IFATS Las Vegas 2018 Conference

16th Annual IFATS Meeting

IFATS

International Federation for Adipose Therapeutics and Science

December 13-15, 2018
The Cosmopolitan of Las Vegas
Las Vegas, Nevada
www.ifats.org

REVOLVE™
Advanced Adipose System

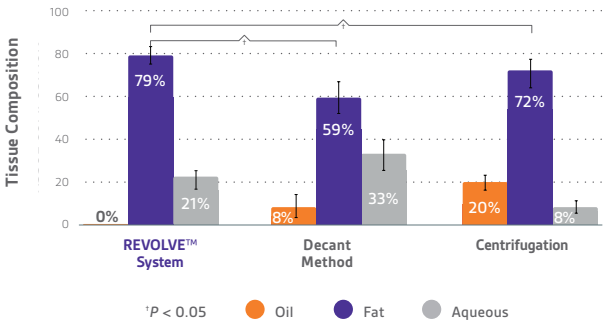
HIGH-QUALITY, PREDICTABLE ADIPOSE GRAFT TISSUE

Results based on laboratory and animal model data

REVOLVE™ System produced a higher concentration of adipose graft tissue[1]

REVOLVE™ System yielded a higher concentration of adipose tissue, eliminating free oil and significantly reducing aqueous fluid and red blood cell debris.[1]

COMPOSITION OF PROCESSED TISSUE[1,*]



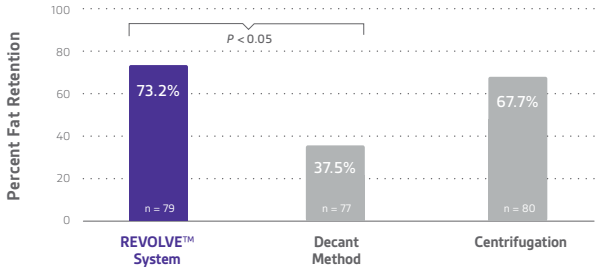
In a laboratory study, fat processed using three different methods was evaluated for adipose tissue concentration, pH, osmolality, hematocrit assays, and percent of oil and aqueous content.

*Correlation of these results to results in humans has not been established.

REVOLVE™ System produced more reliable fat graft retention[1]

In an animal model, REVOLVE™ System yielded significantly higher fat graft retention than decantation and similar results to centrifugation.[1]

PERCENT OF IMPLANTED FAT RETAINED[1,*]



In a preclinical study, human fat was processed using three different methods: REVOLVE™ System, decantation, and centrifugation (processed at 1200 g for 3 minutes). Fat samples from each group were implanted into mice and explanted after 28 days and evaluated for a head-to-head comparison of volume retention.[1]

Ask an Allergan representative to learn more about the

#1 COMMERCIAL DEVICE FOR FAT PROCESSING[2,‡]

‡Market share data through August 2018.

For more information, please call
ALLERGAN CUSTOMER SERVICE AT 1.800.367.5737 or visit
WWW.REVOLVEFATGRAFTING.COM/HCP

REVOLVE™ Advanced Adipose System
Indications and Important Safety Information

INDICATIONS

The REVOLVE™ Advanced Adipose System (REVOLVE™ System) is used for aspiration, harvesting, filtering, and transferring of autologous adipose tissue for aesthetic body contouring. This system should be used with a legally marketed vacuum or aspirator apparatus as a source of suction. If harvested fat is to be re-implanted, the harvested fat is only to be used without any additional manipulation. REVOLVE™ System is intended for use in the following surgical specialties when the aspiration of soft tissue is desired: plastic and reconstructive surgery, gastrointestinal and affiliated organ surgery, urological surgery, general surgery, orthopedic surgery, gynecological surgery, thoracic surgery, and laparoscopic surgery.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Contraindications to autologous fat transfer include the presence of any disease processes that adversely affect wound healing, and poor overall health status of the individual.

WARNINGS

REVOLVE™ System must be used within the same surgical procedure. Reuse of this device in the same patient in a subsequent surgical procedure, or for more than one patient, may result in infection and/or transmission of communicable diseases. Do not use the product if sterile packaging is damaged.

This device will not, in and of itself, produce significant weight reduction. This device should be used with extreme caution in patients with chronic medical conditions such as diabetes, heart, lung, or circulatory system disease or obesity. The volume of blood loss and endogenous body fluid loss may adversely affect intra and/or postoperative hemodynamic stability and patient safety. The capability of providing adequate, timely replacement is essential for patient safety.

PRECAUTIONS

REVOLVE™ System is designed to remove localized deposits of excess fat through small incision and subsequently transfer the tissue back to the patient. Use of this device is limited to those physicians who, by means of formal professional training or sanctioned continuing medical education (including supervised operative experience), have attained proficiency in suction lipoplasty and tissue transfer. Results of this procedure will vary depending upon patient age, surgical site, and experience of the physician. Results of this procedure may or may not be permanent. The amount of fat removed should be limited to that necessary to achieve a desired cosmetic effect. Filling the device with adipose tissue over the maximum fill volume line can lead to occlusion of the mesh resulting in mesh tear.

ADVERSE EFFECTS

Some common adverse effects associated with autologous fat transfer are asymmetry, over- and/or under-correction of the treatment site, tissue lumps, bleeding, and scarring. Potential adverse effects associated with REVOLVE™ System include fat necrosis, cyst formation, infection, chronic foreign body response, allergic reaction, and inflammation.

REVOLVE™ System is available by prescription only.

For more information, please see the Instructions for Use (IFU) and User Manual for REVOLVE™ System available at www.allergan.com/RevolveIFU or call 1.800.678.1605.

To report an adverse reaction, please call Allergan at 1.800.367.5737.

References: 1. Ansorge H, Garza JR, McCormack MC, et al. Autologous fat processing via the Revolve system: quality and quantity of fat retention evaluated in an animal model. *Aesthet Surg J.* 2014;34(3):438-447. **2.** Data on file, Allergan, August 2018. Plastic Surgery Monthly Tracker.

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IFATS
International Federation for Adipose Therapeutics and Science

Welcome to the **16th Annual Meeting of the International Federation for Adipose Therapeutics and Science (IFATS)**.

This organization was founded in 2002 by pioneers following the historical discovery of mesenchymal stem cells in human subcutaneous adipose tissue. Since then, this annual IFATS conference has been an international meeting ground for leading professionals in this exciting field of regenerative medicine. Not only plastic surgeons and cell biologists, but also scientists in industries and physicians in other fields attend this meeting and exchange up-to-date data on basic, translational, and clinical research in adipose-derived products, including adipose-derived stem cells (ASCs).

This year, we welcome the first ***'IFATS Award of Distinction***' lecture by Professor Peter Arner of the Karolinska Institute in Sweden who has made a number of historical discoveries in the physiology and metabolism of human adipose tissue and has been a leader in this field for thirty years. In addition to special and keynote lectures by Drs. Anne Bouloumie and Mark Horowitz on the adipose pathophysiology of human metabolic diseases and adipose stem cells in bone marrow, respectively, the meeting also includes keynote lecturer, Dr. Gregory Hetter, a true pioneer in the history of liposuction in the United States.

IFATS works closely with other leading scientific organizations including the American Association of Blood Banks (AABB), International Society for Cell Therapy (ISCT), and International Society for Plastic and Regenerative Surgeons (ISPRES), and we have collaborating panels with each of these organizations. Faculty from ISPRES and other clinical masters from Europe and Asia will demonstrate the latest aesthetic and reconstructive surgical technologies to improve the beauty and health of tissues and organs.

Accumulated scientific evidence has promoted the clinical application of adipose-derived products all over the world. Currently, just in Tokyo, there are more than 100 clinics providing clinical therapies using the stromal vascular fraction or cultured ASCs. Rapid changes in patient needs appear to be matched by a swiftly responsive supply of stem cell therapies in recent years. You will hear new information on clinical protocols, therapeutic targets, and outcomes of stem cell therapies presented by practitioners from around the world and learn about government regulation for cell-based products in the United States and in Japan.

The IFATS Annual Meeting continues to provide attendees the opportunity to learn about state-of-the-art technology and clinical practice, touch cutting-edge products developed by sponsor companies, and interact with the brightest minds in the field. We thank our participating companies for their support and encourage you to meet with them in our exhibit hall during this conference.

We are very pleased that you have joined us in Las Vegas and are sure that you will learn much and enjoy your time in this exciting city.

Kotaro Yoshimura, MD
IFATS President - 2018

SCIENTIFIC PROGRAM COMMITTEE

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INVITED SPEAKERS AND SESSION MODERATORS

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Joshua Escalante
Gregory Evans, MD, FACS
Hirotaro Fukuoka, MD, PhD
Jaques Galipeau
Jaime R. Garza, MD, FACS, DDS
Jeffrey Gimble, MD, PhD
Benjamin Glenn, JD
Sarah Hagarty, MD
Gregory Hetter, MD
Mark Horowitz, PhD
Cheng-Wei Hsiao
Keita Inoue, MD, PhD
Aaron James, MD, PhD
TaeJo Kang, MD
Adam Katz, MD, FACS
Roger Khouri, MD, FACS
Brian Kinney, MD
Lauren Kokai, PhD
Stig-Frederik Trojahn Kolle, MD, PhD
Kwang Sik Kook, MD
Yur-Ren Kuo, MD, PhD
Hebert Lamblet, MD
Facheng Li, MD, PhD
Tsai-Ming Lin, MD, PhD
Hong-Wei Liu, MD, PhD
Ramon Llull, MD, PhD
Kathy Loper, MHS, MT(ASCP)
Feng Lu, MD, PhD
Guy Magalon, MD
Todd Malan, MD
Keith March, MD, PhD
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Noriko Masuda
Richard McFarland, MD, PhD
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Masanori Mori, MD
Giuseppe Mucci, PhD
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Ahmed Noreldin, MD
Norbert Pallua, MD
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Marc Penn, MD, PhD, FACC
Ivona Percec, MD, PhD
Bob Perry
Nelson Piccolo, MD
Arturo Ramirez-Montanana, MD
J. Peter Rubin, MD, FACS
Gordon Sasaki, MD
Philip Schoettle, MD, PhD
Tawfik Sefrioui, MD
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Nir Shani, PhD
Ewa Anna Siolo, MD, MBChB, FC
Yoshihiro Sowa, PhD
Aris Sterodimas, MD, MSc
H. P. Jeroen Stevens, MD, PhD
Shigeki Sugii, PhD
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International Federation for Adipose Therapeutics and Science

17th Annual Meeting

IFATS MARSEILLE 2019

December 4 - 7, 2019

Palais du Pharo
Marseille, France

Abstract Deadline:

Midnight EST, Wednesday, June 19, 2019

The Call for Abstracts will be sent this winter. All members of IFATS and all registered attendees of the 2018 IFATS Conference will be included in the mailing list. Any others who wish to be reminded to submit papers should contact the IFATS Executive Office.

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Scientific Program in Brief *(This schedule is subject to change)*

Thursday - December 13, 2018

	Room A	Room B
7:30 am	Continental Breakfast in Exhibit Hall	
8:00 am	Welcome Remarks - Kotaro Yoshimura, IFATS President	
8:15 am	Keynote Lecture 1 (Basic) Speaker: Mark Horowitz, PhD - Bone Marrow Adiposity: Orthopedic Clinical Translation Moderator: Jeffrey Gimble, MD, PhD	
9:00 am	Plenary Paper Session - Award Eligible Best Abstracts Moderators: Bruce Bunnell, PhD & Lauren Kokai, PhD Presenters: Jennifer An-Jou Lin, MD; Annie Bowles, PhD; Szu-Hsien Wu, MD; Yan Zhang, MD; Asim Ejaz, PhD; Daria Barwinska, PhD; Kevin Darr, MD; Jeffrey Gusenoff, MD; Joel Aronowitz, MD; William Cimino, PhD	
10:40 am	Coffee Break (Exhibit Hall)	
11:00 am	Special Lecture: Human Adipose Tissues Microenvironment and Obesity Associated Pathologies Moderator: Stuart Williams, PhD Speaker: Ann Bouloumie, PhD	Panel 6: Learn from Asia Moderators: Shigeki Sugii, PhD & Facheng Li, MD, PhD Panelists: Yoshihiro Sowa, PhD; Feng Lu, MD, PhD; Yur-Ren Kuo, MD, PhD; Rintaro Asahi, MD
12:00 pm	Lunch in Exhibit Hall	Lunch in Exhibit Hall
12:05 pm		Sponsored Lunch Session (Dermato Plastica Beauty Co. Ltd.) – Innovation in Fat Grafting Moderator: Brian Kinney, MD Speaker: Tsai-Ming Lin, MD, PhD - The Key to a Successful Fat Grafting - MAFT Gun
12:35 pm		Sponsored Lunch Session (human med) Moderator: Tawfik Sefrioui, MD Speakers: Kotaro Yoshimura, MD - SVF and Other Adipose-Derived Therapeutic Tools Todd Malan, MD - A Novel Point of Care, Automated, and Closed System for Processing Stromal Vascular Fraction Either with or without Collagenase
1:00 pm	Panel 1: Immunomodulatory Properties and Mechanisms of ASC/SVF Moderators: Bruce Bunnell, PhD & Anne Bouloumie, PhD Panelists: Jan Nolta, PhD; J. Peter Rubin, MD, FACS; Bruce Bunnell, PhD; Jaime Garza, MD, FACS, DDS	1:05 pm Free Papers 8: Clinical Trials Moderators: Stig-Frederik Trojahn Kolle, MD, PhD & Hebert Lamblet, MD Presenters: Isaac James, MD; Ramon Castellanos, MD; Luciano Vidal, MD; Todd Malan, MD; Joseph Park, MD; Hongwei Liu, MD, PhD
		2:10 pm Free Papers 9: Clinical Research Moderators: Yur-Ren Kuo, MD & Daria Barwinska, PhD Presenters: Isaac James, MD; Hebert Lamblet, MD; Sherry Collawn, MD, PhD; Summer Hanson, MD, PhD; Dusan Pravica, MD; Katarina Andjelkov, MD, PhD; Angelo Trivisonno, MD; E Xiao
2:30 pm	Free Papers 1: Basic Science - Exosomes, Cell Messaging Moderators: Sherry Collawn, MD, PhD & Shigeki Sugii, PhD Presenters: Aaron James, MD, PhD; Mei Yu, PhD; Srinivas Koduru, PhD; Sophie Veriter, PhD; Matthew Lyes, BS; Jiye Kim, MD, PhD	
3:30 pm	Coffee Break (Exhibit Hall)	Coffee Break (Exhibit Hall)
		Sponsored Afternoon Tea Session (Rohto Pharmaceutical Co., Ltd.) Allogeneic Adipose-Derived Mesenchymal Stem Cell (AD-MSc) Moderator: Kotaro Yoshimura, MD Speakers: Noriko Oki Masuda, MD - The Promises of Allogeneic Adipose-Derived Mesenchymal Stem Cell (AD-MSc) for Treating a Wide Range of Incurable Diseases
4:00 pm	Panel 2: AABB & IFATS: Setting Standards for Adipose Therapies Moderators: Adam Katz, MD, FACS & Ivona Percec, MD, PhD Panelists: Kathy Loper, MHS, MT(ASCP) (AABB); Ramon Llull, MD, PhD (IFATS); Christopher Bocquet (AABB)	Panel 7: Private Cell Therapy Clinics: What are the Methods and are they Compliant with Governing Regulations? Moderators: Keith March, MD, PhD & J. Peter Rubin, MD, FACS Panelists: Marc S. Penn, MD, PhD, FACC; Todd Malan, MD; Hazem Barmada, MD; Guiseppe Mucci, PhD; Mark Berman, MD, FACS; Keita Inoue, MD, PhD; Philip Schoettle, MD, PhD; Borja Sese, PhD
5:00 pm	Free Papers 2: Translational/Clinical Research Moderators: Robert Bowen, MD, FCCP & Shigeki Sugii, PhD Presenters: Marta Kopcewicz, MS; Kacey Marra, PhD; Jeffrey Gimble, MD, PhD; Kamlesh Bajwa, MSc; Anna Wasilewska, MD; Jong-Ho Kim, PhD	
6:30 pm	Adjourn	
7:30 pm	Faculty Dinner (by invitation)	

Friday - December 14, 2018

7:00 am	Continental Breakfast in Exhibit Hall	
7:30 am	Sponsored Breakfast Session (Zen Bio and Theratome Bio) - collaborating with IFATS: ASC Exsomes/Secretome Moderators: Keith March, MD, PhD & Louis Casteilla, PhD Panelists: Kensuke Tashiro, MD; Aaron W. James, MD, PhD Benjamin Beuhrer (Zen Bio); Hirotaro Fukuoka, MD, PhD Michael Coleman, PhD (Theratome Bio); Keith March, MD, PhD	
8:00 am		ISPRES Session Moderators: Sydney Coleman, MD & J. Peter Rubin, MD, FACS Panelists: Sydney Coleman, MD; Brian Kinney, MD; Norbert Pallua, MD (Video); Facheng Li, MD, PhD; Gregory Evans, MD, FACS; Roger Khouri, MD, FACS; Guy Magalon, MD; Nelson Piccolo, MD
9:20 am	Free Papers 3: Basic Research Cell Characterization and Behavior Moderators: Bruce Bunnell, PhD & Torsten Blunk, PhD Presenters: Rosalyn Abbott, PhD; Shigeki Sugii, PhD; Hongwei Liu, MD, PhD Jolanta Norelli, BA; C. Thomas Vangsness, MD; Julia Bachmann, MS; Matthew Potter, BS	
10:30 am	Coffee Break (Exhibit Hall)	
11:00 am	IFATS Award of Distinction Speaker: Peter Arner, MD, PhD - Karolinska Institute, Stockholm, Sweden – Turnover of Human Adipose Tissue Moderator: Kotaro Yoshimura, MD	
12:00 pm	Lunch in Exhibit Hall	Lunch in Room B

	Room A	Room B
		Sponsored Lunch Session I (Tissue Genesis) Moderator: Kotaro Yoshimura, MD Speaker: Marc S. Penn, MD, PhD, FACC - A Novel Approach to the Development of Regenerative Medicine: Okyanos Global Health
		1:05 pm Keynote Lecture 2 (Clinical) Speaker: Gregory Hetter, MD - Lipoplasty: Quo Vadis Moderator: Sydney Coleman, MD
1:20 pm	Panel 3: IFATS & ISCT: Clinical Efficacy Driven by Potency Moderators: Ramon Llull, MD, PhD & Jeffrey Gimble, MD, PhD Panelists: Jacques Galipeau; Jan Nolta, PhD; Louis Casteilla, PhD; Adam Katz, MD, FACS	1:50 pm Panel 8: Reconstructive Adipose Surgery/Limb and Face Moderators: Guy Magalon, MD & Brian Kinney, MD Panelists: Roger Khouri, MD, FACS; Ewa Siolo, MD, MBChB, FC; Frank Chang, MD, MS
3:00 pm	Coffee Break (Exhibit Hall)	
3:30 pm	Free Papers 4: Basic Research Cell Behavior - Preconditioning, Stemness, Senescence Moderators: Nir Shani, PhD & Petra Bauer-Kreisel, PhD Presenters: Rui-Peng Jia, MD, PhD; Bin Fang, MD; Chang Chen, MD; Sudheer Ravuri, PhD; Paul Kingham, PhD; Gregorio Chazenbalk, PhD; Nir Shani, PhD; Anna Barbara Di Stefano, PhD; Natsumi Saito, PhD; Srinivas Koduru, PhD; Michael Badowski, PhD	Panel 9: Reconstructive Adipose Surgery: Breast, Genital and Face Moderators: Gregory Evans, MD, FACS & Frank Chang, MD, MS Panelists: Roger Khouri, MD, FACS; Kotaro Yoshimura, MD; Nelson Piccolo, MD
4:40 pm		4:50 pm Panel 10: Reconstructive Adipose Surgery/Regenerative Moderators: Steven Cohen, MD & Stig Frederik Trojahn Kolle, MD, PhD Panelists: Nelson Piccolo, MD; Guy Magalon, MD; Michele Zocchi, MD; Kwang Sik Kook, MD; Hong-Wei Liu, MD, PhD
6:00 pm	Poster Session and Welcome Reception	
	Dinner on own	
Saturday - December 15, 2018		
7:00 am	Continental Breakfast in Exhibit Hall	
7:30 am		**Sponsored Breakfast Session (MTF Biologics)** Moderator: to be determined Speaker: Marc Long, PhD - Early Clinical Safety and Applications of a Novel Allograft Adipose Matrix
8:00 am	IFATS Members' Meeting	
		8:45 am Panel 11: Mechanical Processing I Moderators: Nelson Piccolo, MD & Gordon Sasaki, MD Panelists: Patrick Tonnard, MD; H. P. Jeroen Stevens MD, PhD; Carlo Tremolada, MD Feng Lu, MD, PhD
9:00 am	Free Papers 5: Translational Research - Cancer, Ischemic Disease Moderators: Kevin Zwezdaryk, PhD & Lauren Kokai, PhD Presenters: Asim Ejaz, PhD; Nada Alaaeddine, PhD; Rachel Sabol, MS; Chi-Ming Pu, MD, PhD; Kaylen Capps, MS	
10:00 am	Coffee Break (Exhibit Hall)	
10:30 am	Panel 4: Regulatory Affairs Moderators: J. Peter Rubin, MD, FACS & Adam Katz, MD, FACS Panelists: Richard McFarland, MD, PhD; Morikuni Tobita, DDS, PhD	Panel 12: Mechanical Processing II Moderators: Michele Zocchi, MD & Ewa Siolo, MD, MBChB, FC Panelists: Gordon Sasaki, MD; Ramon Llull, MD, PhD; Guy Magalon, MD; Steven Cohen, MD; Kevin Darr, MD
12:00 pm	Lunch in Exhibit Hall	**Sponsored Lunch Session (Amano Enzyme)** Effective Collection of Stromal Vascular Fraction (SVF) by Enzymatic Treatment Moderator: Kotaro Yoshimura, MD Speakers: Joshua Escalante - Introduction of Amano's Enzymes for Adipose Tissue Dissociation Masanori Mori - Optimization of Enzyme Blend using Amano's Enzymes
12:35 pm		**Sponsored Lunch Session (Allergan)** Aesthetic Applications of Fat Grafting and Case Based Discussion Speaker: Gaurav Bharti - Innovative Approaches to Aesthetic Fat Grafting and Case Based
		1:15 pm Panel 13: Aesthetic Adipose Surgery/Face I Moderators: Ramon Llull, MD, PhD & Ahmed Adel Noreldin, MD Panelists: Patrick Tonnard, MD; Steven Cohen, MD; Ewa Siolo, MD, MBChB, FC; Tsai-Ming Lin, MD, PhD; Kuang Cheng Chang, MBA; TaeJo Kang, MD
1:30 pm	Panel 5: Innovation and Technology Development: How to Take an Idea to the Finish Line (Sponsored by Allergan) Moderators: Adam Katz, MD, FACS & Sarah Hagarty, MD Panelists: Benjamin Glenn, JD; Faz K. Bashi, MD; Tiffany Wilson, MBA; Steven Brooks	
3:00 pm	Coffee Break (Exhibit Hall)	
3:30 pm	Free Papers 6: Matrix Matters Moderators: Alexandra Conde-Green, MD, FICS & Kacey Marra, PhD Presenters: Suzanne Thomson, BSc, MBChB, MRCSEd, PhD; Benjamin Schilling, MS; Kevin Hopkins, MD, FACS; Omair Mohiuddin, MS; Sophie Veriter, PhD; Manisha Shah, PhD	Panel 14: Cell Assisted Lipotransfer Moderators: Steven Cohen, MD & Aris Sterodimas, MD, MSc Panelists: Gordon Sasaki, MD; Ahmed Adel Noreldin, MD; Tawfik Sefrioui, MD Hyung Min Hahn, MD
		4:10 pm Panel 15: Aesthetic Adipose Surgery/Breast Moderators: Brian Kinney, MD & Patrick Tonnard, MD Panelists: Aris Sterodimas, MD, MSc; Michel Zocchi, MD; Roger Khouri, MD, FACS; Cheng-Wei Hsiao
4:30 pm	Free Papers 7: Hot Topics Moderators: Ali Modaressi, MD & Katarina Andjelkov, MD, PhD Presenters: Adam Katz, MD, FACS; Michelle McCarthy, MS; Oliver Smith, MBChB, MRCS Peter Edenhoffer, MD; Guy Magalon, MD; Giorgio Giatsidis, MD; Rui-Peng Jia, MD, PhD; Sheri Wang, BS	
		5:10 pm Panel 16: Aesthetic Adipose Surgery/Buttock Moderators: J. Peter Rubin, MD, FACS & Nelson Piccolo, MD Panelists: Arturo Ramirez-Montanana, MD; Aris Sterodimas, MD, MSc; Alexandra Conde-Green, MD, FICS
6:20 pm	Concluding Remarks, Award Presentations, Announcement of IFATS 2019 Kotaro Yoshimura, MD & Guy Magalon, MD	
7:30 pm	Farewell Networking Gala Dinner - Wicked Spoon Buffet Restaurant	

NOTES

PROGRAM SCHEDULE

The program is correct at the time of printing; however, the Program Chairman reserves the right to alter the schedule as necessary.

Thursday - December 13, 2018

7:30 am	Continental Breakfast
8:00 am	**Welcome Remarks** - Kotaro Yoshimura, IFATS President
8:15 am	**Keynote Lecture 1 (Basic)**
	Speaker: Mark Horowitz, PhD - Bone Marrow Adiposity: Orthopedic Clinical Translation
	Moderator: Jeffrey Gimble, MD, PhD
9:00 - 10:40 am	**Plenary Paper Session - Award Eligible Best Abstracts**
	Moderators: Bruce Bunnell, PhD & Lauren Kokai, PhD
9:00 am	**1**
	DIABETIC ADIPOSE STEM CELL-DERIVED EXOSOME ACCELERATES CUTANEOUS WOUND HEALING IN DB/DB MICE
	Presenter: Jennifer An-Jou Lin, MD (Taiwan)
	Affiliation: Chang Gung Memorial Hospital
	Authors: Lin JA, Wang AY, Loh CY, Kao HK
9:10 am	**2**
	ENHANCED THERAPEUTIC OUTCOMES OF MSC BY PRIMING AND SELECTION METHODS
	Presenter: Annie Bowles, PhD (USA)
	Affiliation: University of Miami
	Authors: Bowles A, Willman MA, Kouroupis D, Correa D
9:20 am	**3**
	THERAPEUTIC EFFECTS OF HUMAN ADIPOSE-DERIVED PRODUCTS ON IMPAIRED WOUND HEALING IN IRRADIATED TISSUE
	Presenter: Szu-Hsien Wu, MD (Taiwan)
	Affiliation: Taipei Veterans General Hospital and University of Tokyo Hospital
	Authors: Wu SH, Yoshimura K, Mashiko T, Feng J
9:30 am	~~**4**~~
	~~**IDENTIFICATION AND VERIFICATION OF NOVEL ADIPOKINES IN ADIPOSE-DERIVED EXOSOME-LIKE VESICLES**~~
WITHDRAWN	~~Presenter: Yan Zhang, MD (China)~~
	~~Affiliation: Sichuan University~~
	~~Authors: Zhang Y, Yu M, Tian WD~~
9:40 am	**5**
	MOLECULAR BASIS OF ADIPOSE-DERIVED STEM CELL (ASC) THERAPY FOR MANAGEMENT OF RADIATION INDUCED FIBROSIS (RIF)
	Presenter: Asim Ejaz, PhD (USA)
	Affiliation: University of Pittsburgh
	Authors: Ejaz A, Epperly M, Schusterman A, Greenberger J, Rubin P
9:50 am	**6**
	ADIPOSE DERIVED STEM CELLS REGENERATE CIGARETTE SMOKE-INDUCED KIDNEY DAMAGE
	Presenter: Daria Barwinska, PhD (USA)
	Affiliation: Indiana University
	Authors: Barwinska D, Traktuev DO, Cook TG, Saliba J, Bacallao RL, Basile DP, March KL
10:00 am	**7**
	ANALYSIS OF THE SAFETY AND EFFECTIVENESS OF COMBINATION CELL THERAPY FOR THE TREATMENT OF PAIN AND INFLAMMATION ASSOCIATED WITH OSTEOARTHRITIS OF THE KNEE AND HIP
	Presenter: Kevin Darr, MD (USA)
	Affiliation: Covington Orthopedic and Sports Medicine Institute
	Authors: Darr K, Dufresne MD
10:10 am	**8**
	PERFORATING FAT INJECTIONS FOR CHRONIC PLANTAR FASCIITIS: A NOVEL REGENERATIVE TREATMENT OPTION
	Presenter: Jeffrey Gusenoff, MD (USA)
	Affiliation: University of Pittsburgh
	Authors: Gusenoff J, Minteer D, Chen W, Gusenoff B
10:20 am	**9**
	CELL ENRICHED FAT GRAFTING FOR THE TREATMENT OF ANDROGENIC ALOPECIA. THE STYLE TRIAL: MULTICENTER RANDOMIZED CLINICAL STUDY
	Presenter: Joel Aronowitz, MD (USA)
	Affiliation: Cedars Sinai Medical Center
	Authors: Aronowitz J, Daniels ED, Washenik KW
10:30 am	**10**
	SVF TO TREAT OSTEOARTHRITIS: A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, DOSE-ESCALATED, MULTI-SITE, PARALLEL GROUP CLINICAL EVALUATION
	Presenter: William Cimino, PhD (USA)
	Affiliation: The GID Group
	Author: Cimino W
10:40 am	Coffee Break (Exhibit Hall)

11:00 am	**Special Lecture: Human Adipose Tissues Microenvironment and Obesity Associated Pathologies**
Room A	Speaker: Ann Bouloumie, PhD Moderator: Stuart Williams, PhD
11:00 am	**Panel 6: Learn from Asia**
Room B	Moderators: Shigeki Sugii, PhD & Facheng Li, MD, PhD Panelists: Yoshihiro Sowa, PhD *Potential Application of Adipose Tissue in Peripheral Nerve Injury* Feng Lu, MD, PhD *Cryopreservation Changes ECM Content to Inhibit Fat Grafting Survival and SVF-Gel Cryopreservation Technique* Yur-Ren Kuo, MD, PhD *Immunomodulatory Effects of Adipose-Derived Stem Cells* Rintaro Asahi, MD *Pathophysiology of Tissue Damage After Radiation Therapy: Influence of Radiation Dose and Fractionation Protocol on Adipose-Derived Stem Cells*
12:00 pm	Lunch in Exhibit Hall
12:05 pm	**Sponsored Lunch Session (Dermato Plastica Beauty Co. Ltd.) – Innovation in Fat Grafting**
Room B	Moderator: Brian Kinney, MD Speaker: Tsai-Ming Lin, MD, PhD *The Key to a Successful Fat Grafting - MAFT Gun*
12:35 pm	**Sponsored Lunch Session (human med)**
Room B	Moderator: Tawfik Sefrioui, MD Speakers: Kotaro Yoshimura, MD *SVF and Other Adipose-Derived Therapeutic Tools* Todd Malan, MD *A Novel Point of Care, Automated and Closed System for Processing Stromal Vascular Fraction Either with or without Collagenase*
1:00 - 2:30 pm	**Panel 1: Immunomodulatory Properties and Mechanisms of ASC/SVF**
Room A	Moderators: Bruce Bunnell, PhD & Anne Bouloumie, PhD Panelists: Jan Nolta, PhD J. Peter Rubin, MD, FACS Bruce Bunnell, PhD Jaime Garza, MD, FACS, DDS
1:05 - 2:05 pm **Room B**	**Free Papers 8: Clinical Trials** Moderators: Stig-Frederik Trojahn Kolle, MD, PhD & Hebert Lamblet, MD
1:05 pm	**11** **STEM CELL THERAPY ENRICHED FAT GRAFTING FOR THE RECONSTRUCTION OF CRANIOFACIAL DEFICITS** Presenter: Isaac James, MD (USA) Affiliation: University of Pittsburgh Medical Center Authors: Bourne D, Egro FM, Bliley J, James IB, Haas GL, Meyer EM, Donnenberg A, Donnenberg V, Branstetter B, Marra K, Coleman S, Rubin JP
1:15 pm NOT PRESENTED	**12** **A PROSPECTIVE, PILOT STUDY EVALUATING AMNIOTIC MEMBRANE AND UMBILICAL CORD PARTICULATE IN REDUCING PAIN ASSOCIATED WITH KNEE OSTEOARTHRITIS** Presenter: Ramon Castellanos, MD (USA) Affiliation: Castellanos and Associates Author: Castellanos R
1:25 pm	**13** **COMBINED 3D BIOPRINTING OF SKIN AND ADIPOSE TISSUE AS A PROMISING APPROACH FOR NIPPLE AREOLA COMPLEX AND BREAST VOLUME RECONSTRUCTION** Presenter: Luciano Vidal, MD (France) Affiliation: Labskin Creations Authors: Vidal L, Heraud S, Albouy M, Durand C, Thepot A, Dos Santos M, Marquette C
1:35 pm	**14** **A NOVEL POINT OF CARE, AUTOMATED, AND CLOSED SYSTEM FOR PROCESSING STROMAL VASCULAR FRACTION EITHER WITH OR WITHOUT COLLAGENASE** Presenter: Todd Malan, MD (USA) Affiliation: Roxbury Regenerative Author: Malan T
1:45 pm	**15** **THE EFFECT OF STROMAL VASCULAR FRACTION ON SCAR FORMATION OF TRAM FLAP DONOR SITE** Presenter: Joseph K. Park, MD (South Korea) Affiliation: Seoul National University Hospital Authors: Park JK, Jin US
1:55 pm NOT PRESENTED	**16** **USE OF AUTOLOGOUS FAT GRAFTING TO TREAT BURN, TRAUMATIC, AND SURGICAL SCARS: ISSUES AND OUR COUNTERMEASURES** Presenter: Hongwei Liu, MD, PhD (China) Affiliation: The First Affiliated Hospital of Jinan University Author: Liu H

2:10 - 3:30 pm **Free Papers 9: Clinical Research**
Room B Moderators: Yur-Ren Kuo, MD & Daria Barwinska, PhD

2:10 pm **23**
FAT GRAFTING PROMOTES DERMAL REJUVENATION IN PATIENTS WITH FAT PAD ATROPHY OF THE HEEL: DATA FROM A RANDOMIZED CONTROLLED CLINICAL TRIAL
Presenter: Isaac James, MD (USA)
Affiliation: University of Pittsburgh
Authors: James I, Gusenoff BR, Wang S, Dibernardo G, Minteer DM, Gusenoff JA

2:20 pm **24**
AUTOLOGOUS TRANSPLANT FOR FACE AND BODY PRESERVING ADCS: CHEMICAL TO MECHANICAL DISSOCIATION SINCE 2006. A LONG-TERM REVIEW
Presenter: Hebert T. Lamblet, MD (Brazil)
Affiliation: UNIFESP
Author: Lamblet HT

2:30 pm **25**
CLASSIFICATION AND SAFETY OF FAT GRAFTING BY AMOUNT AND LOCATION
Presenter: Sherry Collawn, MD, PhD (USA)
Affiliation: UAB
Authors: Collawn S, Boyd CJ

2:40 pm **26**
BREAST SHAPE CHANGE FOLLOWING AUTOLOGOUS FAT GRAFTING: POTENTIAL OF 3D SURFACE IMAGING FOR QUANTITATIVE ANALYSIS
Presenter: Summer E. Hanson, MD, PhD (USA)
Affiliation: The University of Texas MD Anderson Cancer Center
Authors: Hanson SE, Cheong AL, Reece G, Markey MK, Merchant F

2:50 pm **27**
LIPID CHANGES IN PATIENTS SUBMITTED TO CLASICAL AND RADIOFREQUENCY ASSISTED LIPOSUCTION (RFAL)
NOT PRESENTED
Presenter: Dusan Pravica, MD (Serbia)
Affiliation: Colic Hospital
Authors: Pravica D, Andjelkov K

3:00 pm **28**
COMPARISON OF EARLY POST OPERATIVE TRIGLYCERIDES LEVELS IN PATIENTS SUBMITTED TO LIPOSUCTION AND LIPOSUCTION WITH FAT GRAFTING
Preenter: Katarina Andjelkov, MD, PhD (Serbia)
Affiliation: BelPrime Clinic Belgrade Serbia
Authors: Andjelkov K, Pravica D

3:10 pm **29**
THE FAT IS NOT UNIFORM: SUPERFICIAL FAT PECULIARITY
Presenter: Angelo Trivisonno, MD (Italy)
Affiliation: Sapienza University
Authors: Trivisonno A, Toietta G

3:20 pm **30**
BASIC AND CLINICAL EVIDENCE OF AN ALTERNATIVE METHOD TO PRODUCE VIVO NANOFAT
Presenter: E Xiao
Affiliation: Peking University School and Hospital of Stomatology
Authors: Xiao E, HongSeng B, Gong X

2:30 - 3:30 pm **Free Papers 1: Basic Science - Exosomes, Cell Messaging**
Room A Moderators: Sherry Collawn, MD, PhD & Shigeki Sugii, PhD

2:30 pm **17**
ADIPOSE TISSUE DERIVED PERIVASCULAR VESICULAR SECRETOME INCITES BONE REPAIR
Presenter: Aaron W. James, MD, PhD (USA)
Affiliation: Johns Hopkins University
Authors: Xu J, Meyers C, Wang Y, Chang L, Peault B, James AW

2:40 pm **18**
CELL-FREE ADIPOSE TISSUE REGENERATION BASED ON EXOSOME-LIKE VESICLES DERIVED FROM ADIPOSE TISSUE
Presenter: Mei Yu, PhD (China)
Affiliation: Sichuan University
Authors: Yu M, Dong J, Zhang Y, Dai MJ, Tian WD

2:50 pm **19**
MOLECULAR EVALUATION OF PURIFIED INSULIN PRODUCING BETA CELLS FROM ADIPOSE DERIVED STEM CELLS
Presenter: Srinivas Koduru, PhD (USA)
Affiliation: Pennsylvania State University
Authors: Koduru S, Leberfinger AN, Ozbolat IT, Ravnic DJ

3:00 pm **20**
IMPACT OF THE BONE MATRISOME ON THE ASCS FUNCTION FOR BONE-TISSUE ENGINEERING
Presenter: Sophie Veriter, PhD (Belgium)
Affiliation: Novadip Biosciences
Authors: Veriter S, Mazzucchelli G, LeBrun V, Adnet PY, Cathy C, Dufrane D

3:10 pm **21**

~~**ADIPOSE STEM CELL CROSSTALK WITH CHEMO-RESIDUAL BREAST CANCER CELLS: IMPLICATIONS FOR TUMOR RECURRENCE**~~

WITHDRAWN Presenter: Matthew A. Lyes, BS (USA)
Affiliation: Duke University
Authors: Lyes MA, Payne S, Ferrell P, Pizzo SV, Hollenbeck ST, Bachelder RE

3:20 pm **22**

IMMUNOSUPPRESSIVE EFFECTS OF ADIPOSE TISSUE-DERIVED MESENCHYMAL STEM CELL (ASCS) ON MACROPHAGE-INDUCED IMMUNE REACTIONS THROUGH PROSTAGLANDIN E2
Presenter: Jiye Kim, MD, PhD (South Korea)
Affiliation: Yonsei University Wonju
Authors: Kim J, Eom YW, Kim SW, Chung YK

3:30 pm Coffee Break (Exhibit Hall)

3:30 pm **Sponsored Afternoon Tea Session (Rohto Pharmaceutical Co., Ltd.)**
Room B Allogeneic Adipose-Derived Mesenchymal Stem Cell (AD-MSc)
Moderator: Kotaro Yoshimura, MD
Speaker: Noriko Oki Masuda, MD
The Promises of Allogeneic Adipose-Derived Mesenchymal Stem Cell (AD-MSc) for Treating a Wide Range of Incurable Diseases

4:00 - 5:10 pm **Panel 2: AABB & IFATS: Setting Standards for Adipose Therapies**
Room A Moderators: Adam Katz, MD, FACS & Ivona Percec, MD, PhD
Panelists: Kathy Loper, MHS, MT (AABB)
Ramon Llull, MD, PhD (IFATS)
Christopher Bocquet (AABB)

4:00 - 6:30 pm **Panel 7: Private Cell Therapy Clinics: What are the Methods and are they Compliant with Governing Regulations?**
Room B Moderators: Keith March, MD, PhD & J. Peter Rubin, MD, FACS
Panelists: Marc S. Penn, MD, PhD, FACC
Novel Strategies for Biological Drug Development
Todd Malan, MD
Personal Experience Utilizing SVF for the Treatment of Chronic Spinal Fluid Leak and Dural Tears
Hazem Barmada, MD
Fat-Derived Stem Cell Deployment in Neurological and Autism
Guiseppe Mucci, PhD
Expanded ADSC in Breast Augmentation and Skin
Mark Berman, MD, FACS
A Prospective Study of Adipose Derived Stromal Vascular Fraction for the Treatment of Knee Osteoarthritis
Keita Inoue, MD, PhD
Regenerative Medicine and Cell Therapy at Clinic in Japan: The Impact of Japanese Regulation for Cell Therapy
Philip Schoettle, MD, PhD
The Use of Enzyme Derived MSC in the Different Fields of Orthopaedics and Traumatology - 5 Years Experience
Borja Sese, PhD
Grafts and Inoculi: Two Peas in a Pod?

5:10 - 6:30 pm **Free Papers 2: Translational/Clinical Research**
Room A Moderators: Robert Bowen, MD, FCCP & Shigeki Sugii, PhD

5:10 pm **31**

THE IMPACT OF AGE, SEX AND DIETARY REGIMENT ON THE SKIN WOUND HEALING IN C57BL/6J (B6) MICE
Presenter: Marta M. Kopcewicz, MS (Poland)
Affiliation: Institute of Animal Reproduction and Food Research of PAS
Authors: Kopcewicz MM, Gawronska-Kozak B, Walendzik K, Bukowska J

5:20 pm **32**

ADIPOSE-DERIVED STEM CELLS PARTIALLY MITIGATE MUSCLE ATROPHY AFTER PERIPHERAL NERVE INJURY IN THE RODENT MODEL
Presenter: Kacey Marra, PhD (USA)
Affiliation: University of Pittsburgh
Authors: Marra K, Schilling B, Schusterman M, Kim D, Repko A, Klett K, Christ G

5:30 pm **33**

HUMAN ADIPOSE-DERIVED CELL REPAIR IN A MURINE PRESSURE ULCER MODEL
Presenter: Jeffrey M. Gimble, MD, PhD (USA)
Affiliation: LaCell LLC
Authors: Gimble JM, Bukowska J, Kosnik P, Katz A, Gawronska-Kozak B, Mehrara B, Bunnell BA, Alarcon Uquillas A, Frazier T

~~5:40 pm~~ **34**

~~**REGENERATION OF FRACTURE TIBIAL BONE OF MICE WITH ALLOGENEIC AND XENOGENEIC MESENCHYMAL STEM CELLS**~~

NOT PRESENTED Presenter: Kamlesh K. Bajwa, MSc (India)
Affiliation: National Dairy Research Institute
Authors: Bajwa KK, Potliya S, Saini S, Sharma V, Thakur A, Kumar A, Kumar S, Kumar S, Malakar D

~~5:50 pm~~ **35**
INFLUENCE OF CONTROLLED PHYSICAL ACTIVITY ON SERUM ADIPOKINES CONCENTRATION IN OBESE TEENAGERS
NOT PRESENTED Presenter: Anna Wasilewska, MD (Poland)
Affiliation: Pediatric Nephrology Department
Authors: Wasilewska A, Protas P, Stelmach M, Rybi-Szumińska A, Taranta-Janusz K, Kuroczycka-Saniutycz E, Lemiesz M

6:00 pm **36**
HUMAN ADIPOSE-DERIVED STEM CELLS WITH THYMOSIN B4 ENHANCED NEOVASCULARIZATION IN MOUSE ISCHEMIC HIND LIMB MODEL
Presenter: I-Rang Lim (South Korea)
Affiliation: Korea University College of Medicine
Authors: Kim J, Joo H, Hong S

6:30 pm Adjourn

7:30 pm Faculty Dinner (by invitation)

Friday - December 14, 2018

7:00 am Breakfast in Exhibit Hall

7:30 - 9:20 am **Sponsored Breakfast Session (Zen Bio and Theratome Bio) - Collaborating with IFATS: ASC Exsomes/Secretome**
Room A
Moderators: Keith March, MD, PhD & Louis Casteilla, PhD
Panelists: Kensuke Tashiro, MD
ASC Exosome-Characteristics and Therapeutic Potential
Aaron W. James, MD, PhD
Adipose Tissue Derived Perivascular Vesicular Secretome Incites Bone Repair
Benjamin Beuhrer (Zen Bio)
ASC-Derived Extracellular Vesicles as a Treatment for Inflammatory Diseases
Hirotaro Fukuoka, MD, PhD
Clinical Use of ASC Conditioned Media for Hair Regeneration
Michael Coleman, PhD (Theratome Bio)
Development of an ASC Secretome Derived Biotherapeutic for Acute Organ Injury
Keith March, MD, PhD
Next Generation ASC Therapies: Moving from Cells to Secretome, from Organisms to Organs

8:00 - 10:30 am **ISPRES Session**
Room B
Moderators: Sydney Coleman, MD & J. Peter Rubin, MD, FACS
Panelists: Sydney Coleman, MD
The History of Fat Grafting
Brian Kinney, MD
Innovative Advancements – Off the Shelf Fat, Laser-Drilled Harvesting Cannulae, Processing with Hi-Tech Filters Instead of Enzymes and Centrifuges
Norbert Pallua, MD (Video)
Enhancement of Progenitor Cells by Two Step Centrifugation of Emulsified Lipoaspirates
Facheng Li, MD, PhD
Large Volume Fat Grafting for Total Breast Reconstruction: Experience of 34 Consecutive Cases
Gregory Evans, MD, FACS
The Science of Stem Cells
Roger Khouri, MD, FACS
Fundamental Principles for Successful Large Volume Autologous Fat Transfer
Guy Magalon, MD
Injection of Autologous Fat Tissue: Evolution of Ideas (1997-2018)
Nelson Piccolo, MD
Large Volume Fat Grafting for Obliteration of Large Wound Cavities - Decubiti, Avulsion Injuries and Drained Hematomas

9:20 - 10:30 am **Free Papers 3: Basic Research Cell Characterization and Behavior**
Room A
Moderators: Bruce Bunnell, PhD & Torsten Blunk, PhD

9:20 am **37**
A COMPLEX CO-CULTURE WHITE ADIPOSE TISSUE MODEL
Presenter: Rosalyn D. Abbott, PhD (USA)
Affiliation: Carnegie Mellon University
Authors: Abbott RD, Keyser MN, Debari MK

9:30 am **38**
CD10 IS A PROSPECTIVE MARKER FOR ADIPOCYTE MATURATION OF ADIPOSE-DERIVED STEM CELLS
Presenter: Shigeki Sugii, PhD (Singapore)
Affiliation: Singapore Bioimaging Consortium and Duke NUS Graduate Medical School
Authors: Sugii S, Chakraborty S

~~9:40 am~~ **39**
EFFECTS OF DIFFERENT STORAGE MEDIA AND TEMPERATURES ON THE VIABILITY OF READY-TO-USE HUMAN ADIPOSE-DERIVED STEM CELLS FOR CLINICAL THERAPY
NOT PRESENTED Presenter: Hongwei Liu, MD, PhD (China)
Affiliation: The First Affiliated Hospital of Jinan University
Authors: Liu H, Wu YD

9:50 am **40**
EFFECT OF COMBINED PLATELET-RICH PLASMA AND HYALURONIC ACID ON BONE MARROW-DERIVED MESENCHYMAL STEM AND CHONDROCYTE METABOLISM
NOT PRESENTED
Presenter: Jolanta Norelli, BA (USA)
Affiliation: Northwell Health System
Authors: Norelli J, Plaza D, Satin A, Liang H, Sgaglione N, Grande D

10:00 am **41**
PRE-OSTEOARTHRITIC GENE EXPRESSION CHANGES IN INFRAPATELLAR FAT PADS OF MULTIPAROUS RABBITS
NOT PRESENTED
Presenter: C. Thomas Vangsness, MD (USA)
Affiliation: University of Southern California
Authors: Vangsness CT, Mircheff AK, Lennarz B, Wang Y, Jones IA, Togashi R

10:10 am **42**
ASC IN CELL-ASSISTED LIPOTRANSFER: ANGIOGENIC AND ANTI-APOPTOTIC MARKER EXPRESSION OF ASC UNDER ISCHEMIA-LIKE CONDITIONS AND DEVELOPMENT OF AN ISCHEMIC ADIPOSE TISSUE MODEL IN VITRO
Presenter: Julia Bachmann, MS (Germany)
Affiliation: University of Wuerzburg
Authors: Bachmann J, Ehlert E, Becker M, Radeloff K, Blunk T, Bauer-Kreisel P

10:20 am **43**
RAPAMYCIN EFFECT ON HUMAN ADIPOSE-DERIVED STEM CELLS (ASCS) IN VITRO CONTROLLING FOR AGE, GENDER, AND PASSAGE NUMBER
Presenter: Matthew Potter, BS (USA)
Affiliation: Steadman Philippon Research Institute
Authors: Potter M, Ravuri SR, Mu XM, Huard JH

10:30 am — Coffee Break (Exhibit Hall)

11:00 am **IFATS Award of Distinction**
Room A
Speaker: Peter Arner, MD, PhD - Karolinska Institute, Stockholm, Sweden – Turnover of Human Adipose Tissue
Moderator: Kotaro Yoshimura, MD

12:00 pm — Lunch in Exhibit Hall

12:00 pm **Sponsored Lunch Session (Tissue Genesis)**
Room B
Moderator: Kotaro Yoshimura, MD
Speaker: Marc S. Penn, MD, PhD, FACC - *A Novel Approach to the Development of Regenerative Medicine: Okyanos Global Health*

1:05 - 1:50 pm **Keynote Lecture 2 (Clinical)**
Room A
Speaker: Gregory Hetter, MD - *Lipoplasty: Quo Vadis*
Moderator: Sydney Coleman, MD

1:20 - 3:00 pm **Panel 3: IFATS & ISCT: Clinical Efficacy Driven by Potency**
Room A
Moderators: Ramon Llull, MD, PhD & Jeffrey Gimble, MD, PhD
Panelists: Jacques Galipeau
Jan Nolta, PhD
Louis Casteilla, PhD
Adam Katz, MD, FACS

1:50 - 3:00 pm **Panel 8: Reconstructive Adipose Surgery/Limb and Face**
Room B
Moderators: Guy Magalon, MD & Brian Kinney, MD
Panelists: Roger Khouri, MD, FACS
Treatment Thumb CarpoMetacarpal Joint Arthritis, Dupuytren and other Contractures with AFT
Ewa Siolo, MD, MBChB, FC
Evolution of Aesthetic & Reconstructive Lipofilling to Face – A Decade of Experience
Frank Chang, MD, MS
Reconstructive Adipose Tissue Surgery for Face

3:00 pm — Coffee Break (Exhibit Hall)

3:30 - 6:00 pm **Free Papers 4: Basic Research Cell Behavior - Preconditioning, Stemness, Senescence**
Room A
Moderators: Nir Shani, PhD & Petra Bauer-Kreisel, PhD

3:30 pm **44**
SHORT-TERM HYPOXIC PRECONDITIONING ADIPOSE-DERIVED ENDOTHELIAL PROGENITOR CELLS PROMOTES THE MORPHOLOGICAL REGENERATION AND FUNCTIONAL RESTORATION OF BLADDER DEFECT IN A RAT MODEL
Presenter: Rui-Peng Jia, MD, PhD (China)
Affiliation: Nanjing First Hospital
Author: Jia RP

3:40 pm **45**
ENHANCED IMPAIRED WOUND HEALING BY TREATMENT WITH MECHANICAL STRETCH PRECONDITIONED ADIPOSE-DERIVED STEM CELLS
Presenter: Bin Fang, MD (China)
Affiliation: Shanghai Ninth Hospital
Authors: Fang B, Xie Y, Shan SZ

3:50 pm **46**

PRECONDITIONING BY PROLYL HYDROXYLASE INHIBITION ENHANCES SURVIVABILITY AND ANGIOGENESIS IN HUMAN ADIPOSE DERIVED STEM CELLS

NOT PRESENTED
Presenter: Chang Chen, MD (China)
Affiliation: Sichuan University
Authors: Chen C, Jing W, Tian WD

4:00 pm **47**

REPURPOSING THE ANTHELMINTHIC NICLOSAMIDE AS A SENOLYTIC DRUG FOR ENRICHING HUMAN ADIPOSE-DERIVED STEM CELLS (ASCS)

Presenter: Sudheer Ravuri, PhD (USA)
Affiliation: Steadman Philippon Research Institute
Authors: Ravuri S, Potter MP, Huard JH

4:10 pm **48**

OPTIMISING PROCESSING OF LIPOASPIRATE FOR ISOLATION AND XENO-FREE EXPANSION OF HIGHLY ADIPOGENIC AND ANGIOGENIC CELLS FOR CLINICAL APPLICATION

Presenter: Paul Kingham, PhD (Sweden)
Affiliation: Umea University
Presenter: Kingham P, Lauvrud AT, Gümüscü R, Wiberg R, Kelk P, Wiberg M, Brohlin M

4:20 pm **49**

NOVEL NON-TUMORIGENIC HUMAN PLURIPOTENT STEM CELLS ISOLATED FROM ADIPOSE TISSUE (MUSE-AT CELLS): NEW PARADIGM IN REGENERATIVE MEDICINE

Presenter: Gregorio D. Chazenbalk, PhD (USA)
Affiliation: University of California Los Angeles
Authors: Chazenbalk GD, Gimeno ML, Perone MJ

4:30 pm Discussion

~~4:40 pm~~ **50**

NOTCH SIGNALING ENHANCES STEMNESS BY REGULATING METABOLIC PATHWAYS THROUGH MODIFYING P53, NF-KB, AND HIF-1A

WITHDRAWN
Presenter: Hiroyuki Moriyama, PhD (Japan)
Affiliation: Pharmaceutical Research and Technology Institute
Authors: Moriyama H, Moriyama M, Hayakawa T

4:50 pm **51**

FAS-L PROMOTES THE STEM CELL POTENCY OF ADIPOSE DERIVED MESENCHYMAL CELLS

Presenter: Nir Shani, PhD (Israel)
Affiliation: Tel Aviv Sourasky Medical Center & Cellect Biotherapeutics Ltd.
Authors: Shani N, Solodeev I, Meilik B, Volovitz I, Sela M, Manheim S, Yarkoni S, Gur E

~~5:00 pm~~ **52**

REGENERATIVE PROPERTIES OF HUMAN SPHEROIDS FROM ADIPOSE STEM CELLS (SASCS) IN A XENOGENEIC RABBIT MODEL

NOT PRESENTED
Presenter: Anna Barbara Di Stefano, PhD (Italy)
Affiliation: Plastic and Reconstructive Surgery
Authors: Di Stefano AB, Montesano L, Belmonte B, Gulino A, Grisafi F, Toia F, Gagliardo C, Russo A, Florena AM, Moschella F, Leto Barone AA, Cordova A

5:10 pm **53**

ISOLATION AND CHARACTERIZATION OF MICROVASCULAR ENDOTHELIAL PROGENITOR CELLS FROM HUMAN LIPOASPIRATES

Presenter: Natsumi Saito, PhD (Japan)
Affiliation: Jichi Medical University
Authors: Saito N, Shirado T, Mori M, Asahi R, Yoshimura K

~~5:20 pm~~ **54**

GENETIC STABILITY AND REPLICATIVE SENESCENCE IN ASCS AMPLIFIED FOR CLINICAL APPLICATION

WITHDRAWN
Presenter: Nicolas Theys, PhD (Belgium)
Affiliation: Novadip Biosciences SA
Authors: Theys N, Pierard C, Dufrane D

5:30 pm **55**

HYPERPLASTICITY OF SVF-ISOLATED CD34+ CELLS TOWARDS ADIPO- AND OSTEO- GENESIS

Presenter: Srinivas Koduru, PhD (USA)
Affiliation: Pennsylvania State University
Authors: Koduru S, Leberfinger AN, Hayes DJ, Ravnic DJ

5:40 pm **56**

DONOR AGE AFFECTS STEM CELL RELATED GENE EXPRESSION IN ADIPOSE MSCS

Presenter: Michael Badowski, PhD (USA)
Affiliation: Celebration Stem Cell Center
Authors: Badowski M, Harris DT, Muise A, White L

3:30 pm	**Panel 9: Reconstructive Adipose Surgery: Breast, Genital and Face**
Room B	Moderators: Gregory Evans, MD, FACS & Frank Chang, MD, M Panelists: Roger Khouri, MD, FACS *Tissue Molding with Fat: A New Frontier* Kotaro Yoshimura, MD *How to use Fat Grafting in Asian Breast Reconstruction* Nelson Piccolo, MD *Vaginal Canal and External Female Atrophy Regeneration with Fat Grafting*
4:50 pm	**Panel 10: Reconstructive Adipose Surgery/Regenerative**
Room B	Moderators: Steven Cohen, MD & Stig Frederik Trojahn Kolle, MD, PhD Panelists: Nelson Piccolo, MD *Fat Grafting as an Ancillary Treatment in Burns and Other Complex Wounds and their Sequellae* Guy Magalon, MD *Treatment of Sclerosis. Ten Years Later* Michele Zocchi, MD *A New Approach to Regenerative Medicine and Surgery: The Bio-Active Composite Grafts* Kwang Sik Kook, MD *Clinical Use of SVF for Treating Sskin Complications* Hong-Wei Liu, MD, PhD *Up-To-Date Clinical Trials of Hair Regeneration Using a Combination of Platelet-Rich Plasma and Concentrated Nanofat Graft in Male Androgenetic Alopecia*
6:00 pm	**Poster Session**
NOT PRESENTED	**1P** **A 10-YEAR JOURNEY: TRENDS IN FAT GRAFTING ACROSS THE MAJOR PLASTIC SURGERY JOURNALS** Presenter: Alexandra Conde-Green, MD (USA) Affiliation: Rutgers New Jersey Medical School Authors: Conde-Green A, Liu FL, Gala ZG, Hasbun SH, Arbelaez JA, Mitchell BM, Cansancao AC
NOT PRESENTED	**2P** **SYSTEMATIC REVIEW OF THE EFFICACY OF FAT GRAFTING AND PLATELET-RICH PLASMA FOR WOUND HEALING** Presenter: Oliver J. Smith, MBChB, MRCS (United Kingdom) Affiliation: Royal Free Hospital Authors: Smith OJ, Kanapathy M, Hachach-Haram N, Mann H, Khajuria A, Mosahebi A
	3P **GLUTEOPLASTY WITH IMPLANTS AND LIPO TRANSFERENCE** Presenter: Aristides Arellano, MD (Mexico) Affiliation: Clinica Dermatologica y Cirugia Estetica de Puebla Author: Arellano A
	4P **REGENERATIVE MEDICINE OF MESENCHYMAL STEM CELLS: A PROMISING TREATMENT OF FRACTURE, PARALYSIS AND WOUND OF ANIMALS** Presenter: Kamlesh K. Bajwa, MSc (India) Affiliation: National Dairy Research Institute Authors: Bajwa KK, Saini S, N Malik H, Sharma V, Kumar D, Kumar S, Kumar S
WITHDRAWN	**5P** **BREAST AUGMENTATION USING LOOPS AND LIPOFILLING: HOW I DO IT?** Presenter: Marwan H. Abboud, MD (Belgium) Affiliation: Chu Tivoli Authors: Abboud MH, El Hajj H, Abboud NM
	6P **VALIDATION OF PORCINE ADIPOSE-DERIVED STROMAL/STEM CELLS FOR WOUND HEALING STUDY** Presenter: Joanna Bukowska, PhD (Poland) Affiliation: Institute of Animal Reproduction and Food Research Authors: Bukowska J, Walendzik K, Kopcewicz M, Gawronska-Kozak B
	7P **FACIAL REJUVENATION WITH ADIPOSED DERIVED STEM CELLS ASSISTED LIPOTRANSFER** Presenter: Chao-Chuan Wu, MD (Taiwan) Affiliation: Chai-Yen Plastic and Aesthetic Clinic Author: Wu CC
	8P **ENRICHMENT OF HUMAN AMNIOTIC MEMBRANE WITH ADIPOSE-DERIVED MESENCHYMAL STEM CELLS: FUTURE IN WOUND CARE** Presenter: Angelica Schettino, MD (Brazil) Affiliation: Marcilio Dias Naval Hospital Authors: Schettino A, Fusco MA, Franco D, Bueno DF, Pinheiro C, Sant'Ana L, Fonseca AC, Gregorio ML

9P

THREE-DIMENSIONAL EVALUATION OF BREAST VOLUMES: A NOVEL APPROACH TO ASSESS FAT GRAFTING OUTCOMES

Presenter: Carlo M. Oranges, MD (Switzerland)
Affiliation: Basel University Hospital
Authors: Oranges CM, Harder Y, Haug M, Kalbermatten DF, Schaefer DJ, Thieringer FM

10P

ENHANCING THE RESULTS OF LOWER BLEPHAROPLASTY WITH FAT TRANSPLANTATION

Presenter: Yu-Hsiu Yen, MD; PhD (Taiwan)
Affiliation: Cathay General Hospital
Authors: Yen YH, Pu CM, Lu SY

11P

TRENDING FAT GRAFTING ACROSS THE WORLD: ANALYSIS OF THREE ANNUAL MAJOR PLASTIC SURGERY MEETINGS

Presenter: Farrah C. Liu, BS (USA)
Affiliation: Rutgers New Jersey Medical School
Authors: Liu FC, Arbelaez JA, Gala ZG, Hasbun SH, Cansancao AC, Conde-Green AC

12P

~~**A SIMPLE METHOD FOR CONCENTRATING NANOFAT GRAFT BY CENTRIFUGATION AND NEGATIVE PRESSURE**~~

NOT PRESENTED

Presenter: Hongwei Liu, MD, PhD (China)
Affiliation: The First Affiliated Hospital of Jinan University
Authors: Liu H, Wu YD

13P

THE EFFECTS OF INTRAVENOUS INSULIN ADMINISTRATION ON THE INCREASE IN SVF CELL DENSITY

Presenter: Agus Budi, MD (Indonesia)
Affiliation: Faculty of Medicine Airlangga University
Author: Budi A

14P

CLINICAL USE OF CRYOPRESERVED WHOLE ADIPOSE TISSUE

Presenter: Michael Badowski, PhD (USA)
Affiliation: Celebration Stem Cell Center
Authors: Badowski M, Harris DT, Muise A

15P

PURIFICATION OF EXOSOMES FROM ADIPOSE-DERIVED CONDITIONED MEDIA

Presenter: Sherry Collawn, MD, PhD (USA)
Affiliation: UAB
Authors: Collawn S, Banerjee NS, Chow LT

16P

ADIPOSE-DERIVED STEM CELLS ATTENUATE ATOPIC DERMATITIS-LIKE SKIN LESIONS IN NC/NGA MICE

Presenter: Ji-Ung Park, MD (South Korea)
Affiliation: Seoul National University Boramae Hospital
Authors: Park JU, Park HS, Son YS, Hong HS, Kim SD

17P

CUTANEOUS WOUND HEALING EFFECTS OF MESENCHYMAL STEM CELLS AND THEIR SHEETS OVEREXPRESSING PLATELET-DERIVED GROWTH FACTOR IN DOGS

Presenter: Namyul Kim, DVM (South Korea)
Affiliation: Seoul National University
Author: Kim N

18P

ADIPOSE-DERIVED STEM CELL INDUCED ENDOTHELIAL PROGENITOR CELL SALVAGE ISCHEMIC SKIN FLAP BY PROMOTING ANGIOGENESIS

Presenter: Yuan-Yu Hsueh, MD, PhD (Taiwan)
Affiliation: National Cheng Kung University Hospital
Authors: Hsueh YY, Wang D, Chang Y, Lin S, Wu C

19P

~~**A PAPER-SUPPORTED APTASENSOR BASED ON UPCONVERSION LUMINESCENCE RESONANCE ENERGY TRANSFER FOR THE ACCESSIBLE DETERMINATION OF EXOSOMES**~~

NOT PRESENTED

Presenter: Xiaosong Chen, MD, PHD (China)
Affiliation: Fujian Medical University Union Hospital
Author: Chen X

20P

OBESITY AND THE SKIN: DOES EPIDERMAL FOXN1 REGULATE DERMAL WHITE ADIPOSE TISSUE (DWAT)

Presenter: Katarzyna Walendzik, MS (Poland)
Affiliation: Institute of Animal Reproduction and Food Research
Authors: Walendzik K, Bukowska J, Kopcewicz M, Gimble J, Gawronska-Kozak B

21P
IN VIVO AND CLINICAL EVALUATION OF THE EFFECT OF STROMAL VASCULAR FRACTION-ENHANCED FAT GRAFTING ON SOFT TISSUE AUGMENTATION
NOT PRESENTED
Presenter: Hyung Min Hahn, MD (South Korea)
Affiliation: Ajou University Hospital
Authors: Hahn HM, Ha N, Lee L, Yeom Y

22P
STUDY FOR THE POTENTIAL OF HYPOXIA-CULTURED ASCS IN NERVE REGENERATION
Presenter: Szu-Hsien Wu, MD (Taiwan)
Affiliation: Taipei Veterans General Hospital and University of Tokyo Hospita
Authors: Wu SH, Wang J

23P
THE EFFECT OF ADIPOSE TISSUE DERIVED STEM CELLS WITH CONDITIONED MEDIA FOR THE TREATMENT OF ACNE VULGARIS SCAR ON RABBIT EAR MODEL
NOT PRESENTED
Presenter: Jomg-Won Rhie, MD, PhD (South Korea)
Affiliation: Catholic University of Korea Seoul St Mary Hospital
Author: Rhie JW

24P
EFFICACY EVALUATION OF TRANSPLANTATION OF THREE-DIMENSIONAL ADIPOSE-DERIVED STEM CELL SHEET WITH ENHANCED ANGIOGENESIS INTO ISCHEMIC VASCULAR DISEASE
Presenter: Jong-Ho Kim, PhD (South Korea)
Affiliation: Korea University College of Medicine
Authors: Kim JH, Lim I, Park C, Joo H, Hong S, Lim D

25P
MOUSE ADIPOSE STEM CELLS TRANSPLANTED INTO INFARCTED MYOCARDIUM IMPROVE CARDIAC FUNCTION
Presenter: Chi-Yeon Park, PhD (South Korea)
Affiliation: Korea University College of Medicine
Authors: Park CY, Kim J, Choi J, Choi S, Joo H, Lim D

26P
EFFECT OF MATURE ADIPOCYTE-DERIVED DEDIFFERENTIATED FAT (DFAT) CELLS ON ISCHEMIC TISSUE OF NORMAL AND DIABETIC RATS
Presenter: Tsutomu Kashimura, PhD (Japan)
Affiliation: Nihon University School of Medicine
Authors: Kashimura T, Soejima K, Kikuchi Y, Kazama T, Matsumoto T, Nakazawa H

27P
3D BIOPRINTING THE CARDIAC PURKINJE SYSTEM USING HUMAN ADIPOGENIC MESENCHYMAL STEM CELL DERIVED PURKINJE CELLS
Presenter: Evan P. Tracy, BS (USA)
Affiliation: University of Louisville School of Medicine
Authors: Tracy EP, Gettler BC, Zakhari JS, Birla RK, Schwartz RJ, Williams SK

28P
PATHOPHYSIOLOGY OF TISSUE DAMAGE AFTER RADIATION THERAPY: INFLUENCE OF RADIATION DOSE AND FRACTIONATION PROTOCOL ON ADIPOSE-DERIVED STEM CELLS IN VITRO AND IN VIVO
NOT PRESENTED
Presenter: Rintaro Asahi, MD (Japan)
Affiliation: Jichi Medical University
Authors: Asahi R, Shirado T, Moriya K, Yoshimura K

6:00 pm — Poster Session and Welcome Reception

Dinner on own

Saturday - December 15 - DAY 3

7:00 am — Breakfast in Exhibit Hall

7:30 am — Sponsored Breakfast Session (MTF Biologics)
Room B
Moderator: to be determined
Speaker: Marc Long, PhD - *Early Clinical Safety and Applications of a Novel Allograft Adipose Matrix*

8:00 am — **IFATS Members' Meeting** - Room A

8:45 - 10:00 am — **Panel 11: Mechanical Processing I**
Room B
Moderators: Nelson Piccolo, MD & Gordon Sasaki, MD
Panelists: Patrick Tonnard, MD
Processing, Indications and Results of Nanofat grafting
H. P. Jeroen Stevens MD, PhD
Fractionation of Adipose Tissue (FAT-Procedure) and Platelet Rich Stroma (PRS)
Carlo Tremolada, MD
Intact Microfragmented Fat as an Ideal Way to Process Adipose Tissue for Regenerative Purpose
Feng Lu, MD, PhD
Clinical Applications of SVF Gel in Skin Rejuvenation and Precise Filling

9:00 - 10:00 am Room A	**Free Papers 5: Translational Research - Cancer, Ischemic Disease** Moderators: Kevin Zwezdaryk, PhD & Lauren Kokai, PhD
9:00 am	**57** **THE EFFECT OF CELL-CELL CONTACT DEPENDENT LIPOASPIRATE CO-CULTURE ON BREAST CANCER CELLS PROLIFERATION: IMPLICATIONS FOR CELL-ASSISTED LIPOTRANSFERS IN BREAST RECONSTRUCTION** Presenter: Asim Ejaz, PhD (USA) Affiliation: University of Pittsburgh Authors: Ejaz A, Egro F, Johngrass M, Silva M, Kokai L, Rubin JP
9:10 am	**58** **ADIPOSE DERIVED MESENCHYMAL STEM CELLS INHIBITS CARCINOGENESIS AND INVASIVENESS IN HEPATOCELLULAR CARCINOMA CELL LINES** Presenter: Nada Alaaeddine, PhD (Lebanon) Affiliation: University of St Joseph Authors: Alaaeddine N, Serhal R, Moussa M, Hilal G, Alhassan G, Elatat O
9:20 am	**59** **OBESITY-ALTERED ADIPOSE STEM CELLS PROMOTE RADIORESISTANCE OF ER+ BREAST CANCER** Presenter: Rachel Sabol, MS (USA) Affiliation: Tulane University School of Medicine Authors: Sabol R, Cote A, Bunnell BA
9:30 am	**60** **ADIPOSE-DERIVED STEM CELLS PROTECT SKIN FLAPS AGAINST ISCHEMIA/REPERFUSION INJURY VIA IL-6 EXPRESSION** Presenter: Chi-Ming Pu, MD, PhD (Taiwan) Affiliation: Cathay General Hospital Authors: Pu CM, Chen YL, Yen YH
9:40 am	**61** **A UNIQUE APPROACH TO TREATING CATASTROPHIC DISTAL-LIMB WOUNDS WITH ADIPOSE STEM CELLS, PLATELET-RICH-PLASMA, AND VETAP-17 (SM-1997)** Presenter: Kaylen M. Capps, MS (USA) Affiliation: Trinity Research Institute Authors: Capps KM, Murnane JM, Jirakittissonthon T, Snyder II OJ, Andrews N, Stottlemire BJ
10:00 am	Coffee Break (Exhibit Hall)
10:30 am	**Panel 4: Regulatory Affairs**
Room A	Moderators: J. Peter Rubin, MD, FACS & Adam Katz, MD, FACS Panelists: Richard McFarland, MD, PhD Morikuni Tobita, DDS, PhD *Regulatory Frame Work of Regenerative Medicine in Japan: "The Act on Safety of Regenerative Medicine"*
10:30 am	**Panel 12: Mechanical Processing II**
Room B	Moderators: Michele Zocchi, MD & Ewa Siolo, MD, MBChB, FC Panelists: Gordon Sasaki, MD *The Significance of Lower Total Nucleated Cell Counts (tSVF) in Adipose Tissue after "Mechanical" Centrifugation of Filtration Processing in Midface Fat Graft Retention and PRP/SVF "Rescue"* Ramon Llull, MD, PhD *Cell Aggregates: Achieving Potent and Ultra High Cell Concentrations with Mechanical Disaggregation* Guy Magalon, MD *Emulsified Fat Protocol and Quality Control* Steven Cohen, MD *Options for Mechanical Processing of Fat- Millifat, Microfat, Nanofat, Mechanical SVF* Kevin Darr, MD *Analysis of the Safety and Effectiveness of Autologous Micro-Fragmented Adipose Tissue in the Treatment of Osteoarthritis*
12:00 pm	Lunch in Exhibit Hall
12:00 pm	**Sponsored Lunch Session (Amano Enzyme)**
Room B	Effective Collection of Stromal Vascular Fraction (SVF) by Enzymatic Treatment Moderator: Kotaro Yoshimura, MD Speakers: Joshua Escalante *Introduction of Amano's Enzymes for Adipose Tissue Dissociation* Masanori Mori *Optimization of Enzyme Blend using Amano's Enzymes*
12:35 pm	**Sponsored Lunch Session (Allergan)**
Room B	Aesthetic Applications of Fat Grafting and Case Based Discussion Speaker: Gaurav Bharti *Innovative Approaches to Aesthetic Fat Grafting and Case Based*

1:15 pm	**Panel 13: Aesthetic Adipose Surgery/Face I**
Room B	Moderators: Ramon Llull, MD, PhD & Ahmed Adel Noreldin, MD Panelists: Patrick Tonnard, MD *Microfat, SNIF and Nanofat Grafting: from Volume Augmentation to Cell Therapy in Every Facial Rejuvenation Procedure* Steven Cohen, MD *Injectable Tissue Replacement and Regeneration: A New Strategy in Facial Rejuvenation* Ewa Siolo, MD, MBChB, FC *Perioral Rejuvenation With Adipose Tissue - How, What, Where & How Much* Tsai-Ming Lin, MD, PhD *The Innovative Treatment of Gummy Smile – Micro-Autologous Fat Transplantation (MAFT)* Kuang Cheng Chang, MBA *Combined Treatment to Increase Satisfaction in Fat Grafting to Nasolabal Fold and Glabella* TaeJo Kang, MD *Facial Rejuvenation With Fat Grafting and Barbed Suture*
1:30 pm	**Panel 5: Innovation and Technology Development: How to Take an Idea to the Finish Line (Sponsored by Allergan)**
Room A	Moderators: Adam Katz, MD, FACS & Sarah Hagarty, MD Panelists: Benjamin Glenn, JD Faz K. Bashi, MD Tiffany Wilson, MBA Steven Brooks Bob Perry
3:00 pm	Coffee Break (Exhibit Hall)
3:30 pm Room A	**Free Papers 6: Matrix Matters** Moderators: Alexandra Conde-Green, MD, FICS & Kacey Marra, PhD
3:30 pm	**62** **IN VITRO AND IN VIVO EVALUATION OF A BIOENGINEERED NERVE CONDUIT COMBINING TOPOGRAPHICAL CUES AND ADIPOSE TISSUE-DERIVED SUPPORT CELLS** Presenter: Suzanne E. Thomson, BSc, MBChB, MRCSEd, PhD (United Kingdom) Affiliation: Canniesburn Plastic Surgery Unit Authors: Thomson SE, Jetter N, Charalambous C, Smith CA, Riddell J, Wallace R, Nottelet B, Hart AM, Kingham PJ, Riehle MO
3:40 pm	**63** **IN VITRO AND CLINICAL STUDIES WITH LONGITUDINAL ANALYSIS OF FUNCTIONAL ADIPOSE TISSUE REGENERATION USING ADIPOSE ALLOGRAFT MATRIX** Presenter: Benjamin K. Schilling, MS (USA) Affiliation: University of Pittsburgh Authors: Schilling BK, Kokai LE, Sivak WN, Johngrass M, Faust A, Minteer DM, Simon D, Egro F, Schusterman MA, Chnari E, Jacobs M, Marra KG, Rubin JP
3:50 pm	**64** **CLINICAL EXPERIENCE WITH ALLOGRAFT ADIPOSE MATRIX GRAFTING IN THE PEDIATRIC PATIENT** Presenter: Kevin Hopkins, MD, FACS (USA) Affiliation: Driscoll Childrens Hospital Authors: Hopkins K, Dimas V
4:00 pm	**65** **STRUCTURAL ANALYSIS AND CYTOCOMPATIBILITY OF HUMAN DECELLULARIZED ADIPOSE TISSUE DERIVED HYDROGEL** Presenter: Omair A. Mohiuddin, MS (USA) Affiliation: Tulane University Authors: Mohiuddin OA, Dabagian H, Hayes D, Bunnell B, Gimble J
4:10 pm	**66** **KEY ROLE OF ADIPOSE STEM CELLS FOR OSTEOGENESIS IN A SCAFFOLD-FREE GRAFT FOR LARGE CRITICAL SIZE BONE DEFECT** Presenter: Sophie Veriter, PhD (Belgium) Affiliation: Novadip Biosciences Authors: Veriter S, Thirion G, LeBrun V, Adnet PY, Cathy C, Dufrane D
4:20 pm	**67** **DEVELOPMENT OF XENO-FREE EPITHELIAL DIFFERENTIATION MEDIA FOR ADHERENT, NON-EXPANDED ADIPOSE STROMAL VASCULAR CELL CULTURES** Presenter: Manisha K. Shah, PhD (USA) Affiliation: Mayo Clinic Arizona Authors: Shah MK, Hintze JM, Tchoukalova YD, Sista R, Zhang N, Lott DG
3:30 pm	**Panel 14: Cell Assisted Lipotransfer**
Room B	Moderators: Steven Cohen, MD & Aris Sterodimas, MD, MSc Panelists: Gordon Sasaki, MD *The Safety and Efficacy of Cell-Assisted Fat Grafting in the Hands: Dermal and 3D Imaging Volumetric Rejuvenation (24 Month Split-Hand)* Ahmed Adel Noreldin, MD *Aesthetic Outcome of Cell Assisted Lipografting for the Treatment of Facial Scars* Tawfik Sefrioui, MD *Scarless Vaginal Rejuvenation With Micronized Fat Transfer, Enhancement of Sexual Arousal of Gspot Amplification and Treatment of Stress* Hyung Min Hahn, MD *In Vivo and Clinical Evaluation of the Effect of Stromal Vascular Fraction-Enhanced Fat Grafting on Soft Tissue Augmentation*

4:25 pm	**Panel 15: Aesthetic Adipose Surgery/Breast**
Room B	Moderators: Brian Kinney, MD & Patrick Tonnard, MD Panelists: Aris Sterodimas, MD, MSc *Hybrid Breast Augmentation: An Analysis of 745 Consecutive Cases* Michel Zocchi, MD *27 Years Experience in Large Volume Breast Fat Transfer: Technical and Clinical Aspects* Roger Khouri, MD, FACS *Treatment of Implant Complications with Fat Grafts* Cheng-Wei Hsiao *Single Session Fat Graft Breast Augmentation Using Space-Creating Concept*
4:30 pm	**Free Papers 7: Hot Topics**
Room A	Moderators: Ali Modaressi, MD & Katarina Andjelkov, MD, PhD
4:30 pm	**68** **OIL AND WATER: A RANDOMIZED, BLINDED, PLACEBO-CONTROLLED STUDY OF AUTOLOGOUS FAT GRAFTING FOR SCAR PREVENTION AND REMODELING** Presenter: Adam J. Katz, MD (USA) Affiliation: University of Florida Authors: Katz AJ, Brown JC, Shang H, Yang N, Pierson J, Ratliff C, Prince N, Roney N, Chan R, Mankoff G, Gittleman H, Vincek V, Barnholtz-Sloan JS
4:40 pm	**69** **FAT ON A CHIP MODEL OF HUMAN SUBCUTANEOUS ADIPOSE TISSUE** Presenter: Michelle McCarthy, MS (USA) Affiliation: Tulane University School of Medicine Authors: McCarthy M, Bender R, Brown T, Bukowska J, Smith S, Abbott R, Kaplan D, Williams C, Wade J, Alarcon A, Wu X, Lau F, Gimble J, Frazier T
~~4:50 pm~~ NOT PRESENTED	**70** **A SYSTEMATIC REVIEW OF AUTOLOGOUS PLATELET-RICH PLASMA AND FAT GRAFT PREPARATION METHODS** Presenter: Oliver J. Smith, MBChB MRCS (United Kingdom) Affiliation: Royal Free Hospital Authors: Smith OJ, Luck J, Mosahebi A
5:00 pm NOT PRESENTED	**71** **THE ROUTE BY WHICH INTRANASALLY DELIVERED STEM CELLS ENTER THE CENTRAL NERVOUS SYSTEM** Presenter: Peter Edenhoffer, MD (USA) Affiliation: Barshop Institute Authors: Edenhoffer P, Galeano C, Qiu Z, Mishra A, Farnsworth S, Hemmi J, Moreira A, Hornsby P
5:10 pm	**72** **REGENERATIVE MEDICINE AND WRIST OSTEOARTHRITIS: INTRA-ARTICULAR INJECTION TREATMENT OF A MIXTURE OF AUTOLOGOUS MICROFAT ASSOCIATED WITH AUTOLOGOUS PLASMA-ENRICHED PLATELETS** Presenter: Guy Magalon, MD (France) Affiliation: Culture and Cell Therapy Unit INSERM CBT1409 Authors: Eraud JE, Kachouh NK, Curvale CC, Iniesta AI, Mayoly AM, Casanova DC, Sabatier FS, Veran JV, Magalon JM, Legre RL
5:20 pm	**73** **DEVELOPMENT OF A HUMAN-DERIVED ADIPOSE ACELLULAR ALLOGENIC FLAP (AAFS) USING PERFUSION DECELLULARIZATION: TOWARDS UNIVERSAL, SHELF-READY FLAPS?** Presenter: Giorgio Giatsidis, MD (USA) Affiliation: Brigham and Women s Hospital - Harvard Medical School Authors: Giatsidis G, Orgill DP, Guyette J, Ott HC
5:30 pm	**74** **CONSTRUCTION OF VASCULARIZED TISSUE ENGINEERING BLADDER WITH AUTOLOGOUS ADIPOSE DERIVED STROMAL VASCULAR FRACTION COMBINED WITH BLADDER ACELLULAR MATRIX** Presenter: Rui-Peng Jia, MD, PhD (China) Affiliation: Nanjing First Hospital Author: Jia RP
5:40 pm	**75** **PEDAL FAT GRAFTING: CORRELATING ADIPOSE TISSUE CHARACTERISTICS TO CLINICAL OUTCOMES AND VOLUME RETENTION** Presenter: Sheri Wang, BS (USA) Affiliation: University of Pittsburgh Authors: Wang S, DiBernardo GD, James IJ, Minteer DM, Zhang WZ, Gusenoff BG, Marra KM, Kokai LK, Gusenoff JG
5:10 pm	**Panel 16: Aesthetic Adipose Surgery/Buttock**
Room B	Moderators: J. Peter Rubin, MD, FACS & Nelson Piccolo, MD Panelists: Arturo Ramirez-Montanana, MD *Up to Date in Gluteal Fat Grafting: ASERF Report and Guidelines* Aris Sterodimas, MD, MSc *Shaping the European Buttock: Combining Liposuction and Lipografting by Stromal Enriched Lipogrft™* Alexandra Conde-Green, MD, FICS *Postoperative Measurement of Fat Graft Retention to the Gluteal Region Using Ultrasound Technique*
6:20 pm	Concluding Remarks, Award Presentations, Announcement of IFATS 2019 Kotaro Yoshimura, MD & Guy Magalon, MD
7:30 pm	Farewell Networking Gala Dinner - Wicked Spoon Buffet Restaurant

AUTHOR INDEX

PAPER PRESENTATIONS

1

DIABETIC ADIPOSE STEM CELL-DERIVED EXOSOME ACCELERATES CUTANEOUS WOUND HEALING IN DB/DB MICE

Presenter: Jennifer An-Jou Lin, MD (Taiwan)
Affiliation: Chang Gung Memorial Hospital
Authors: Lin JA, Wang AY, Loh CY, Kao HK

Introduction: Paracrine secretion from ASCs contains membrane-bound nano-vesicles called exosomes (ASC-exo). The mechanism of exosomal-cell communication for these effects remains unclear. This study aims to identify the in vitro characteristics and functional properties of diabetic ASC derived exosomes and the in vivo mechanistic basis of ASC-exo treatment in accelerating cutaneous wound healing in diabetic mice.

Methods: In vitro, the ASC-exo and dermal fibroblast-derived exosome (DFb-exo) were isolated by differential centrifugation and are characterized further by flow cytometry, immunoblotting, electron microscopy (EM), and nanoparticle tracking analysis. The dynamic course of exosome attachment onto the wound was tested using IVIS spectrum in conjunction with octadecyl rhodamine B chloride (R18) during exosomal uptake. In vivo, full thickness wounds in diabetic mice were treated either with ASC-exo, DFb-exo, or phosphate buffered saline (PBS) through topical administration. Wound healing kinetics, including wound contraction, re-epithelialization and microscopic metrics such as cell proliferation, angiogenesis, and granulation growth were investigated. Expression of proinflammatory factors, profibrotic factors, growth factors, and extracellular matrix components were measured in wound tissues.

Result: ASC-exo and DFb-exo exhibited a cup-shaped morphology with an average 30–100 nm size characteristic of exosomes. Typical surface proteins were identified, including CD63, CD9, and CD81. R18-labeled exosomes had strong fluorescent signal within 1 hour and showed a time-dependent attenuation till 21 days after treatment. ASC-exo stimulated wound healing by dermal cell proliferation, keratinocyte proliferation with re-epithelialization, and angiogenesis compared with DFb-exo and PBS treated wounds. Expression of angiogenesis markers (VEGF and b-FGF), growth factors (TGF-β, PDGF-A, and FGF-7), chemokines (MCP-1 and MIP-1α), and extracellular matrix (collagen-I and α-SMA) were upregulated in ASC-exo treated wounds.

Conclusions: The application of ASC-exo may represent a novel cell-free therapy in wound regeneration. ASC-exo can accelerate wound healing by stimulating cell proliferation, re-epithelialization, and angiogenesis in a diabetic mice experimental model.

2

ENHANCED THERAPEUTIC OUTCOMES OF MSC BY PRIMING AND SELECTION METHODS

Presenter: Annie Bowles, PhD (USA)
Affiliation: University of Miami
Authors: Bowles A, Willman MA, Kouroupis D, Correa D

Introduction: Mesenchymal stem cells (MSCs) have the innate ability to sense and respond to their environment through the dynamic spectrum of secreted paracrine signals. Nevertheless, clinical reproducibility and predictability are still significant challenges, due in part to the inherent heterogeneity within donors and the lack of standardization regarding "ideal" characteristics and attributes of the cell-based product during manufacturing. To overcome these limitations, we propose to refine a more uniform and reproducible cell-based product by pre-disposing MSCs to a defined inflammatory environment in vitro (i.e., cell priming) followed by active selection of the enriched cell subset.

Methods: Human adipose and bone marrow-derived MSCs were isolated and designated to groups defined as naïve (control), primed and magnetic-activated cell sorted (selected CD146+) MSCs. All groups were highly characterized, including complete immunophenotype, growth kinetic and gene expression profiles. All cell groups were then co-cultured with CD3/CD28 activated human T cells or peripheral blood mononuclear cells to demonstrate immunomodulatory potential, cellular phenotypic skewing, and molecular response curves. Secretome analysis of proteins and high throughput analysis of secreted and exosomes-derived miRNA profiles were performed to obtain a deeper insight into the inherent qualities of the primed and selected groups compared to the naïve controls.

Results: Priming of MSCs generated a consistent, reproducible, and distinguished cellular phenotype across donors, defined by a robust secretory profile and enhanced immunomodulatory effects. The selected CD146+ fraction exhibited an enrichment in similar markers while reproducing the anti-inflammatory secretory profile and immunomodulatory behavior even without prior priming. Furthermore, primed and selected MSCs secreted key proteins and miRNAs implicated in immunoregulatory pathways.

Conclusion: Together, these findings suggest that cell priming and selection produce highly effective, reproducible, uniform, and robust phenotypes of MSCs with superior in vitro immunomodulatory outcomes. These discriminatory responses by the MSCs may limit potential secondary effects after administration. Finally, these acquired attribute

3

THERAPEUTIC EFFECTS OF HUMAN ADIPOSE-DERIVED PRODUCTS ON IMPAIRED WOUND HEALING IN IRRADIATED TISSUE

Presenter: Szu-Hsien Wu, MD (Taiwan)
Affiliation: Taipei Veterans General Hospital and University of Tokyo Hospital
Authors: Wu, SH, Yoshimura K, Mashiko T, Feng J

Objective: Clinical sequelae of irradiation (e.g., ischemia, fibrosis, and atrophy) result in tissue devitalization, where wound healing capacity is impaired. Fat or fat-derived products may work to treat such abnormality.

Methods: Nonlethal irradiation at various doses (5, 10, and 15 Gy) and frequencies (one to three times on sequential days) was delivered to dorsal skin of 7-week-old nude mice, and subsequent gross and microscopic changes were evaluated for up to 4 weeks. Cutaneous punch wounds were then created to compare wound healing in irradiated and nonirradiated states. Wounds were also locally injected with vehicle, cultured adipose-derived stem cells, centrifuged fat tissue, or micronized cellular adipose matrix, and the therapeutic impact was monitored for up to 15 days.

Results: Nude mice given total doses greater than 15 Gy spontaneously developed skin ulcers approximately 2 weeks after exposure, and radiation damage was dose-dependent; however, a fractionated irradiation protocol could reduce the damage. Histologic assessment revealed dose-dependent dermal fibrosis/thickening and subcutaneous atrophy. Dose-dependent (5 to 15 Gy) impairment of wound healing was also evident. At the highest dosage (15 Gy three times), open wounds persisted on day 15. However, wounds injected with cultured adipose-derived stem cells were nearly healed on day 12, and those treated with injection of centrifuged fat or micronized connective tissue healed faster than untreated controls ($p < 0.05$).

Conclusion: Three types of human adipose-derived injectable products (i.e., cultured adipose-derived stem cells, centrifuged fat, and micronized connective tissue) were examined for their therapeutic potentials for cutaneous wounds in the irradiated tissue. All of them significantly accelerated wound healing, suggesting the revitalizing effects of adipose derived stem cell–containing products.

4

IDENTIFICATION AND VERIFICATION OF NOVEL ADIPOKINES IN ADIPOSE-DERIVED EXOSOME-LIKE VESICLES

Presenter: Yan Zhang, MD (China)
Affiliation: Sichuan University
Authors: Zhang Y, Yu M, Tian WD

NOT PRESENTED

5

MOLECULAR BASIS OF ADIPOSE-DERIVED STEM CELL (ASC) THERAPY FOR MANAGEMENT OF RADIATION INDUCED FIBROSIS (RIF)

Presenter: Asim Ejaz, PhD (USA)
Affiliation: University of Pittsburgh
Authors: Ejaz A, Epperly M, Schusterman A, Greenberger J, Rubin P

Radiation therapy is one of the most important tools in cancer treatment, however iatrogenic comorbidities including RIF can significantly impair patient healing and life quality. Several published case studies suggest that application of autologous adipose tissue aspirates and adipose stem cells at the irradiation sites can ameliorate RIF, though the mechanism is not clear. In this study, we evaluated the efficacy of adipose tissue aspirates and/or ASCs in management of radiation fibrosis in a mouse model and investigated the underlying molecular mechanism.

Transwell co-cultures were performed using irradiated human foreskin fibroblasts (HFFs) and ASCs to determine changes in fibrosis related genes expression. Female C57BL/6 mice were irradiated with 35 Gray (Gy) at the flank region and monitored for expression of fibrosis related genes by quantitative RT PCR at days 1 and 14 post irradiations. Fibrosis was confirmed by histological analyses and range of limb motion measure. To assess ASCs intervention efficacy, irradiated mice were injected with adipose tissue aspirates from luciferase+ GFP+ mice at day 28 post irradiations.

Successful development of RIF in C57BL/6 mouse model was confirmed by histological staining of collagens using Masson's Trichrome stain which confirmed collagens deposition at the site of irradiation. At day 14 post irradiations we observed an upregulation of fibrosis related genes TGF β (500 fold), CTGF (60 fold), Collagen1 (400 fold), Collagen3 (500 fold) and collagen4 (500 fold) as compared to non-irradiated mouse skin. We observed a loss of limb flexibility in irradiated mice and these mice showed range of limb extension to only 11.4 ± 2.7 degree as compared to 57.0 ± 2.5 ($p < 0.0001$) degree in non-irradiated mice. A single ASCs injection significantly restored the limb flexibility to 42.5 ± 2.5 degree ($p = 0.0013$). In addition, a single intraperitoneal injection of ASCs lead to a significant enhanced survival of 9.25 Gy total body irradiated mice ($P = 0.047$). Transwell cultures with ASCs demonstrated significant down regulation of pro-fibrotic genes in irradiated fibroblasts. We determined hepatocyte growth factor (HGF) as the key mediator secreted by ASCs in irradiated HFF co-culture. Further, addition of recombinant HGF signific

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ADIPOSE DERIVED STEM CELLS REGENERATE CIGARETTE SMOKE-INDUCED KIDNEY DAMAGE

Presenter: Daria Barwinska, PhD (USA)
Affiliation: Indiana University
Authors: Barwinska D, Traktuev DO, Cook TG, Saliba J, Bacallao RL, Basile DP, March KL

Background: Approximately 10% of the worldwide population is diagnosed with chronic kidney disease. We previously demonstrated that administration of adipose stem cells (ASC) to rats with kidney ischemia/reperfusion injury protects and regenerates renal morphology and function. Cigarette smoking (CS) has been associated with decline in kidney function in patient population, however little has been done to elucidate the effect of CS on kidney homeostasis and subsequent application of ASC to treat CS-induced renal damage.

Methods: C57Bl/6 mice (10-week old) were exposed to CS for five months (five hours a day, five days a week). In parallel, a subset of mice was exposed to ambient air to serve as Control. Following CS-exposure regiment, mice received an i.p. injection of either 3x105 human ASC, or ASC-derived conditioned medium (ASC-CM), or Vehicle once a week for four consecutive weeks. Seven days after last injection, blood flow in kidneys was evaluated by Laser Doppler Perfusion Imager (LDI). Then, kidneys were harvested, weighed, and analyzed for macrophage accumulation (M1, M2 populations), collagen (PicroSirius Red) and iron (Perl's Iron) deposition using histology.

Results: When compared to the kidneys of the Control cohort of mice, kidneys of CS-exposed mice manifested decrease in weight by 20% and cortical blood flow by 37% ($p<0.01$), but 2.2-fold increase in collagen deposition, a sign of fibrotic changes. Iron deposition was also observed, while no M1M2 macrophages were detected. However, post CS-exposure treatment of mice with in vitro expanded human ASC reversed damages caused by CS and restored kidney perfusion to the level of Control cohort, while fibrosis was ameliorated by 3.8 fold.

Discussion: Our data shows that systemic administration of human ASC reversed the damage caused by CS which significantly compromised both renal structure and function by decreasing capillary density and inducing collagen and iron deposition, which leads to decrease in kidney perfusion, function and nephrotoxicity. We have shown that ASC are able to mitigate CS-induced renal pathology, thus providing additional evidence that ASC-based therapy will benefit patients with compromised renal function.

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ANALYSIS OF THE SAFETY AND EFFECTIVENESS OF COMBINATION CELL THERAPY FOR THE TREATMENT OF PAIN AND INFLAMMATION ASSOCIATED WITH OSTEOARTHRITIS OF THE KNEE AND HIP

Presenter: Kevin Darr, MD (USA)
Affiliation: Covington Orthopedic and Sports Medicine Institute
Authors: Darr K, Dufresne MD

Objectives: To assess the clinical outcome of participants receiving bone marrow-aspirate concentrate(BMAC), adipose (fat graft) and concomitant Platelet-Rich Plasma (PRP) for the treatment of pain associated with osteoarthritis.

Methods: This is a safety and efficacy study with a single treatment group. We evaluated 176 knee and hip patients, age 23-90, diagnosed with osteoarthritis. We followed a well established protocol for extracting, preparing, and administering autologous BMAC, a fat graft, and PRP using ultrasound guidance. Participants returned for a follow-up after 6, 18, 52, and 108 weeks and completed the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and a visual analog scale (VAS) to serve as the primary outcomes.

Results: 146 knee and 30 hip patients received combination cell therapy. 82% reported some improvement at all follow-up appointments. After 18 weeks, 104 knee patients reported an average of 41.2% improvement in function ($p < .001$) and 41.5% improvement in pain ($p < .001$). and 19 hip patients saw an average of 31.2% improvement in function ($p < .001$) and 32.5% improvement in pain ($p < .001$). 76 knee patients followed-up after 1 year and reported an average of 48.3% improvement in function ($p < .001$) and 42.5% improvement in pain ($p < .001$). 9 hip patients reported an average of 31% improvement in function ($p < .05$) and 49% improvement in pain ($p < .001$). 17 knee patients followed-up after 2 years and reported an average of 69.4% improvement in function ($p < .001$) and 67.9% improvement in pain ($p < .001$). 3 hip patients reported an average of 52.4% improvement in function ($p < .05$) and a 25.1% improvement in pain. Patients with a BMI of less than 31 or who were younger than 70 years old had better results in function and pain. After 1 year, 45% of MRIs showed improvement in lesion size and edema. We evaluated cell count in 60 patients and found no correlation between cell count and percent improvement in function or pain. There were no serious complications reported.

Conclusion: Cell based biologic treatment of osteoarthritis continues to show considerable improvement from baseline in this group of patients with an excellent safety record.

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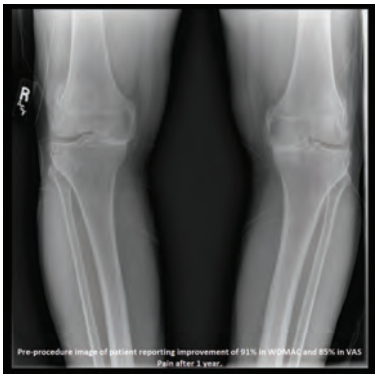
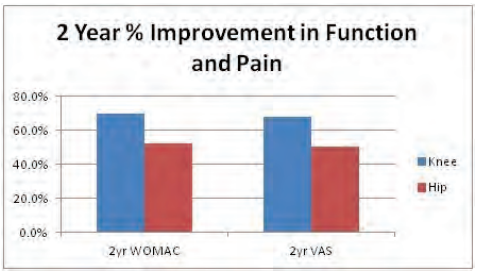
ANALYSIS OF THE SAFETY AND EFFECTIVENESS OF COMBINATION CELL THERAPY FOR THE TREATMENT OF PAIN AND INFLAMMATION ASSOCIATED WITH OSTEOARTHRITIS OF THE KNEE AND HIP

Presenter: Kevin Darr, MD (USA)
Affiliation: Covington Orthopedic and Sports Medicine Institute
Authors: Darr K, Dufresne MD





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PERFORATING FAT INJECTIONS FOR CHRONIC PLANTAR FASCIITIS: A NOVEL REGENERATIVE TREATMENT OPTION

Presenter: Jeffrey Gusenoff, MD (USA)
Affiliation: University of Pittsburgh
Authors: Gusenoff J, Minteer D, Chen W, Gusenoff B

Introduction: Plantar fasciitis (PF) is the most common cause of heel pain, and chronic PF is a painful condition resulting from recurrent inflammation and degeneration of the plantar fascia insertion at the calcaneal tuberosity. Fascial thickening can cause tremendous pain and reduce quality of life. Current treatment options can be invasive, with complication risks, or non-invasive with inconsistent results. We evaluated a novel method of perforating fat injections to regenerate the plantar fascia and reduce pain and improve quality of life.

Methods: We report a prospective, randomized cross-over pilot study. Included patients had chronic PF with thickening (>4mm) and failed standard treatment for 6 months. Subjects were randomized to either observation or intervention groups. Intervention involved perforating autologous fat injections to the PF at multiple sites. Subjects were evaluated at baseline, 1-/2-/6-months. Outcomes included validated foot pain and function questionnaires, plantar fascia thickness, and physical exam. Unpaired t-test was used ($p<0.05$).

Results: 15 human subjects were enrolled and randomized (14 female; mean age 49.9±12.4 years, mean BMI 29.1±4.8; observation, n=6; intervention, n=9) following a diagnosis of chronic PF for >4 years. Mean injection volume was 2.6±1.6 cc/foot. At baseline, there were no significant differences between the groups. Six and 12 months after intervention, experimental group had significantly less thick plantar fascia measured by ultrasound ($p<0.05$), while the observational group displayed no change in plantar fascia thickness ($p>0.05$). The experimental group had improvements in pain at 1, 2, 6, and 12 months post-operative ($p<0.05$) while the observational group reported the same pain levels compared to pre-op at 1 and 2 months ($p>0.05$), then improvement at 6 months after the procedure ($p=0.03$). Both groups reported improved functionality following the procedure ($p<0.05$). No unanticipated complications occurred.

Conclusion: Perforating fat injections to the plantar fascia demonstrate promising improvements in pain and daily activities. Autologous fat grafting proves to have a regenerative potential in remodeling chronically thickened plantar fascia and eliminating pain.

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CELL ENRICHED FAT GRAFTING FOR THE TREATMENT OF ANDROGENIC ALOPECIA. THE STYLE TRIAL: MULTICENTER RANDOMIZED CLINICAL STUDY

Presenter: Joel Aronowitz, MD (USA)
Affiliation: Cedars Sinai Medical Center
Authors: Aronowitz J, Daniels ED, Washenik KW

Research demonstrates the role of adipose cells surrounding the hair bulb in maintaining the continuity of the hair cycle. AA involves a reduction in these adipose cells and adipose-derived regenerative cells (ADRCs). By replenishing adipose and ADRCs to the tissue surrounding the hair bulb, it is hypothesized that progression of AA will be slowed and growth of terminal hair will be increased.

We conducted an IRB approved, controlled and randomized multicenter clinical study to assess the safety and efficacy of ADRC-enriched autologous fat grafts in the treatment of early-stage AA.

71 male and female subjects diagnosed with early-stage AA (Norwood-Hamilton and Ludwig scales) randomized to 4 treatment groups:
Group 1: Puregraft fat + 1.0 x 106 ADRC/cm2 scalp; n = 16
Group 2: Puregraft fat + 0.5 x 106 ADRC/cm2 scalp; n = 22
Group 3: Puregraft fat alone; n = 24
Group 4: Saline (Control); n = 9

Lipoaspirate was harvested from subjects and ADRCs isolated with Kerastem technology. Cell count was measured prior to injection, and fat grafts prepared using Puregraft. Subjects received treatments to 40cm2 of the scalp including Puregraft (0.1ml/cm2) and pre-determined dose of ADRCs. Controls received saline injections. Hair shaft width, endpoint data and terminal hair counts were taken at baseline, 6, 24, and 52 weeks from a standardized system of global and macro scalp photographs.

71 subjects completed the trial. No unforeseen adverse events were documented. A statistically significant increase in terminal hair count ($p=0.013$) was observed in Puregraft + Low Dose ADRCs group compared to Control at 24 weeks in males with early stage loss (n=22), representing an average increase of 17 terminal hairs/cm2. The Puregraft + Low Dose ADRCs group also exhibited a trend toward increased hair width ($p=0.065$) compared to Control in this same group.

The hypothesis that early AA can be treated by restoring adipocytes and ADRCs to the follicular niche is clearly supported by this trial. Puregraft + Low Dose ADRCs for the treatment of early-stage AA showed statistically significant increase ($p=0.013$) in terminal hairs at week 24. Further research using a protocol such as represented by STYLE is expected to reveal a dose-response curve for ADRC fat grafting for AA.

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SVF TO TREAT OSTEOARTHRITIS: A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED, DOSE-ESCALATED, MULTI-SITE, PARALLEL GROUP CLINICAL EVALUATION

Presenter: William Cimino, PhD (USA)
Affiliation: The GID Group
Author: Cimino W

Background: Stromal vascular fraction progenitor cells have significant potential for therapy of degenerative diseases of the stromal and vascular tissues, such as osteoarthritis. This clinical trial evaluated use of autologous SVF cells generated at point-of-care for treatment of osteoarthritis of the knee. This clinical trial was conducted under an IDE approval by the FDA, and an IRB approval at each of the study sites. Level of evidence: 1.

Methods: Stromal vascular fraction cells were extracted at point-of-care from freshly harvested adipose tissue using GID SVF technology. 39 subjects in 3 groups of 13 received placebo, 15 million SVF cells, or 30 million SVF cells in one osteoarthritic knee with KL score II or III. Subjects completed WOMAC analysis of pain at baseline, 3 months, 6 months, with additional follow-up at 1 and 2 years. Safety and efficacy evaluation was completed at 6 months. The SVF was characterized acutely with yield, viability, gram contamination, and endotoxin level. SVF was further characterized in a laboratory using CFU analysis, flow cytometry, cultured sterility, residual collagenase, and cytokine/growth factor analysis.

Results: No significant adverse events were reported. Evaluation of efficacy showed that the active treatment groups improvement was statistically significant relative to the placebo group. Evaluation of effect size and confidence intervals showed that that active treatment groups were statistically superior to the placebo group. The MCID for the study was 33% change from baseline. Both active treatment groups were superior to the MCID while the placebo group was inferior to the MCID.

Conclusions: Use of SVF to treat pain due to osteoarthritis of the knee has been shown to be a clinically effective therapy. This study demonstrated statistically and clinically significant reductions of pain at 6 months. Evaluation of 1-year results showed continued improvement relative to 6-month results for both active treatment groups, with the higher dose showing a more significant improvement.

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STEM CELL THERAPY ENRICHED FAT GRAFTING FOR THE RECONSTRUCTION OF CRANIOFACIAL DEFICITS

Presenter: Isaac James, MD (USA)
Affiliation: University of Pittsburgh Medical Center
Authors: Bourne D, Egro FM, Bliley J, James IB, Haas GL, Meyer EM, Donnenberg A, Donnenberg V, Branstetter B, Marra K, Coleman S, Rubin JP

Purpose: Fat grafting is an effective treatment for craniofacial deformities. Stromal vascular fraction (SVF) is a concentrated form of adipose derived stem cells (ASC) that can be isolated from fat through collagenase based procedures. The aim of this clinical trial is to assess the impact of SVF enrichment on craniofacial fat grafting.

Methods: This IRB-approved prospective cohort study was funded by the Department of Defense. Twelve subjects with at least two regions of craniofacial volume deficit were enrolled and underwent fat grafting with SVF-enriched or standard fat grafting to each area. All patients had bilateral malar regions injected with SVF-enriched graft on one side and control standard fat grafting to the contralateral side. Outcome assessments included: 1) demographic information; 2) volume retention determined by CT scans; 3) SVF cell populations assessed by flow cytometry; 4) cell viability; 5) SVF cell yield; and, 6) adverse events. Follow-up was nine months.

Results: All patients had subjective improvement in appearance (Figure 1). There were no serious adverse events. Surgery lasted 253.8±40.3 minutes and SVF processing took 99.8±14.2 minutes. The mean volume grafted was 153.3±113.9mL. Overall volume retention was 54.2±19.0% at nine months. There was no significant difference in volume retention between the SVF-enriched and control regions overall (50.3% vs 57.3%, p=0.269) or comparing malar regions (51.4% vs 56.7%, p=0.494). Patient age, obesity, and smoking status did not impact volume retention. Cell viability was 77.4±7.3%. Cell yield was 5.1x105±3.4x105 cells per gram of fat. Cellular subpopulations were 60.1±11.2% ASCs, 12.2±7.0% endothelial cells, and 9.2±4.4% pericytes. There was no significant correlation between cell viability, yield or subpopulations and volume retention.

Conclusions: Autologous fat transfer for reconstruction of craniofacial defects is effective and safe. SVF enrichment does not significantly impact volume retention.

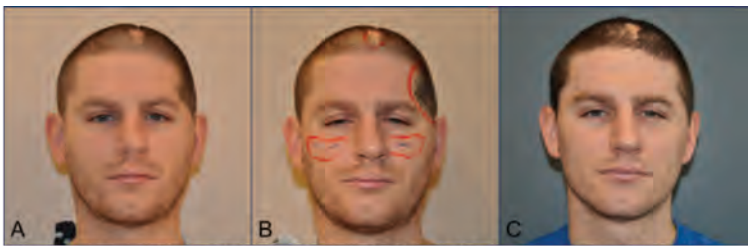

Figure 1. 25 year old man who suffered from a blast injury while serving in Iraq requiring left craniotomy. **A)** Preoperative appearance. Note soft tissue deficits most pronounced in the left temple. **B)** Soft tissue deficits are marked and numbered in order following a clockwise pattern. Either even or odd numbers are assigned enrichment with stromal vascular fraction at random. Malar regions serve as a control as one side is enriched and the other is treated with standard fat grafting. **C)** Postoperative appearance. Note improvement in the left temple hollowing as well as other regions of volume enhancement.

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A PROSPECTIVE, PILOT STUDY EVALUATING AMNIOTIC MEMBRANE AND UMBILICAL CORD PARTICULATE IN REDUCING PAIN ASSOCIATED WITH KNEE OSTEOARTHRITIS

Presenter: Ramon Castellanos, MD (USA)
Affiliation: Castellanos and Associates
Author: Castellanos R

NOT PRESENTED

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COMBINED 3D BIOPRINTING OF SKIN AND ADIPOSE TISSUE AS A PROMISING APPROACH FOR NIPPLE AREOLA COMPLEX AND BREAST VOLUME RECONSTRUCTION

Presenter: Luciano Vidal, MD (France)
Affiliation: Labskin Creations
Authors: Vidal L, Heraud S, Albouy M, Durand C, Thepot A, Dos Santos M, Marquette C

In the past few decades, breast reconstruction became an important component of breast cancer treatment due to the combined effect of its high prevalence and the significant improvements in patient survival. Current options for breast volume and nipple areola complex reconstruction post-mastectomy are based on different surgical procedures such as autologous skin and adipose tissue flaps, lipofilling or implant based. However, these conventional reconstructive techniques have inconsistent long-term outcomes regarding maintenance of the shape and projection over time. To overcome these limitations, novel regenerative medicine technology based on three-dimensional bioprinting approach, which combines advanced tissue engineering with 3D printing platform, provides a potential solution for unmet clinical needs in breast reconstruction. Our laboratory developed a 3D bioprinting approach to accurately deposit cells and biomaterials into precise geometries with the goal of creating anatomically correct biological vascularized adipose tissue and NAC constructs for breast reconstruction. Human fibroblasts, keratinocytes, and adipose derived stem cells combined with human microvascular endothelial cells were printed in a bioink composed of 3 biopolymers with optimal printing conditions. Histological characterisation of the 3D bioprinted adipose tissue showed adipocytes cells forming droplets and capillary-like structures homogeneously distributed within the tissue. Nil red staining highlighted the formation of large lipid droplets-containing cells. Immunostaining analysis confirmed mature adipose tissue markers expression such as FABP4 and perilipin-1 on the surface of lipid droplets. The bioprinted adipose tissue released adipose tissue-specific adipocytokines, leptin and adiponectin, demonstrating the functionality of the bioprinted tissue. The 3D bioprinted skin was morphologically and biologically representative of the normal human skin. The printed dermis presented a microvascular network expressing CD31 and supported epidermal formation to produce a full thickness, well-organ and terminally differentiated epidermis. This work paths the way to the promising development of autologous vascularised adipose tissue and skin for personalized breast volume and NAC reconstruction.

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A NOVEL POINT OF CARE, AUTOMATED, AND CLOSED SYSTEM FOR PROCESSING STROMAL VASCULAR FRACTION EITHER WITH OR WITHOUT COLLAGENASE

Presenter: Todd Malan, MD (USA)
Affiliation: Roxbury Regenerative
Author: Malan T

Stromal Vascular Fraction (SVF) is a component of lipoaspirate that can serve as a rich source of multipotent elements with phenotypic and gene expression profiles similar to human Mesenchymal stem cells (hMSCs) and Pericytes. SVF enriched fat grafts have demonstrated improved survival as compared to native fat as well as significant wound and scar healing properties.

Currently a reliable, automated, and entirely closed point of care system for SVF processing technique does not exist.

Here, we present the Q-Graft device from HumanMed AG.

The Q-Graft is an entirely closed and sterile point of care automated SVF processing device that can be used either with or without collagenase digestion. Adipose tissue is harvested directly into the device which is placed within the sterile OR field. The device then automates the incubation, filtration, washing, and suspension of the SVF pellet.

We will present pre-clinical data gathered in our testing of the Q-Graft device to identify the cellular characterization of SVF product, growth kinetics and self-renewal assay, differentiation potential, ability to maintain sterility, and measures of residual collagenase. Comparisons will also be made in using the device either with or without collagenase.

An evaluation as to the feasibility of direct point of care use of the Q-Graft device as an alternative to currently available manual and automated processing techniques will also be discussed.

In addition we will review data for the first 50 patients treated outside the US for an indication of Osteoarthritis.

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THE EFFECT OF STROMAL VASCULAR FRACTION ON SCAR FORMATION OF TRAM FLAP DONOR SITE

Presenter: Joseph K. Park, MD (South Korea)
Affiliation: Seoul National University Hospital
Authors: Park JK, Jin US

Introduction: A long donor site scar is inevitable in breast reconstruction with free transverse rectus abdominis myocutaneous (TRAM) flap. Several studies have shown that many patients are unsatisfied with the appearance of their abdomen after the surgeries, and scar formation contributes greatly to their dissatisfaction. Mesenchymal stromal cells are known to participate in wound healing by reducing inflammation and suppressing fibrosis, thereby potentially reducing scar formation. In this study, stromal vascular fraction (SVF), which contains mesenchymal stromal cells, are harvested from remnant tissue of elevated TRAM flap and injected along the abdominal wound to evaluate the effect of SVF on scar formation.

Method: Thirty patients undergoing breast reconstruction with free TRAM flap by a single surgeon were enrolled. Patients were randomly selected into two groups and a half-side test was conducted on the incisional scar. In the first group, SVF was injected to the right half of the abdomen while normal saline was injected to the left; in the second group, the injection sides were reversed. Scar is evaluated using 3D imaging, Vancouver Scar Scale, PSAQ, and immunohistochemical analysis at 1month, 4~6 months, and 12 months after the operation.

Results/Conclusion: All patients have undergone their reconstructive surgery. Some patients have yet to undergone their scar evaluation at 12 months postoperative follow-up, and data collection is to be completed in Q3 of 2018. As a prospective, randomized controlled trial, this study hopes to evaluate to effect of SVF on scar formation.

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USE OF AUTOLOGOUS FAT GRAFTING TO TREAT BURN, TRAUMATIC, AND SURGICAL SCARS: ISSUES AND OUR COUNTERMEASURES

Presenter: Hongwei Liu, MD, PhD (China)
Affiliation: The First Affiliated Hospital of Jinan University
Author: Liu H

NOT PRESENTED

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ADIPOSE TISSUE DERIVED PERIVASCULAR VESICULAR SECRETOME INCITES BONE REPAIR

Presenter: Aaron W. James, MD, PhD (USA)
Affiliation: Johns Hopkins University
Authors: Xu J, Meyers C, Wang Y, Chang L, Peault B, James AW

Adipose tissue resident human perivascular stem/stromal cells (PSC) are known to incite bone defect healing, predominantly via paracrine means. Here, we detail how extracellular vesicles obtained from the perivasculature incite bone healing. Human white adipose tissue was FACS processed using established protocols to isolate PSC, including CD146+CD34-CD45-CD31- pericytes and CD34+C146-CD45-CD31- adventitial cells. PSC were first examined in non-contact co-culture with human BMSC. Next, PSC derived extracellular vesicles (PSC-EV) were obtained by ultracentrifugation. Validation was performed based on ISEV minimal experimental requirements, including Western blot, size analysis, and electron microscopy. The effects of PSC-EV were either examined in vitro, or in vivo in a mouse calvarial defect. For in vitro studies, BMSC proliferation, migration and osteogenic differentiation were assessed. Clariom D microarray examined the BMSC transcriptome before and after PSC-EV treatment. For in vivo studies, PSC-EV were applied by injection to mouse calvarial bone defects, and healing was assessed by microCT and histology. Results showed that human PSC induced significant changes in BMSC behavior in non-contact co-culture, including an increase in proliferation, migration, and osteodifferentiation. These in vitro effects were accompanied by release of fluorescently labelled extracellular vesicles (PSC-EV), which fused with recipient cells. These findings were replicated by addition of PSC-EV to BMSC cultures. Depletion of surface-associated proteins on EVs, or neutralizing antibodies to CD9 and CD81, reversed these effects. Transcriptomic analysis of PSC-EV treated BMSC demonstrated a robust change in key signaling pathways, as observed by principal component analysis and ingenuity pathway analysis. When applied to a calvarial defect model, PSC-EV led to a marked increase in bone healing overtime, accompanied by increased progenitor proliferation, migration, and osteogenic differentiation. Our data suggest that adipose tissue PSC derived extracellular vesicles (PSC-EV) retain the osteoinductive effects of their parent cell, and could be used as an 'off the shelf' therapy for bone defect repair.

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CELL-FREE ADIPOSE TISSUE REGENERATION BASED ON EXOSOME-LIKE VESICLES DERIVED FROM ADIPOSE TISSUE

Presenter: Mei Yu, PhD (China)
Affiliation: Sichuan University
Authors: Yu M, Dong J, Zhang Y, Dai MJ, Tian WD

Introduction: Previous results have shown that adipose tissue extract (ATE) promote adipogenesis and angiogenesis in vivo without the need of additional growth factors. In this study, we investigated whether exosome-like vesicles derived from adipose tissue (ELV-AT) could act as a bioactive component of ATE to direct cell differentiation and trigger adipose tissue regeneration.

Method: ELV-AT were isolated from ATE and characterized by transmission electron microscopy, NanoSight technology and presence of exosome specific marker. To assess the regenerative potential of ELV-AT, Matrigel-filled chambers containing ELV-AT were placed subcutaneously on the back of Nude mice and SD rat. At different time points post-transplantation, Nude mice and SD rat were killed and implanted chambers were harvested for morphometric, histologic, and immune-histochemical analysis.

Results: The internalization of ELV-AT into adipose tissue-derived stem cells (ADSCs) enhanced the proliferation and adipogenic differentiation of ADSCs. ELV-AT could also significantly enhance endothelial cells' proliferation, migration, and angiogenic tubule formation. In vivo adipose neotissue formation, neovascularization, and volume stability were evaluated over a period of 12 weeks. The results showed that ELV-AT facilitated the infiltration of host cell into chamber area, reduced the thickness of capsule, significantly enhanced the formation of vessels and neo-adipose tissues.

Conclusions: Our findings indicated that ELV-AT could provide an appropriate microenvironment to recruit host cell and induce adipose tissue regeneration effectively.

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MOLECULAR EVALUATION OF PURIFIED INSULIN PRODUCING BETA CELLS FROM ADIPOSE DERIVED STEM CELLS

Presenter: Srinivas Koduru, PhD (USA)
Affiliation: Pennsylvania State University
Authors: Koduru S, Leberfinger AN, Ozbolat IT, Ravnic DJ

Introduction: Type 1 diabetes (T1D) affects over one million people in the United States. It results from autoimmune destruction of pancreatic beta cells leading to lack of insulin production. Treatment requires daily insulin injections, which can be cumbersome for patients. Therefore, a cellular replacement strategy would be welcomed. Recently, we have demonstrated the potential of adipose derived stem cells (ADSCs) for beta cell replacement. However, their molecular profile is unknown. We hypothesize that ADSC-beta cells will demonstrate a similar molecular signature to native human beta cells.

Methods: Abdominal adipose tissue was obtained from patients (n>15) undergoing lipectomy. Following digestion, the stromal vascular fraction was obtained. CD90+ cells were isolated by microbeads and subsequently underwent in vitro differentiation. ADSC-beta cells were evaluated for insulin and c-peptide expression using single cell Imagestream and multi-color flow cytometry. Comprehensive molecular evaluation of sorted cells was performed by RNA sequencing and validated by 3D digital PCR. RNA sequencing data of native human beta cells was obtained from publically available sources and used for comparison.

Results: RNA-seq and 3D dPCR confirmed the presence of insulin transcripts in ADSC-beta cells when compared to undifferentiated ADSCs. Further investigation revealed similar signaling pathways to those commonly seen in native beta cells. We observed the presence of markers such as INS, IGF2, IGF1, ISL1, MAF, SH2B1, and Sox9. RNA-seq data was validated by dPCR documented upregulation of INS, ISL and Sox9 in ADSC-beta cells. The molecular validity was confirmed by the presence of both insulin and c-peptide on multicolor flow cytometry and single cell immunofluorescence.

Conclusion: ADSC-beta cells would represent a significant breakthrough in the management of patients afflicted with T1D. Our results suggest that purified insulin producing ADSC-beta cells exhibit a similar molecular signature to native human beta cells. Further molecular evaluation can enhance the development of ADSC-based cellular replacement therapies.

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IMPACT OF THE BONE MATRISOME ON THE ASCS FUNCTION FOR BONE-TISSUE ENGINEERING

Presenter: Sophie Veriter, PhD (Belgium)
Affiliation: Novadip Biosciences
Authors: Veriter S, Mazzucchelli G, LeBrun V, Adnet PY, Cathy C, Dufrane D

Bone allograft remains a suitable and competitive scaffold to vehicle adipose stem cells (ASCs) and to improve the cellular homing and survival rate for bone tissue engineering. This study investigated the impact of the bone proteins content on the osteogenicity and angiogenicity of ASCs.

Both mineralized and demineralized (HCl treatment for 12 hours) bone allografts were firstly studied in terms of (i) growth factors content (ELISA for VEGF, SDF-1α, IGF-1, osteoprotegerin(OPG), BMP-7) and (ii) matrisome analysis (by ELISA and LC-ESI-MS/MS) in view to be compare to a classical bone substitute as HA/bTCP (65/35%). Human ASCs were then seeded on each scaffold to assess (i) the graft colonization (after 15 days of incubation) by scanning electron microscopy (SEM), histology, DNA quantification and (ii) the ASCs function for genes expression (qRT-PCR for skeletal genes development) and osteogenic/angiogenic growth factors (content/secretion of VEGF, SDF1a, IGF1, OPG).

The bone demineralization revealed a significant increase of VEGF, IGF1 and OPG contents ($p \leq 0.05$) and significantly affected the matrisome by the loss of 107 proteins (exclusively found in the mineralized bone). Indeed, the structural proteins (extracellular matrix, collagen) were over-expressed in mineralized bone and specific pathways as the response to stress proteins and the PI3K-Akt signaling pathway–related proteins were mainly identified in the mineralized bone. HA/bTCP substitute did not revealed any content of structural/function proteins. At the molecular level, the skeletal development of ASCs was not impacted by the ASC's adhesion on both de-/mineralized bones versus HA/bTCP substitutes. A better ASCs' adhesion (by DNA quantification) and spreading (by SEM) was demonstrated on demineralized bones while a significant loss of VEGF/IGF-1 and increase of SDF-1α contents was found in ASCs seeded on bone demineralized allograft. A very low level of growth factors content was found for ASCs seeded on HA/bTCP blocks.

In conclusion, the protein composition of the bone substitute affects significantly the ASCs function and modulates the specific bioactivity of a bone-tissue engineered product.

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ADIPOSE STEM CELL CROSSTALK WITH CHEMO-RESIDUAL BREAST CANCER CELLS: IMPLICATIONS FOR TUMOR RECURRENCE

Presenter: Matthew A. Lyes, BS (USA)
Affiliation: Duke University
Authors: Lyes MA, Payne S, Ferrell P, Pizzo SV, Hollenbeck ST, Bachelder RE

NOT PRESENTED

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IMMUNOSUPPRESSIVE EFFECTS OF ADIPOSE TISSUE-DERIVED MESENCHYMAL STEM CELL (ASCS) ON MACROPHAGE-INDUCED IMMUNE REACTIONS THROUGH PROSTAGLANDIN E2

Presenter: Jiye Kim, MD, PhD (South Korea)
Affiliation: Yonsei University Wonju
Authors: Kim J, Eom YW, Kim SW, Chung YK

Introduction: Suppression or regulation of inflammation is very important in treatment of autoimmune disease or intractable chronic wound. Mesenchymal stem cells (MSCs) have been highlighted as new candidates for treating various inflammatory diseases based on their immunomodulatory properties. In this study, we investigated the anti-inflammatory mechanisms and therapeutic effects of adipose tissue-derived MSCs (ASCs) using THP-1 macrophages.

Method: ASCs was isolated and cultured from aspirated fat of healthy donor. Macrophage differentiation of THP-1 was co-cultured with or without ASCs in transwell plate. To analyze inflammatory cytokines or PGE2, conditioned medium was collected, filtered (0.45um), and stored at -80°C until needed.

Result:

- LPS increased the expression of CD11b, a marker of M1 macrophage, in THP-1 macrophages, but the expression of CD206, CD68, CCL18, Legumain, and IL-10 (M2 markers) was increased in THP-1 macrphages co-cultured with ASCs. This result suggested that ASCs induce M1 to M2 transition of macrophages. (Fig. 1)
- LPS expressed Cox-2, IL-1B, IL-8, TNF-A in PMA-treated THP-1 cells. However, the expression of inflammatory cytokine's mRNAs such as IL-1B and TNF-A was not decreased significantly. (Fig. 2)
- ASCs have immunosuppressive effects through inhibiting the secretion of inflammatory cytokines (i.e. IL-1B and IL-18) and that PGE2 can regulate this process. (Fig. 3)
- PGE2 play inhibitory role in inflammasome formation leading to suppress inflammatory cytokines (i.e. IL-1B and IL-18) activation. Analysis of immune modulation of ASCs in condition of co-culture with macrophage. (Fig. 4)

Conclusion: ASCs have been shown to modulate the inflammatory response of macrophages by transferring M1 to M2. Expression of M2 markers and PGE2 was markedly increased, but activated IL-1β and IL-18 was dramatically decreased in THP-1 co-cultured with ASCs. Our results suggest that ASCs can suppress the inflammatory response by controlling the M1/M2 transition and inflammasome formation through PGE2 in THP-1 macrophages. Therefore, PGE2 or ASC therapy is expected to be useful for the treatment of inflammatory diseases through regulation of macrophage activity.

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IMMUNOSUPPRESSIVE EFFECTS OF ADIPOSE TISSUE-DERIVED MESENCHYMAL STEM CELL (ASCS) ON MACROPHAGE-INDUCED IMMUNE REACTIONS THROUGH PROSTAGLANDIN E2

Presenter: Jiye Kim, MD, PhD (South Korea)
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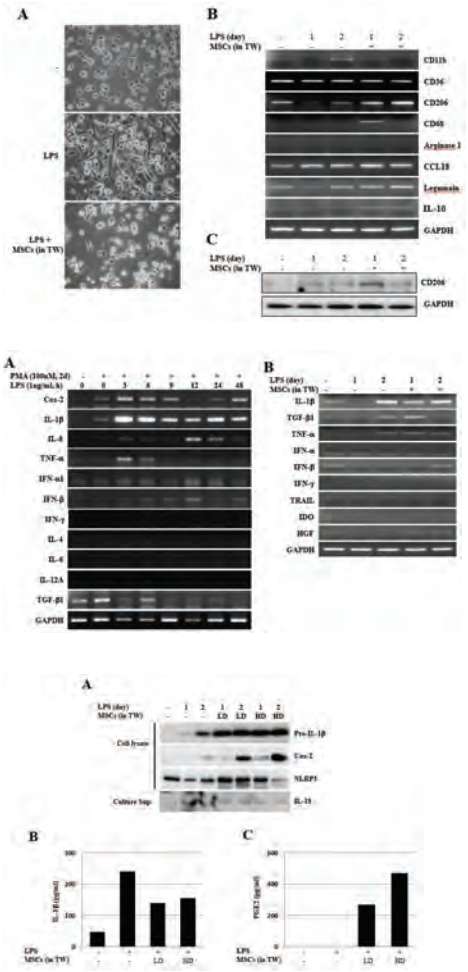


23

FAT GRAFTING PROMOTES DERMAL REJUVENATION IN PATIENTS WITH FAT PAD ATROPHY OF THE HEEL: DATA FROM A RANDOMIZED CONTROLLED CLINICAL TRIAL

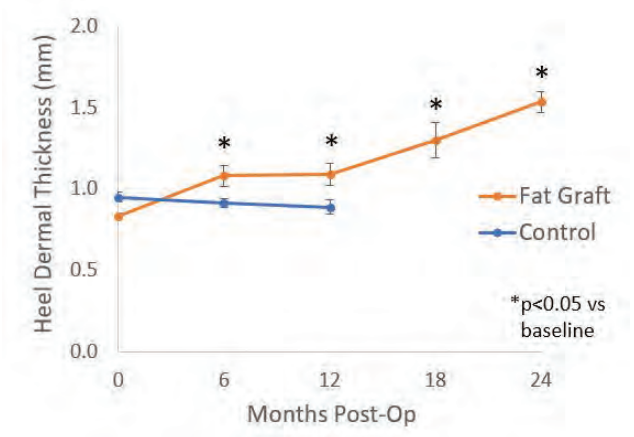
Presenter: Isaac James, MD (USA)
Affiliation: University of Pittsburgh
Authors: James I, Gusenoff BR, Wang S, Dibernardo G, Minteer DM, Gusenoff JA

Background: The shock absorbing soft tissues of the heel are composed of dermis and two specialized fat pads–a thin, superficial microchamber (MIC), and a thicker, deep macrochamber (MAC). Atrophy of these soft tissues is common and can be painful and debilitating. In our previous work, fat grafting to the MAC improved patient-reported pain scores at 1-year, despite loss of most of the initial increase in MAC thickness. Fat grafts have been shown to have remarkable regenerative properties, and our work in the forefoot has shown long term improvements in dermal thickness. In this study, we investigate the impact of autologous fat grafting to the heel on the overlying dermis.

Methods: Fat was harvested from the abdomen using manual liposuction then processed and injected by Coleman technique into the MAC of 7 patients (10 feet) with an average volume of 6.9cc grafted per heel. Patients were offloaded for 4wks post-operatively using a customized Darco shoe. Ultrasound-measured tissue thickness and Manchester Foot Pain and Disability Index (MFPDI) were obtained pre-operatively and followed for 1 year post-operatively with a subset of patients following up for up to 2 years post-operative. Outcomes were compared against 6 randomly selected control patients (8 feet) who received standard-of-care offloading only.

Results: Average age was 56. Average BMI was 30. 50% of patients were female. No patients were active smokers or diabetic. Average baseline dermal thickness in the affected foot was 0.875mm, which is much thinner than what has been reported in the general population. Subjects receiving fat grafting had significantly increased dermal thickness beginning at 6 months ($p=0.019$) which continued to trend upward at 18 and 24 months (Figure 1). This change was also significant when compared to controls ($p<0.05$), who saw no change in dermal thickness over the course of the study. Improvement in dermal thickness was also correlated to reductions in patient reported pain scores (Spearman's rho= -0.659, $p=0.038$).

Conclusion: Our data suggest that fat grafting of the heel helps to rejuvenate the overlying dermis. These changes are also correlated to improvements seen in patient-reported pain scores.



24

AUTOLOGOUS TRANSPLANT FOR FACE AND BODY PRESERVING ADCS: CHEMICAL TO MECHANICAL DISSOCIATION SINCE 2006. A LONG-TERM REVIEW

Presenter: Hebert T. Lamblet, MD (Brazil)
Affiliation: UNIFESP
Author: Lamblet HT

Goal/Purpose: Besides the fact that fat grafting gained popularity, isolation of ADCs (Adipose Derived Cells) and fat tissue manipulation still remains controversial. In 2001, a putative Stem cell population was isolated within the adipose stromal compartment. Since then, many studies exhibited and confirmed the abundance of adult mesenchymal cells, endothelial progenitor cells and growth factor-producing cells derived from fat tissue. Isolation of those cells, its activation and their immediate use for fat transplant still remain a challenge. The purpose of this study is to show our evolution from chemical to mechanical dissociation of those cells from the fat tissue stroma since 2002.

Methods/Technique: Adipose tissue is collected from the abdomen of patients undergoing liposuction. The fat is harvested and processed using two selective methods. Chemical: Half of the collected fat is left to decant, the other half is submitted to the collagenase isolation method. The stromal vascular fraction is centrifuge and the infranated pellet is added to the fresh fat tissue. Mechanical: After the washing process with saline solution, a collagenase free Mechanical shear Force maneuver is made, generating a gradient force that detaches the adcs from the fat tissue stroma. The presence of mesenchymal stem cells isolated in the pellet was confirmed by Indirect Immunofluorescence and Flow Cytometer analysis in a selective sample data in both methods.

Results/Complications: From February 2002 to October 2017, 667 patients benefited from autologous fat transplant preserving ADCs. The first 72 patients with Chemical Dissociation, from 2002 to 2006, and 595 patients, from 2006 to 2017, with Mechanical Dissociation. The donor site was the abdomen. An average of 40 to 50 millions of mesenchymal stem cells/100ml of processed lipoaspirate was isolated with the Mechanical method.

Conclusion: Up to now, adipose-derived cells isolation and fat tissue manipulation was mainly be done in the lab or using expensive processing machines and collagenase. The mechanical method has shown to be reproducible is collagenase free and have been used since 2006 in a long-term evaluation.

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CLASSIFICATION AND SAFETY OF FAT GRAFTING BY AMOUNT AND LOCATION

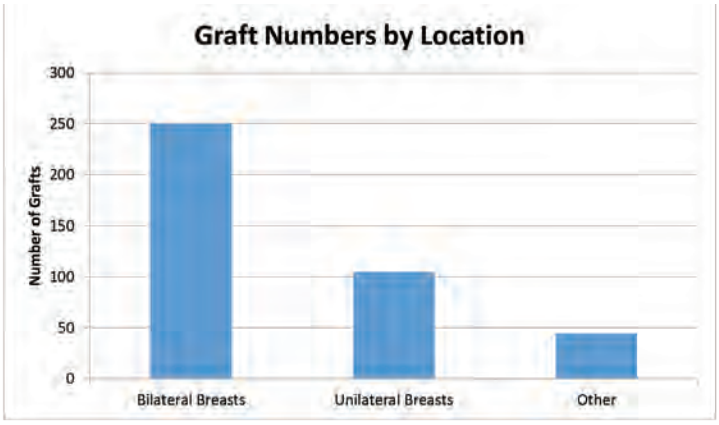
Presenter: Sherry Collawn, MD, PhD (USA)
Affiliation: UAB
Authors: Collawn S, Boyd CJ

Introduction: Fat grafting is a popular volumizing agent in the face, breasts, and other tissue deficient areas in the body. Fat grafting has been used for volume replacement in the face and breasts and in our series has shown improved results. Patients undergoing removal of breast implants with fat grafting replacement have also had successful results and none of the patients have requested a second session for breast enhancement. In our patient series there have been no complications such as infection, skin loss, paresthesias, vascular compromise, embolization or blindness.

Methods: A total of 534 patients have had fat grafting of the face and body from January 2015 through July 2018. Of these, 399 patients had completely documented records of the fat graft recipient site, donor site, and amount grafted available to our investigators. Fat harvest is generally from the abdomen, thighs, and flanks using toomey syringes or an enclosed power-assisted system with 3.7 or 3.0mm cannulas.

Results: The average amount of fat grafted for all grafts was 125.5 ml. 250 (62.7%) of the grafts involved the bilateral breasts, while 105 (26.3%) of the grafts involved a unilateral breast. There was an average amount of 126.4 ml of fat grafted in procedures involving the breasts. The remaining 44 (11.0%) fat grafts did not involve a breast. Of the grafts that did not involve the breasts, 27 (61.4%) of those were solely to the face or temporal region for which the average amount of fat grafted was 15.9 ml. Of the total 399 fat grafts studied, only 22 (5.51%) of all procedures involved fat grafts to multiple sites.

Conclusions: Fat grafting is a safe and reliable method for volumization. In this series there has been no infection or occurrence of embolization.



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BREAST SHAPE CHANGE FOLLOWING AUTOLOGOUS FAT GRAFTING: POTENTIAL OF 3D SURFACE IMAGING FOR QUANTITATIVE ANALYSIS

Presenter: Summer E. Hanson, MD, PhD (USA)
Affiliation: The University of Texas MD Anderson Cancer Center
Authors: Hanson SE, Cheong AL, Reece G, Markey MK, Merchant F

Introduction: Autologous fat grafting (AFG) following breast cancer treatment is increasingly used to address asymmetry and contour irregularities. Despite the increase in procedural volume, graft retention and predictability are highly variable in AFG. Furthermore, there are no well-established quantitative tools to accurately measure longitudinal change in breast volume and shape following AFG.

Methods: Quantitative analysis was performed before and after AFG as an adjunct to implant-based breast reconstruction in two participants. Three-dimensional surface torso images were captured using a stereo-photogrammetric imaging system (3dMDTorso, 3dMD Inc., Atlanta, GA). Surface Gaussian curvature was computed and changes as a result of AFG were analyzed using the curvature difference image. The difference image was normalized such that intensity values from 0 to 255 represent changes in the surface curvature, with no change shown in black (0), and maximal change shown in white (255).

Results: As demonstrated below, breast volume can be measured and the normalized difference in the Gaussian curvature between the before and after fat grafting images can be used to visualize changes in breast shape due to fat grafting. Differences in the surface curvature (white) can be seen in the fat graft area (delineated by red outlines).

Conclusions: Gaussian curvature analysis revealed changes in breast shape in the regions that were fat grafted. Changes were also seen in other parts of the breast (e.g. IMF, nipple) due to factors, such as breathing and posture differences. As opposed to measuring the entire breast mound volume, future analysis can also restrict quantitative measurements to the specific regions of the breast that are fat grafted to monitor changes in breast shape and rates of graft resorption. Further analysis will advance our understanding of breast shape and volume changes with the goal of improving predictability and outcomes of fat grafting in breast reconstruction.

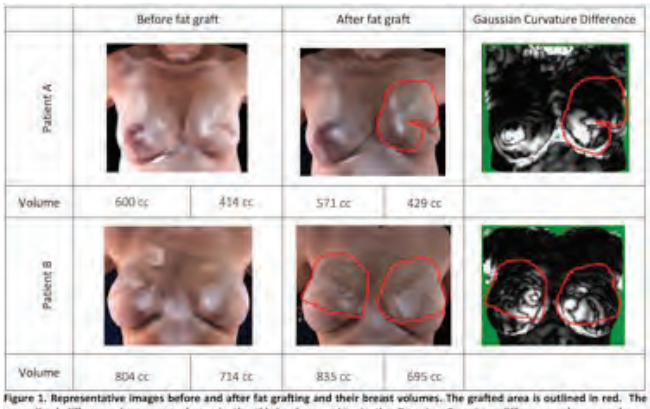

Figure 1. Representative images before and after fat grafting and their breast volumes. The grafted area is outlined in red. The normalized difference images are shown in the third column, wherein the Gaussian Curvature difference values are shown overlaid on the after images. White areas represent high discrepancies in the Gaussian curvature between the before and after images, whereas the gray shades represent smaller differences.

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LIPID CHANGES IN PATIENTS SUBMITTED TO CLASICAL AND RADIOFREQUENCY ASSISTED LIPOSUCTION (RFAL)

Presenter: Dusan Pravica, MD (Serbia)
Affiliation: Colic Hospital
Authors: Pravica D, Andjelkov K

NOT PRESENTED

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COMPARISON OF EARLY POST OPERATIVE TRIGLYCERIDES LEVELS IN PATIENTS SUBMITTED TO LIPOSUCTION AND LIPOSUCTION WITH FAT GRAFTING

Presenter: Katarina Andjelkov, MD PhD (Serbia)
Affiliation: BelPrime Clinic Belgrade Serbia
Authors: Andjelkov K, Pravica D

Introduction: Several previously published studies examined changes in lipid levels and showed no immediate significant changes after liposuction. [1] In a light of increased concerns of safety of fat grafting and standardization of fat grafts, we tried to determine if there were increased triglycerides levels when fat grafting was associated to liposuction.

Methods: We hypothesized that circulating TG concentrations would worsen following fat grafting. We studied 55 patients (7 male and 48 female) seeking liposuction and fat grafting. We performed prospective study that included two groups of patients: The control group (30 patients) was submitted to liposuction only while the study group (25 patients) had additional fat grafting. All patients were healthy individuals with normal preoperative levels of triglycerides, non-obese (BMI<30 kg/m2), sedentary to moderate physically active (exercise up to 2h/week), weight stable and not using lipid-lowering medication. Prior to enrollment each patient provided signed consent form. Liposuction treatment areas were, depending on patients' request: abdomen, flanks, male chest, back, thighs, knees and upper arms. Fat grafts were washed and left to sedimentation. The excess fluids and oils were discharged prior to grafting. Fat grafted areas were: breasts, buttock and calves. Preoperative fasting blood tests were taken immediately before the surgery. Follow up fasting blood tests were drawn immediately after the procedure, 24h after and 7 days after. Repeated measures were computed and analyzed. Only patients with all 3 time points were included.

Results: Patient data, clinical signs and blood test data are presented and statistically analyzed. McNemar tests were used to access changes in categorical variables for repeated measures. The chi-squared test of independence was used for other categorical variables. Independent t-test was used to compare means between two different groups, and paired t test were used for repeated measures. A value of $p<0.05$ was considered significant. There were no deep venous thrombosis, no pulmonary emboli and no deaths.

1. Klein S, Fontana L, Young VL, et al. Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. N Engl J Med. 2004;350(25)

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THE FAT IS NOT UNIFORM: SUPERFICIAL FAT PECULIARITY

Presenter: Angelo Trivisonno, MD (Italy)
Affiliation: Sapienza University
Authors: Trivisonno A, Toietta G

Introduction: The fat is not uniform, the shape, size, color, and arrangement of fat lobules are different in different locations. We can distinguish between brown, brite/beige and white. Subcutaneous and visceral. There are differences in relationship to its site (in a study considered three different types: deposit, structural and fibrous), but also in relationship to its profundity. The adipose tissue contains ADSCs that have regenerative and reparative functions. Many efforts have aimed to obtain a better yield of these cells, in minimal manipulation, including the choice of the best harvesting site. The superficial fat is more vascularized, so has more staminality than deeper, as observed in our study. But these ADSCs proliferate faster and present higher differentiation potential. Moreover this superficial fat called dermal white adipose tissue dWAT is considered dermal tissue, different from subcutaneous tissue, and interact with skin stem cells to regenerate the skin, encases mature hair follicles and influences hair growth. It has also role in other processes including protection of skin from bacterial infection, with production of antimicrobial peptide cathelicidin; in thermogenic response to cold stress expand in thickness; is significantly more resistant to apoptosis. These superficial ADSCs have a higher proportion of CD105 positive cells, a marker of skeletal lineage.

Materials and Methods: We have harvested 12 samples of adipose tissue by microcannula in 6 patientes, in superficial and deep layers of adipose tissue. And after culture we observed that the superficial ADSCs proliferate faster than those isolated in deeper layer.

Result: The fat shows morphological and functional differences within the same depot. The superficial fat has more staminality, but also an higher proliferation rate. In fact the more superficial layer of the body are more exposed to traumatism and than to regeneration. Of course in firsth the skin, but after the more external layer of the fat.

Conclusion: The DWAT is a more exposed mechanical stress and stimulated to repair, so is a good source for regenerative purpose. Not only for more yield of ADSCs, but also for the capacity to proliferate faster and greater resistance to apoptosis. These peculiarities contribute

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THE IMPACT OF AGE, SEX AND DIETARY REGIMENT ON THE SKIN WOUND HEALING IN C57BL/6J (B6) MICE

Presenter: Marta M. Kopcewicz, MS (Poland)
Affiliation: Institute of Animal Reproduction and Food Research of PAS
Authors: Kopcewicz MM, Gawronska-Kozak B, Walendzik K, Bukowska J

Age, obesity and diabetes are the main risk factors for impaired skin wound healing. Moreover, elderly male subjects have the highest incidence of chronic non-healing wounds.

Present study were designated to explore the effect of age, sex and dietary regiment on the skin wound healing in C57BL/6J (B6) mice. Young (2 months) and old (18 months) male and female B6 mice that were fed regular chow diet were assigned into separated groups fed for a period of 8 weeks low fat diet (LFD 11kcal% fat) or high fat diet (HFD 58 kcal% fat). HFD males, displayed stable, linear increase in body mass, regardless of age. The increase in body mass for young males was a result of lean and fat mass expansion whereas for old males it was achieved mainly through fat mass gain. The glucose tolerance test (GTT) performed at the end of 8th week showed impaired glucose tolerance for HFD mice. The most severe glucose intolerance was observed for males. Postmortem analysis of histological skin sections demonstrated reduced dermal thickness in old animals, regardless of diet. The diet had the most prominent effect on the hypodermis which was significantly thicker in mice fed HFD.

After 8 weeks of diet, mice were injured with a 4mm biopsy punch. Skin tissues were collected at Day 3, 7, 14 and 21 after wounding. Masson's trichrome stained sections revealed that old, HFD animals displayed greater collagen deposition comparing to LFD. The collagen 1 and 3 mRNA expression levels were significantly higher in unwounded and postwounded tissues of male mice. Moreover, the profile of collagen 1 and 3 mRNA expression differed between sexes during skin healing process: (i) postwounded collagen deposition was delayed in males comparing to females; (ii) collagen 1 and 3 mRNA levels were significantly higher in the skin of females on HFD than on LFD at post-wounded Day7th.

The data revealed that impact of HFD on glucose tolerance, body mass gain an histomorphology of the skin, is more prominent for male than female. However, the differences in skin collagen expression between males and females may suggest diverse mechanisms of healing and dependency on the metabolic status of animals.

Work was supported by the grant of KNOW Consortium ""Healthy Animal - Safe Food"", MS&HE Decision No. 05-1/KNOW2/2015.

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ADIPOSE-DERIVED STEM CELLS PARTIALLY MITIGATE MUSCLE ATROPHY AFTER PERIPHERAL NERVE INJURY IN THE RODENT MODEL

Presenter: Kacey Marra, PhD (USA)
Affiliation: University of Pittsburgh
Authors: Marra K, Schilling B, Schusterman M, Kim D, Repko A, Klett K, Christ G

Introduction: Muscle recovery after long-gap peripheral nerve injury poses an exceptional challenge for regenerative medicine. Nearly $150 billion is spent annually on peripheral nerve injury and its related ailments such as muscular atrophy after denervation. Successful regrowth of the injured nerve does not necessarily lead to regeneration of muscle, especially if combinative therapies addressing both the nerve injury and the muscle atrophy are not used.

Methods: Here, a rodent model for muscle atrophy of the gastrocnemius results from a 1.5cm defect to the sciatic nerve. To address the nerve injury, an autograft was placed into the defect consistent with the standard of care. Additionally, allogeneic rodent adipose-derived stem cells were injected into the gastrocnemius post-operatively in two cohorts, one receiving a single injection, and the other receiving two injections, post-operatively and at three weeks.

Results: At six weeks, the cohorts having received an ASCs injection post-operatively had a higher muscle mass percentage retained, had larger average fiber area, and was shown to have less overall lipid content accumulated throughout the musculature. Additionally, muscles having received ASCs injection showed increased presence of IL-10 (anti-inflammatory cytokine) and Ki67 (cell proliferation marker), with decreased presence of iNOS (pro-inflammatory cytokine).

Conclusion: Collectively this investigation is suggestive that an ASC injection into denervated muscle post-operatively is able to partially mitigate the onset of atrophy as determined by relative muscle mass measurements being corroborated by average fiber area size. Further, IL-10 appear to have greater upregulation in the ASC-injected condition, suggestive of being further in the healing cascade.

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HUMAN ADIPOSE-DERIVED CELL REPAIR IN A MURINE PRESSURE ULCER MODEL

Presenter: Jeffrey M. Gimble, MD, PhD (USA)
Affiliation: LaCell LLC
Authors: Gimble JM, Bukowska J, Kosnik P, Katz A, Gawronska-Kozak B, Mehrara B, Bunnell BA, Alarcon Uquillas A, Frazier T

Introduction: Pressure ulcers occur at high frequency in elderly and bed-ridden patients due, in part, to repetitive cycles of ischemia/reperfusion (IR) that compromise flow within blood vessels and lymphatics, thereby compromising tissue integrity at the levels of the epidermis, dermis, and subcutaneous adipose tissue and skeletal muscle. Current treatment relies primarily on preventive care or surgical debridement and wound vacuums. This study explores the safety and efficacy of adipose-derived cell therapeutics.

Methods: Stromal vascular fraction (SVF) cells were isolated from human lipoaspirates using a closed system device (Icellator, Tissue Genesis, Honolulu HI) and culture expanded to adipose-derived stromal/stem cells (ASC). C57BL/6 mice of both genders were subjected to two consecutive cycles of IR created by 12 hr placement and removal of circular magnets to the dorsal skin. The resulting injuries were injected subcutaneously with PBS solution alone (Control) or containing up to 2 X 106 SVF cells. The rate of wound closure and tissue architecture were monitored over the subsequent 20-day period.

Results: The introduction of human SVF cells accelerated the rate of wound healing in young female mice relative to PBS-treated controls. The wound closure rate in female mice was accelerated compared to male mice. Introduction of SVF cells in male mice did not show the same level of efficacy as seen in female mice.

Conclusions: The immunocompetent mouse displayed utility as a model system for evaluation of human cell therapies in the context of pressure ulcer injury. There are gender-specific differences in the response to adipose-derived cell treatment. This may reflect differences in the tissue architecture between genders since the dermal and epidermal layers are thicker in males as compared to age-matched females of the C57BL/6 background.

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REGENERATION OF FRACTURE TIBIAL BONE OF MICE WITH ALLOGENEIC AND XENOGENEIC MESENCHYMAL STEM CELLS

Presenter: Kamlesh K. Bajwa, M Sc (India)
Affiliation: National Dairy Research Institute
Authors: Bajwa KK, Potliya S, Saini S, Sharma V, Thakur A, Kumar A, Kumar S, Kumar S, Malakar D

NOT PRESENTED

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REGENERATION OF FRACTURE TIBIAL BONE OF MICE WITH ALLOGENEIC AND XENOGENEIC MESENCHYMAL STEM CELLS

Presenter: Kamlesh K. Bajwa, M Sc (India)
Affiliation: National Dairy Research Institute
Authors: Bajwa KK, Potliya S, Saini S, Sharma V, Thakur A, Kumar A, Kumar S, Kumar S, Malakar D

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INFLUENCE OF CONTROLLED PHYSICAL ACTIVITY ON SERUM ADIPOKINES CONCENTRATION IN OBESE TEENAGERS

Presenter: Anna Wasilewska, MD (Poland)
Affiliation: Pediatric Nephrology Department
Authors: Wasilewska A, Protas P, Stelmach M, Rybi-Szumińska A, Taranta-Janusz K, Kuroczycka-Saniutycz E, Lemiesz M

NOT PRESENTED

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HUMAN ADIPOSE-DERIVED STEM CELLS WITH THYMOSIN B4 ENHANCED NEOVASCULARIZATION IN MOUSE ISCHEMIC HIND LIMB MODEL

Presenter: I-Rang Lim (South Korea)
Affiliation: Korea University College of Medicine
Authors: Kim JH, Kim J, Joo H, Hong S

Human adipose-derived stem cells (hASCs) have potential of differentiating into endothelial lineage and are easily obtainable, therefore they are promising candidates for stem cell therapy. Thymosin β4 (Tβ4) is G-actin sequestering protein that exerts a broad range of functions such as cell migration and angiogenesis. In this study, we investigated the effects of Tβ4 on angiogenic and endothelial differentiation potential of hASCs. Exogenous treatment of Tβ4 (100 ng/mL) induced a significant increase in endogenous mRNA expression of Tβ4, and morphological changes with increased cell length in hASCs. In addition, Tβ4-treated hASCs showed significantly higher endothelial differentiation potential than untreated hASCs after the induction of endothelial differentiation for 3 weeks. The expression of endothelial markers such as PDGFRb and CD144 were significantly enhanced by the treatment of Tβ4 with the endothelial differentiation induction media compared to untreated hASCs. Indeed, Tβ4-treated hASCs expressed higher expression of angiogenic genes including Ang-1, vWF, Tie1, CXCR4, uPAR, FGFR4, IGFR2, and VE-Cadherin than untreated hASCs, both cultured in the endothelial differentiation induction media. Moreover, a scratch wound healing assay revealed that the treatment of Tβ4 significantly increased cell migration compared to untreated and Tβ4-siRNA transfected hASCs. In the microbead sprouting assay, the treatment of Tβ4 significantly augmented the number of sprouts per bead and the length of sprouts compared to untreated and Tβ4-siRNA transfected hASCs. Futhermore, transplantation of hASCs with Tβ4 induced neovascularization and significantly improved the blood flow in mouse ischemic hind limb models compared to sham, hASC-transplanted, and Tβ4-transplanted groups. Taken together, therapeutic application of hASCs with Tβ4 could be useful to enhance endothelial differentiation and neovascularization.

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A COMPLEX CO-CULTURE WHITE ADIPOSE TISSUE MODEL

Presenter: Rosalyn D. Abbott, PhD (USA)
Affiliation: Carnegie Mellon University
Authors: Abbott RD, Keyser MN, Debari MK

Introduction: Current progress in targeting drug therapeutics is hindered by the lack of physiologically-relevant human adipose tissue models. Multiple cell types are residents of adipose tissue including adipocytes, preadipocytes, endothelial cells, fibroblasts, and vascular smooth muscle cells. However, current adipose tissue engineered systems generally incorporate only one cell type (differentiated adipoctyes) [1-9] or two (differentiated adipocytes and endothelial cells) [10-12]. Culturing multiple cell types has been suggested as a method to improve the accuracy of tissue engineered systems [13]. Therefore, a tissue engineered system that incorporates all of the cell types in adipose tissue will likely have improved physiological relevance over current systems. Our hypothesis was that integrating multiple cell types, including human primary mature adipocytes and stromal vascular cells (SVF: endothelial cells, pericytes and preadipocytes) in a 3D silk matrix will improve functional readouts (specifically glycerol secretion).

Methods: The tissue engineered systems were prepared as described previously [14]. Silk scaffolds were cut (2mm x 4mm) soaked in lipoaspirate with or without the SVF and cultured in minimally supplemented media (DMEM/F12, 10%FBS, 1X PSF). To quantify lipolysis, glycerol secretion was quantified with an Adipolysis Assay (BioAssay Systems).

Results: Co-cultures were verified with immunohistochemistry indicating endothelial cells (CD31), stem cells (PREF1), and pericytes (αSMA) were maintained [14]. Adipocytes cultured with cells from the SVF displayed enhanced lipolysis from adipocytes cultured alone (Figure 1), suggesting paracrine signaling from different cell types is essential to maintain functionality ex vivo. Ongoing studies are evaluating co-culture effects on other physiologically relevant parameters including: free fatty acid secretion, isoproterenol stimulated lipolysis, and glucose uptake.

Conclusions: Our novel 3D approach establishes that co-culturing adipocytes with the stromal vascular fraction enhances lipolysis, making this methodology useful for developing more physiologically relevant adipose systems ex vivo.

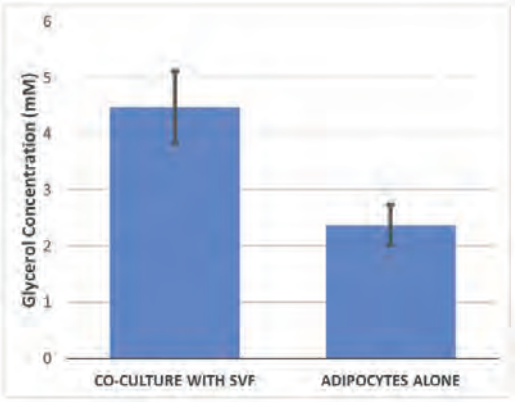

Figure 1. Enhanced glycerol secretion was measured in adipocytes co-cultured with the stromal vascular fraction (SVF) versus adipocytes alone. n=5 samples over 3 days of culture, error bars represent standard error of the mean.

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CD10 IS A PROSPECTIVE MARKER FOR ADIPOCYTE MATURATION OF ADIPOSE-DERIVED STEM CELLS

Presenter: Shigeki Sugii, PhD (Singapore)
Affiliation: Singapore Bioimaging Consortium and Duke NUS Graduate Medical School
Authors: Sugii S, Chakraborty S

It is relatively challenging to find biomarkers for specific human stem cell population that can undergo better differentiation into mature cells upon stimulation. Recently, we identified selective cell surface markers of human adipose-derived stem cells (ASCs) from different fat depots. We identified CD10 as a marker of subcutaneous ASCs, which undergo robust adipogenesis and may account for its better pathophysiological properties. By investigating knock-down and over-expression lines and various human samples, we established an intrinsic CD10 level as a positive determinant of adipocyte quality after differentiation of ASCs. Stem cell CD10 levels also predicted the browning (beiging) differentiation capacity of ASCs. Furthermore, as a proof-of-concept study of CD10 as a prospective marker, we performed high content image-based screening with nuclear receptor ligands library, and identified dexamethasone and retinoic acid as stimulatory and inhibitory adipogenic drugs, respectively. Thus, CD10 is a prospective biomarker for adipocyte maturation of ASCs, which would be useful for convenient drug screening, trilineage differentiation assay and clinical applications.

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EFFECTS OF DIFFERENT STORAGE MEDIA AND TEMPERATURES ON THE VIABILITY OF READY-TO-USE HUMAN ADIPOSE-DERIVED STEM CELLS FOR CLINICAL THERAPY

Presenter: Hongwei Liu, MD, PhD (China)
Affiliation: The First Affiliated Hospital of Jinan University
Authors: Liu H, Wu YD

NOT PRESENTED

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EFFECT OF COMBINED PLATELET-RICH PLASMA AND HYALURONIC ACID ON BONE MARROW-DERIVED MESENCHYMAL STEM AND CHONDROCYTE METABOLISM

Presenter: Jolanta Norelli, BA (USA)
Affiliation: Northwell Health System
Authors: Norelli J, Plaza D, Satin A, Liang H, Sgaglione N, Grande D

NOT PRESENTED

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PRE-OSTEOARTHRITIC GENE EXPRESSION CHANGES IN INFRAPATELLAR FAT PADS OF MULTIPAROUS RABBITS

Presenter: C. Thomas Vangsness, MD (USA)
Affiliation: University of Southern California
Authors: Vangsness CT, Mircheff AK, Lennarz B, Wang Y, Jones IA, Togashi R

NOT PRESENTED

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ASC IN CELL-ASSISTED LIPOTRANSFER: ANGIOGENIC AND ANTI-APOPTOTIC MARKER EXPRESSION OF ASC UNDER ISCHEMIA-LIKE CONDITIONS AND DEVELOPMENT OF AN ISCHEMIC ADIPOSE TISSUE MODEL IN VITRO

Presenter: Julia Bachmann, MS (Germany)
Affiliation: University of Wuerzburg
Authors: Bachmann J, Ehlert E, Becker M, Radeloff K, Blunk T, Bauer-Kreisel P

Introduction: Cell-assisted lipotransfer (CAL) employing ASC holds great promise to improve graft survival in free fat transplantation. However, the role of ASC remains unclear in the transplantation environment characterized by ischemic conditions (i.e., deprivation of oxygen and nutrients) leading to reduced cell viability and altered cell behavior. In this context, we investigated the viability and secretion of angiogenic and anti-apoptotic factors of ASC under varying conditions of oxygen, glucose, and serum depletion in vitro. Further, we aimed to establish an adipose tissue culture model for detailed investigations on the function of ASC in CAL.

Methods: Human ASC were cultured under standard (DMEM with glucose 3.15 g/l, 10% FCS, 21% O2) or under deprivation conditions (0.5 or 0 g/l glucose, 0% FCS, 2% or 0.2% O2). Viability was monitored using live/dead staining and MTT assay. Expression of angiogenic and anti-apoptotic marker genes was analyzed using qRT-PCR (d4, d7). Human adipose tissue was cultured as standardized tissue fragments in agarose-coated wells under standard or deprivation conditions up to 28 days. Tissue viability and structure was assessed by live/dead and whole-mount staining and resazurin assay.

Results: Deprivation conditions distinctly altered the expression of angiogenic and anti-apoptotic marker genes of ASC. Expression of VEGF, STC-1, and HGF was significantly upregulated under hypoxia (2% O2, 0.2% O2), while HGF was also distinctly upregulated under serum depletion. Glucose depletion strongly impacted cell viability with minor influence on marker expression. Adipose tissue culture under standard conditions displayed viable tissue with intact structure over 28 days. In contrast, applying deprivation conditions resulted in distinct decline in viability and structure integrity, mainly dependent on glucose deprivation. Ongoing experiments investigate the impact of ASC in the adipose tissue model.

Conclusion: ASC displayed an expression profile of angiogenic and anti-apoptotic marker genes mainly influenced by oxygen and serum concentration. An in vitro model of ischemic adipose tissue was established enabling investigations of the influence of ASC on viability and structure of adipose tissue under deprivation conditions in CAL.

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RAPAMYCIN EFFECT ON HUMAN ADIPOSE-DERIVED STEM CELLS (ASCS) IN VITRO CONTROLLING FOR AGE, GENDER, AND PASSAGE NUMBER

Presenter: Matthew Potter, BS (USA)
Affiliation: Steadman Philippon Research Institute
Authors: Potter M, Ravuri SR, Mu XM, Huard JH

Introduction: Rapamycin has been shown to extend the lifespan of many species and emerged as potential anti-aging drug. Rapamycin mechanistically targets mTORC1 pathway and persistent mTORC1 signaling is thought to accelerate stem cell exhaustion. Although the effects of Rapamycin have been studied on many cell types, its mechanistic effect on ASCs is unclear. This study investigates the effects of Rapamycin on ASCs gene expression profile to characterize rejuvenation potential of ASCs with regenerative medicine implications.

Methods: ASCs isolated from human subcutaneous fat were cultured as per standard laboratory optimized protocols. ASCs from young, old, male, female subjects at early and late passages were subsequently treated with Rapamycin at 1nM, 10 nM and 100 nM concentrations, beginning at 24 hours and ending at 72 hours. Throughout the study, sample groups were controlled for gender (male vs female), age (young vs old), and passage number (low passage vs high passage). mRNA was extracted from drug treated and untreated ASCs by Trizol method and qRT-PCR was conducted.

Results: ASCs gene expression profile was analyzed by ddCT method and data showed notable results for several transcripts of interest. The heat map depicted in figure-1 showed results for young, male, and late passage ASCs (Group A) and for old, female, and early passage ASCs (Group B) seemed to have significant correlation. Cell cycle regulators (p53 and p21) and pro-inflammatory factors (IL6 and IL1B) were increased across all groups but higher levels among Group A. Additional cell cycle regulators (p16 and pRb), mitochondria detoxifier (MnSOD), telomerase gene (TERT), and anti-inflammatory factor (Klotho) were found to be increased in Group A but decreased in Group B.

Conclusion: Preliminary results suggest that Rapamycin treatment of ASCs does have an effect at the transcript level on key genes associated with cell cycle, inflammation, and aging. Rapamycin seems to elicite slightly differing responses among young, male, and late passage cells versus old, female, and early passage cells. The increase in p53 transcript levels is an interesting finding that warrants further investigation to understand novel mechanism of Rapamycin mediated mTORC1 antagonism.

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SHORT-TERM HYPOXIC PRECONDITIONING ADIPOSE-DERIVED ENDOTHELIAL PROGENITOR CELLS PROMOTES THE MORPHOLOGICAL REGENERATION AND FUNCTIONAL RESTORATION OF BLADDER DEFECT IN A RAT MODEL

Presenter: Rui-Peng Jia, MD, PhD (China)
Affiliation: Nanjing First Hospital
Author: Jia RP

Introduction: A transplant currently may fail to generate sufficient blood vessels in the course of repair of large bladder defects through tissue engineering. Although the application of endothelial progenitor cells (EPCs) may improve vascular formation to some extent, it still has minimal effects. Recent evidence has shown that short-term hypoxic preconditioning is an effective method to strengthen the angiogenic effect of stem/progenitor cells. Additionally, we have previously cultured adipose tissue derived EPCs (ADEPCs) with high proliferative potential and angiogenic effect. In this study, bladder defect is constructed by partial cystectomy and replaced with hypoxic preconditioning ADEPCs (hp-ADEPCs) seeded bladder acellular matrices (BAM). Meanwhile, its mechanism was researched.

Methods: ADEPCs were maintained at 37°C in either normoxic or hypoxic for 24h, and then seeded into the BAM scaffolds. The rats were divided into three groups: hp-ADEPCs-BAM group, ADEPCs-BAM group, and BAM group. Partial cystectomy was performed by removing 50% of the bladder followed by augmenting the cystectomized defects with hp-ADEPCs-BAM, ADEPCs-BAM, or BAM. The histological and functional assessments of neobladders were performed 4 and 12 weeks after surgery.

Results: ADEPCs expressed both progenitor and endothelial cell marker, and formed capillary-like structures in Matrigel (Fig.1). Immunohistochemical analysis revealed that the hp-ADEPCs-BAM could significantly promote urothelium, blood vessels, smooth muscles and nerve cells regeneration in the regenerated bladder. Regarding functional restoration, the hp-ADEPCs-BAM group exhibited higher bladder compliance and relatively normal micturition pattern compared to the ADEPCs-BAM or BAM group (Fig.2). In addition, ADEPCs secreted more VEGF, bFGF and HIF1α in anoxic condition and strengthened ability of migration and angiogenesis of rat endothelial cells (Fig.3).

Conclusion: This is the first study demonstrates that a combination of ADEPCs and BAM with short-term hypoxic preconditioning is capable of strengthening angiogenesis and functional recovery of defected bladder reconstructed by tissue engineering techniques. Hypoxic preconditioning of ADEPCs might be a potential method for bladder tissue engineering.

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SHORT-TERM HYPOXIC PRECONDITIONING ADIPOSE-DERIVED ENDOTHELIAL PROGENITOR CELLS PROMOTES THE MORPHOLOGICAL REGENERATION AND FUNCTIONAL RESTORATION OF BLADDER DEFECT IN A RAT MODEL

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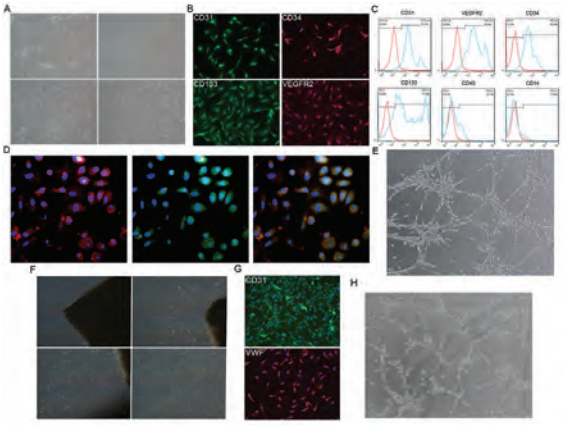

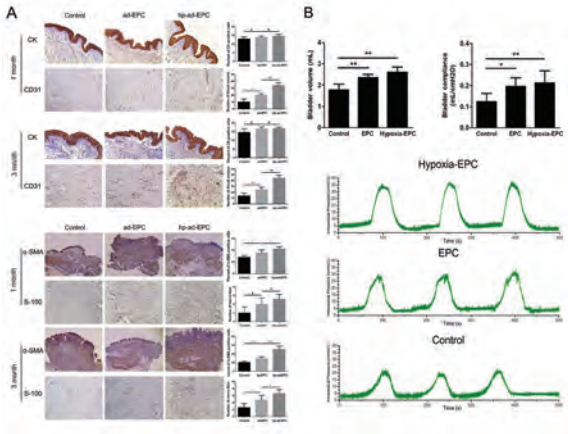

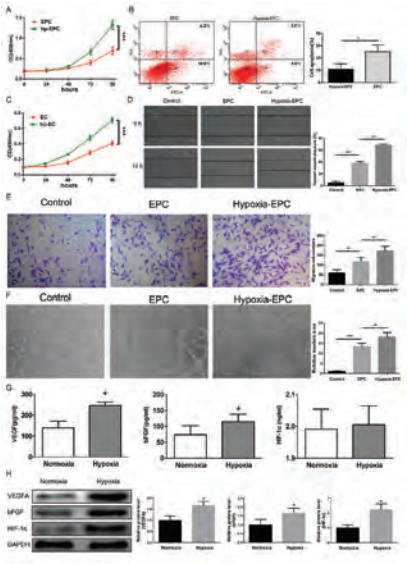

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ENHANCED IMPAIRED WOUND HEALING BY TREATMENT WITH MECHANICAL STRETCH PRECONDITIONED ADIPOSE-DERIVED STEM CELLS

Presenter: Bin Fang, MD (China)
Affiliation: Shanghai Ninth Hospital
Authors: Fang B, Xie Y, Shan SZ

Introduction: Previous studies have shown the therapeutic potential of adipose-derived stem cells (ADSCs) in repairing wound healing. However, when stem cells were transplanted into the unfavorable wound environment caused by infection and low blood flow, the cellular viability, adhesion and migration are remarkably low, but the mortality is high. This have obviously reduced the effect of ADSCs in impaired wound healing. Cyclic stretch is one of mechanical stimuli and involved in many physiological and pathological processes. It is a known modulator of self-renewal and differentiation for many cells. We have previously shown that mechanical stretch preconditioning can promote the cellular viability, proliferation, adhesion, migration and paracrine factor production, but inhibit apoptosis of ADSCs in vitro.

Aim: To study the effect of mechanical stretch preconditioning on the therapeutic capability of ADSCs in accelerating the impaired wound healing process.

Methods: Mouse ADSCs were obtained and preconditioned into two groups, the cyclic equibiaxial mechanical stretched group (ms-ADSCs) and no stretched group (con-ADSCs). 8mm diameter full-thickness excision wounds were made on the dorsal skin of db/db diabetic mice as a delayed wound healing model. db/db diabetic mice were treated by intradermal injections of ms-ADSCs around wound margins while control mice received con-ADSCs injections. The re-epithelialization, collagen deposition and angiogenesis of the wound were tested to evaluate the therapeutic effects.

Results: HE-staining showed that the re-epithelialization was significantly improved in ms-ADSCs-treated wounds compared with con-ADSCs-treated wounds. Masson trichrome staining of ms-ADSCs-treated wounds on day 7 showed thick and densely packed collagen fibers, whereas thin and loosely packed basket-weaved collagen bundles were more apparent in con-ADSCs-treated wounds. And ms-ADSCs-treated wounds expressed more CD31+ endothelial cells than con-ADSCs-treated wounds. Overall, the wounds of mice treated with ms-ADSCs closed significantly faster than the mice treated with st-ADSCs.

Conclusion: Transplantation of ADSCs preconditioned with mechanical stretch accelerates impaired wound healing, which will bring new insights into the regeneration medicine.

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ENHANCED IMPAIRED WOUND HEALING BY TREATMENT WITH MECHANICAL STRETCH PRECONDITIONED ADIPOSE-DERIVED STEM CELLS

Presenter: Bin Fang, MD (China)
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Authors: Fang B, Xie Y, Shan SZ

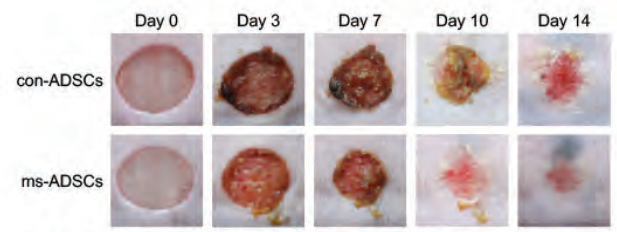

Figure 1. Representative clinical images of wound healing at day 0, day 3, day 7, day 10 and day 14 after the transplantation of con-ADSCs or ms-ADSCs.

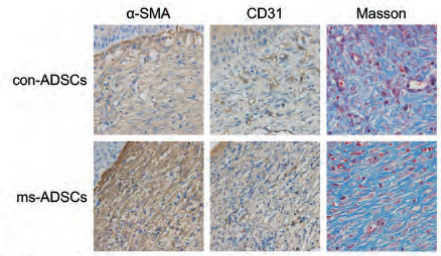

Figure 2. Representative immunohistochemistry staining for α-SMA, CD31 and masson trichrome staining in the con-ADSCs group and in the ms-ADSCs group.

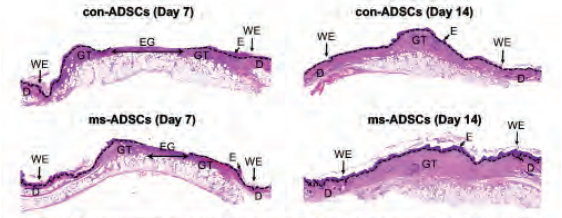

Figure 3. Representative histologic images of con-ADSCs and ms-ADSCs treated wounds at day 7 (Left) and day 14 (Right). D, dermis; E, epidermis; EG, epidermal gap; GT, granulation tissue. (Scale bar: 500 μm.)

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PRECONDITIONING BY PROLYL HYDROXYLASE INHIBITION ENHANCES SURVIVABILITY AND ANGIOGENESIS IN HUMAN ADIPOSE DERIVED STEM CELLS

Presenter: Chang Chen, MD (China)
Affiliation: Sichuan University
Authors: Chen C, Jing W, Tian WD

Introduction: In cell therapy the transplanted cells must survive in a low oxygen, glucose, and pH microenvironment which is called ischemic microenvironment. Hypoxia-inducible factor 1 (HIF-1) is one of the key factors that has crucial effects on the cells vitality, proliferation and differentiation in ischemic circumstance. In this study, we explored the role of hypoxia-inducible factor 1 (HIF-1) on adipose-derived stem cells (ADSCs) survival and angiogenesis ability and its underlining mechanisms by treating cells with dimethyloxalylglycine (DMOG), an α-ketoglutarate antagonist that the intracellular HIF-1 concentration.

Methods: ADSCs were identified for the stemness and treated by DMOG with different concentration and the best concentration was employed to partly mimic the in vivo hypoxia circumstance in vitro. For survival research, we used cck-8 and live/dead cell staining assay to study the variation of cell survivability under an ischemic environment mimicked in vitro by changing the pH value and glucose concentration. And nude mouse model were used to investigate the survival of ADSCs after DMOG preincubation in vivo. Angiogenesis and cell metabolism were determined by tube formation assay, flow cytometry, fluorescence microscopy and real-time PCR respectively.

Results: DMOG-treated ADSCs have a significant promotion of cell survivability under ischemic microenvironment in vivo and in vitro via HIF-1α-induced metabolic alteration characterized by decreased ROS, increased intracellular pH value, enhanced glucose uptake and glycogen synthesis. Result of tube formation assay presents a higher angiogenesis ability in the DMOG treatment group. The angiogenic-related gene expressions were promoted as well according to the date of real-time-PCR test after DMOG treatment.

Conclusion: This research indicates that DMOG, a prolyl hydroxylase inhibitor, increases intracellular HIF-1 concentration and metabolic alteration including decreased reactive oxygen species (ROS) and increased glucose uptake, glycogen storage and intracellular pH in ADSCs. And this approach presents a positive impact on the cell survivability and angiogenesis in ischemic condition. The results suggest a potential strategy for improving cell efficiency in cell therapy.

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REPURPOSING THE ANTHELMINTHIC NICLOSAMIDE AS A SENOLYTIC DRUG FOR ENRICHING HUMAN ADIPOSE-DERIVED STEM CELLS (ASCS)

Presenter: Sudheer Ravuri, PhD (USA)
Affiliation: Steadman Philippon Research Institute
Authors: Ravuri S, Potter MP, Huard JH

Introduction: Several groups have recently found success repurposing Niclosamide for treatment of malignancy. As cancer and aging increasingly appear to have commonalities at the cellular level, the repurposing of Niclosamide as potential senolytic drug for application in anti-aging therapy naturally warrants investigation. This study focuses on understanding molecular mechanism of Niclosamide on ASCs and more specifically to enrich ASCs by targeting senescent cells during expansion in vitro for subsequent autogenic therapies. We aimed to elucidate the senolytic potential of Niclosamide and enrich ASCs.

Methods: ASCs isolated from human subcutaneous fat were cultured as per standard laboratory optimized protocols. Normal proliferating ASCs treated with Niclosamide, ASCs treated with Niclosamide prior to senescence induction and ASCs treated with Niclosamide after senescence induction were evaluated at 0 μM, 1 μM and 10 μM concentrations of drug beginning at 6 hours and ending at 72 hours. mRNA was extracted from ASCs by Trizol method and qRT-PCR was performed with ddCT analysis. ASCs were quantified for senescence marker SA-βgal and cell proliferation by MTS assay.

Results: qRT-PCR analysis showed a large increase in cell cycle regulators (p53, p21 and p16) and pro-inflammatory factors (IL6 and IL1B) in normal proliferating ASCs (Figure-1). Senescent ASCs showed an increase in cell cycle regulators (p53, p21 and p16) but instead showed a decrease in pro-inflammatory factors (IL6 and IL1B). SA-βgal quantification showed decreased senescence in normal proliferating ASCs and senescence induced ASCs (Figure-2). Cell proliferation assay showed proliferation of normal ASCs under 1 uM Niclosamide, while Niclosamide dosing over 1 uM caused decreasing levels of senescent ASCs.

Conclusion: Increasing levels of cell cycle regulators could imply senescence induction, but these preliminary results suggest Niclosamide elicits senolytic response within ASCs. Corroborating this conclusion is the observed decrease in pro-inflammatory factors which are known to be associated with the senescence-associated secretome phenotype. Furthermore, a decrease observed in SA-βgal also implies senolytic activity. Apoptosis assays are in progress to confirm senolytic activity.

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REPURPOSING THE ANTHELMINTHIC NICLOSAMIDE AS A SENOLYTIC DRUG FOR ENRICHING HUMAN ADIPOSE-DERIVED STEM CELLS (ASCS)

Presenter: Sudheer Ravuri, PhD (USA)
Affiliation: Steadman Philippon Research Institute
Authors: Ravuri S, Potter MP, Huard JH

Figure 1

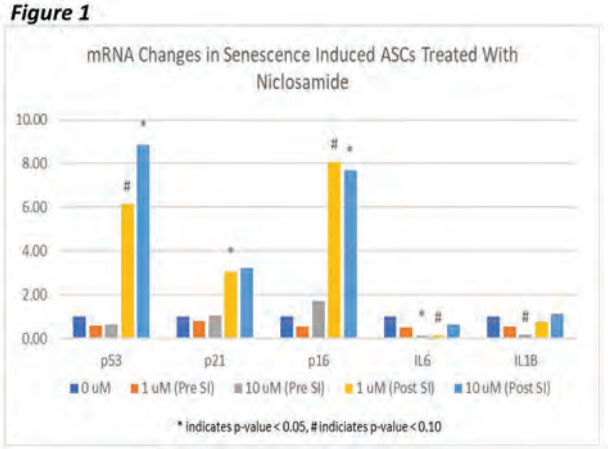
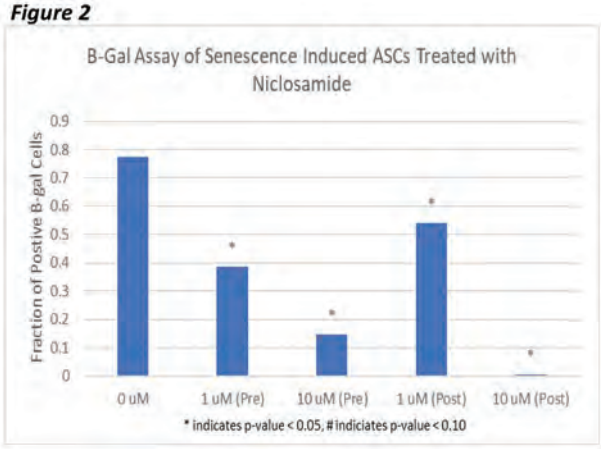


Figure 2



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OPTIMISING PROCESSING OF LIPOASPIRATE FOR ISOLATION AND XENO-FREE EXPANSION OF HIGHLY ADIPOGENIC AND ANGIOGENIC CELLS FOR CLINICAL APPLICATION

Presenter: Paul Kingham, PhD (Sweden)
Affiliation: Umea University
Authors: Kingham P, Lauvrud AT, Gümüscü R, Wiberg R, Kelk P, Wiberg M, Brohlin M

Background: The benefits of cell-assisted lipotransfer (CAL) compared with conventional fat grafting are inconclusive and there is no single standardised procedure used to isolate adipose stem cells. With the goal of obtaining optimal highly adipogenic and angiogenic cells, we have investigated the influence of i) liposuction method, ii) automated cell processing and iii) a xeno-free, GMP-compliant cell culture expansion protocol.

Methods: First, ten women underwent liposuction of subcutaneous abdominal fat. On one side manual liposuction was performed and on the other side water-jet (WJ) assisted liposuction (Body-jet®, Human Med). Cell proliferation, adipogenic differentiation and angiogenic activity were compared. Next, WJ aspirates were processed using a regular centrifugation protocol or Sepax-2 Cell Separation System (Biosafe, GE Healthcare). Cells were then expanded in MEM medium with 10% FBS (Gibco™, Thermo Fisher Scientific) or in Prime-XV® MSC expansion XSFM medium (Irvine Scientific).

Results: Both WJ and manual liposuction yielded cell mixes containing >95% cells expressing CD73, CD90 and CD105 whereas WJ preparations showed 2-fold higher levels of CD146 positive cells. Both cell preparations proliferated at similar rates and secreted various active angiogenic factors. Robust adipogenic differentiation was observed in cultures expanded from both manual and WJ-aspirated fat but the latter group showed higher expression of the mature adipocyte markers GLUT4 and aP2. WJ aspirates processed using the Sepax-2 system showed similar stem cell CD marker profile as those in cells isolated by regular centrifugation. The type of culture medium did not influence this at early passage but at late passage CD105 expression was markedly reduced in Prime-XV® MSC expansion XSFM medium. Cumulative population doublings and CFU-F were higher in Prime-XV® MSC expansion XSFM medium. The medium composition differentially influenced angiogenic protein expression.

Conclusions: Our data indicate that WJ assisted liposuction yields high levels of cells suitable for CAL. Furthermore, we have developed a procedure which incorporates an automated processing device and GMP compliant cell expansion protocol, both of which are necessary prerequisites for Advanced Therapies.

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NOVEL NON-TUMORIGENIC HUMAN PLURIPOTENT STEM CELLS ISOLATED FROM ADIPOSE TISSUE (MUSE-AT CELLS): NEW PARADIGM IN REGENERATIVE MEDICINE

Presenter: Gregorio D. Chazenbalk, PhD (USA)
Affiliation: University of California Los Angeles
Authors: Chazenbalk GD, Gimeno ML, Perone MJ

Significant progress has occurred since Multi-Lineage Differentiating Stress Enduring cells isolated from adipose tissue (Muse-AT) cells, a novel human non-tumorigenic pluripotent stem cells, were introduce to the scientific community in 2013. Muse-AT cells can be obtained under severe cellular stress conditions such as lack of nutrients, hypoxia, long collagenase treatment, and low temperatures. Muse-AT cell expansion is not required due to the abundance of highly purified Muse-AT cells obtained (25-50 million cells /100 gr of lipoaspirate material). Muse-AT cells are present in both adipocyte and stromal vascular fractions. Additionally, the purification of Muse-AT cells does not require cell sorting, magnetic beads, or special devices. Muse-AT cells grow in suspension as cell clusters, expressing the classical pluripotent stem cell markers SSEA3/4, NANOG, Oct3/4, and Sox2, although in much lower levels than relative to embryonic stem cells (ES) or induced pluripotent stem cells (iPS). Furthermore, Muse-AT cells can spontaneously or induced differentiate into the three germ cell layers. Muse-AT cells preferentially spontaneously differentiate into adipocytes, indicating that they retain an epigenetic memory, of their tissue of origin. Importantly, Muse-AT cells do not undergo tumorigenesis or form teratomas "in vivo". Additionally, the microRNA Let-7 seems to be a critical master regulator of Muse-AT proliferation without teratogenesis. Muse-AT cells also display a stable normal karyotype in culture, as indicated by their normal chromosome number and integrity. Muse-AT cells highly express significant amounts of TGF-beta1, a key cytokine governing down-modulation of T lymphocytes and macrophages. Furthermore, Muse-AT cells have immunomodulatory properties mediated by their secretion of specific cytokines/growth factors. Our preliminary results indicate the beneficial effects of Muse-AT cells in an experimental mice model of type 1 diabetes. Because naive Muse-AT cells are normally in a quiescent state, they are innate resilient to severe cellular stress and therefore can survive when transplanted back into the host organism. All these qualities and vast potential make Muse-AT cells an "optimal" candidate for tissue regeneration and stem cell therapy.

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NOTCH SIGNALING ENHANCES STEMNESS BY REGULATING METABOLIC PATHWAYS THROUGH MODIFYING P53, NF-KB, AND HIF-1A

Presenter: Hiroyuki Moriyama, PhD (Japan)
Affiliation: Pharmaceutical Research and Technology Institute
Authors: Moriyama H, Moriyama M, Hayakawa T

WITHDRAWN

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FAS-L PROMOTES THE STEM CELL POTENCY OF ADIPOSE DERIVED MESENCHYMAL CELLS

Presenter: Nir Shani, PhD (Israel)
Affiliation: Tel Aviv Sourasky Medical Center & Cellect Biotherapeutics Ltd.
Authors: Shani N, Solodeev I, Meilik B, Volovitz I, Sela M, Manheim S, Yarkoni S, Gur E

Introduction: Fas-L is a TNF family member known to trigger cell death. It has recently become evident that Fas-L can transduce also nonapoptotic signals. Mesenchymal stem cells (MSCs) are multipotent cells that are derived from various adult tissues. Although MSCs from different tissues display common properties they also display tissue-specific characteristics. Previous works have demonstrated massive apoptosis following Fas-L treatment of bone marrow (BM)-derived MSCs both in vitro and following their administration in vivo. We therefore set to examine Fas-L-induced responses in adipose derived stem cells (ASCs).

Methods: Human ASCs were isolated from lipoaspirates and their reactivity to Fas-L treatment was examined.

Results: ASCs responded to Fas-L by simultaneous apoptosis and proliferation, which yielded a net doubling of cell quantities and a phenotypic shift, including reduced expression of CD105 and increased expression of CD73, in association with increased bone differentiation potential. Treatment of freshly isolated ASCs led to an increase in large colony forming unit fibroblasts (CFU-F), likely produced by early stem cell progenitor cells. Fas-L-induced apoptosis and proliferation signaling were found to be independent as caspase inhibition attenuated Fas-L-induced apoptosis without impacting proliferation, while inhibition of PI3K and MEK, but not of JNK, attenuated Fas-L-dependent proliferation, but not apoptosis.

Conclusions: Thus, Fas-L signaling in ASCs leads to their expansion and phenotypic shift towards a more potent stem cell state. We speculate that these reactions ensure the survival of ASC progenitor cells encountering Fas-L-enriched environments during tissue damage and inflammation and may also enhance ASC survival following their administration in vivo.

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REGENERATIVE PROPERTIES OF HUMAN SPHEROIDS FROM ADIPOSE STEM CELLS (SASCS) IN A XENOGENEIC RABBIT MODEL

Presenter: Anna Barbara Di Stefano, PhD (Italy)
Affiliation: Plastic and Reconstructive Surgery
Authors: Di Stefano AB, Montesano L, Belmonte B, Gulino A, Grisafi F, Toia F, Gagliardo C, Russo A, Florena AM, Moschella F, Leto Barone AA, Cordova A

NOT PRESENTED

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ISOLATION AND CHARACTERIZATION OF MICROVASCULAR ENDOTHELIAL PROGENITOR CELLS FROM HUMAN LIPOASPIRATES

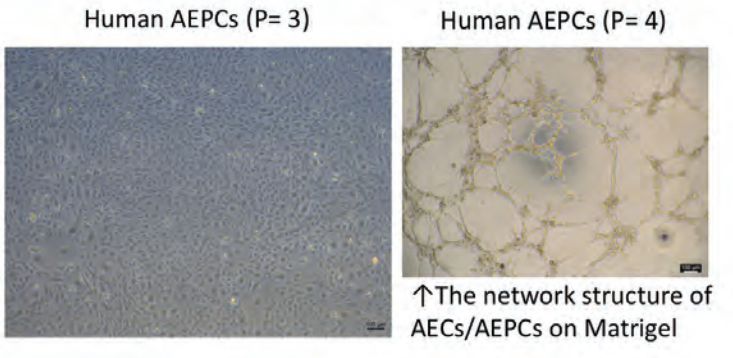
Presenter: Natsumi Saito, PhD (Japan)
Affiliation: Jichi Medical University
Authors: Saito N, Shirado T, Mori M, Asahi R, Yoshimura K

Introduction: Vascular endothelial progenitor cells (VEPCs) are one of important cell populations to play pivotal roles in angiogenesis and wound healing. Thus, VEPCs are expected to be a potent therapeutic tool in regenerative medicine. For the first time, we succeeded in isolation and culture expansion of microvascular EPCs from human lipoaspirates (adipose-derived EPCs; AEPCs).

Methods: There are three steps to isolated human AEPCs. First, stromal vascular fraction (SVF) was extracted from lipoaspirates through regular enzymatic digestion. Second, CD45−/CD31+ fraction was collected with magnetic-activated cell sorting (MACS). Finally, the CD45−/CD31+ cell fraction was cultured under appropriate medium for 2-4 days, followed by the second MACS using CD31 antibody alone. We tested some culture media for expansion, banking and recovery culture. We also performed characterization and functional analysis of expanded AEPCs with comparison to HUVECs (Lonza).

Results: AEPCs were successfully isolated and expanded only when performed the second MACS to further purify AEPCs at the level of >90%. Otherwise, AEPCs were overwhelmed by ASCs over culture period. EGM-2MV medium significantly increased (>1.5 times) AEPCs proliferation compared with EGM-2 at 5 days in culture, while a remarkable difference was not seen in HUVECs culture. Colony forming unit (CFU) assay using AEPCs at passage 5 showed 47.7±4.8% of colony formation, while HUVECs at passage 5 culture was 37.9%±4.4%. Tube formation assay showed that both AEPCs and HUVECs formed honeycomb-like network on Matrigel gel although the total tube length is relatively longer in HUVECs.

Conclusions: We found that a high level (>90%) purification of AEPCs is a key factor to isolate and expand AEPCs from human lipoaspirates. The AEPCs can be expanded and recovered after cryopreservation, and maintained a high colony-forming capacity at least up to the passage 5.



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GENETIC STABILITY AND REPLICATIVE SENESCENCE IN ASCS AMPLIFIED FOR CLINICAL APPLICATION

Presenter: Nicolas Theys, PhD (Belgium)
Affiliation: Novadip Biosciences SA
Authors: Theys N, Pierard C, Dufrane D

WITHDRAWN

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HYPERPLASTICITY OF SVF-ISOLATED CD34+ CELLS TOWARDS ADIPO- AND OSTEO- GENESIS

Presenter: Srinivas Koduru, PhD (USA)
Affiliation: Pennsylvania State University
Authors: Koduru S, Leberfinger AN, Hayes DJ, Ravnic DJ

Introduction: The stromal vascular fraction (SVF) is a multicellular isolate of adipose tissue that includes adipose derived stem cells (ADSCs). ADSCs are defined as exhibiting CD73 and CD90 positivity with potential for both adipo- and osteo- genesis. However, other cellular progenitors present in the SVF may offer better differentiation potential than ADSCs. CD34 is a marker for bone marrow-derived progenitor cells and these cells are noted in the SVF as well. However, their utility in directed adipo- and osteo- genesis is ill-defined. We hypothesized that adipose derived CD90-/CD31-/CD34+ cells could offer an alternative to standard ADSCs for in vitro adipose and bone differentiation.

Methods: Excised adipose tissue was obtained from ten consecutive patients undergoing lipectomy under IRB approval. The SVF was retrieved via mechanical and enzymatic digestion, and subjected to magnetic activated cell sorting. CD90+ cells were retrieved and followed by depletion of CD31+ cells. CD34+ cells were then extracted from the CD90/CD31 depleted SVF. CD90+ and CD90-/CD31-/CD34+ subpopulations were differentiated into adipocytes and osteoblasts in vitro using 2D and 3D cultures. At two weeks the differentiation capacity was noted using both standard histology and immunofluorescence. Cellular populations were verified by flow cytometry prior to and after directed differentiation. Image analysis was performed with Image J software.

Results: Following standardization, representative sections of both 2D and 3D cultured cells suggested a higher differentiation capacity of CD90-/CD31-/CD34+ cells into both adipocytes and osteoblasts. Perilipin staining of CD90-/CD31-/CD34+ derived adipocytes demonstrated approximately a four-fold increase compared to CD90+ derived adipocytes. Similarly, osteocalcin staining in differentiated osteoblasts was noted to be doubled (area per HPF).

Conclusion: Purified CD90+ cells have been shown to demonstrate robust mesenchymal differentiation potential. However, our results indicate that the CD90-/CD31-/CD34+ fraction of the SVF exhibits an even stronger propensity for directed adipo- and osteo- genesis. Therefore, this cellular subpopulation should be considered for adipose and bone engineering applications.

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DONOR AGE AFFECTS STEM CELL RELATED GENE EXPRESSION IN ADIPOSE MSCS

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Introduction: Aging is a complex process characterized by many disorders, and inability of body to maintain tissue turnover and homeostasis. As implied by stem cell dysfunction in natural aging, donor age must be considered as a critical factor for laboratory and clinical cell therapies. Aged patients, prone to many diseases and disorders, are the main target population for cell based therapies. Since autologous cell sources are preferred, investigating the effect of donor age on the potential utility of cells is useful. In recent years, various clinical and preclinical investigations urge use of mesenchymal stem cells (MSCs) from several sources including adipose tissue.

Methods: Here we sought to study mRNA transcription characteristics of adipose derived MSCs (Ad-MSCs) obtained from young or aged patients. Previously cryopreserved tissue was thawed, digested, and the resulting cells plated. RNA was extracted from P1 cells and used in phenotyping by FACS and in RT2 Profiler PCR arrays (Qiagen).

Results: Cells were similar morphologically and immunophenotypically regardless of donor age. However, upregulation of several MSC related genes such as NOTCH1, BMP6, GCSF was noted in MSCs from aged individuals. Lower levels of mRNA for factors such as IL-10, IL-6, Endoglin and FGF2 was also seen from aged samples.

Conclusions: These data, in conjunction with known changes in MSC doubling time, senescence and apoptosis point to potentially significant alterations in cell therapy strategies when using cells from aged patients.

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THE EFFECT OF CELL-CELL CONTACT DEPENDENT LIPOASPIRATE CO-CULTURE ON BREAST CANCER CELLS PROLIFERATION: IMPLICATIONS FOR CELL-ASSISTED LIPOTRANSFERS IN BREAST RECONSTRUCTION

Presenter: Asim Ejaz, PhD (USA)
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Background: Approximately 1 in 8 U.S. women develop invasive breast cancer over the course of their lifetime. Clinical outcomes suggest that post-oncologic reconstruction with fat graft yields comparable cumulative incidence curves to standard of care procedures, however results from experimental research studies are discordant. In this study, we employed our unique cell culture and mouse model to study the cell-cell contact dependent interactions between lipoaspirate and breast cancer cells.

Methods: Lipoaspirates from human subjects (n=3) were co-cultured using direct or in-direct contact with breast cancer cells MCF-7, MDA-MB 231 and BT474 using T12.5 cm2 flask. The effect of the co-culture on proliferation of cancer cells was recorded by counting the cells using hemocytometer. GFP transfected stable MCF-7 and MDA-MB 231 cell lines were generated to study cell-cell interaction with adipose derived stem cells. The outcome of co-culture was monitored by direct visualization of GFP positive cells using fluorescence microscopy and counting the number of GFP positive cells for 60 seconds at a constant flow rate on a LSRFortessa cytometer. For in vivo studies mammary fat pads of female NOD-SCID gamma mice were injected with MCF-7 cells in Matrigel. Tumors were allowed to engraft for 2 weeks, after which time either saline or human fat graft were injected adjacent to tumor sites. After 8 weeks, tumor volume was measured.

Results: A significant decrease in the proliferation of MCF-7, MDA-MB 231 and BT474 cells was observed upon contact co-culture with lipoaspirates. Upon paracrine culture with lipoaspirates only MCF-7 cells showed a significant lower proliferation rate. Cell-cell contact culture of ASCs with breast cancer cells also resulted in lower proliferation of breast cancer cells. On contrary, ASCs paracrine culture enhances breast cancer cells proliferation. In line with in vitro results, in vivo results demonstrated that animals receiving lipofilling after tumor cell engraftment had lower tumor volume and mass.

Conclusion: This study suggests the possibility of oncologic safety of lipofilling as part of the surgical platform for breast reconstruction after cancer therapy.

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ADIPOSE DERIVED MESENCHYMAL STEM CELLS INHIBITS CARCINOGENESIS AND INVASIVENESS IN HEPATOCELLULAR CARCINOMA CELL LINES

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Background: Hepatocellular carcinoma (HCC) is a malignant condition with higher incidence and no effective treatment. Adipose derived stem cells (ADMSCs) have been shown to exhibit therapeutic efficacy in many diseases; however, their influence on cancer is not clear. In this study, we investigated the effect of ADMSCs and their conditioned media (CM) on biological responses of HCC cell lines, namely HepG2 and PLC-PRF-5 cells.

Methods: Proliferation rate was measured using cell counting kit-8. Apoptosis level and intracellular interleukin expression were determined by flow cytometry. Protein and mRNA expressions were measured by ELISA and real time PCR respectively. Migration and invasion rates were detected by transwell migration and invasion assay.

Results: Our data demonstrated that ADMSCs and their CM significantly inhibited the proliferation and increased the apoptosis of HepG2 and PLC-PRF-5 cells, along with an upregulation of the P53/Retinoblastoma mRNA and a downregulation of that of c-Myc/hTERT. Co-culturing HCC cell lines with ADMSCs or treating them with ADMSCs CM also suppressed their expression of alpha-fetoprotein and Des-γ-carboxyprothrombin, two important markers of carcinogenicity in HCC. Moreover, ADMSCs and ADMSCs CM diminished migration and invasion levels of the HepG2 and PLC-PRF-5cells, possibly through increased expression of tissue inhibitor metalloproteinases, namely TIMP-1, TIMP-2 and TIMP-3 and anti-inflammatory cytokines, namely IL-4, IL-10 and IL-13.

Conclusion: These findings highlight an important role for ADMSCs and their CM in controlling the invasiveness and carcinogenesis of HCC, and suggest their therapeutic efficiency in the treatment of the disease.

Keywords: hepatocellular carcinoma; adipose derived mesenchymal stem cells; adipose derived mesenchymal stem cells conditioned media; proliferation; apoptosis; invasion.

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OBESITY-ALTERED ADIPOSE STEM CELLS PROMOTE RADIORESISTANCE OF ER+ BREAST CANCER

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Hypothesis: Adipose stem cells from obese individuals (obASCs) promote breast cancer radioresistance through IL-6 JAK/STAT pathways.

Purpose/Objective(s): Adipose stem cells (ASCs) are recruited to sites of inflammation where they act as immunomodulators. ASCs modulate their environment through the secretion of adipokines, cytokines and growth factors. Obesity alters the biology of resident ASCs. ASCs from obesity-altered ASCs (obASCs) have been shown to promote proliferation and metastasis of breast cancer compared to lean ASCs (lnASCS) in vitro and in vivo. The pro-survival secretome secreted by ASCs led us to investigate the role of lnASCs and obASCs in breast cancer radioresistance. Estrogen receptor positive (ER+) breast cancer cells (MCF7) were co-cultured for 96 hours in a transwell system (0.4 μm pore size, Costar) with pooled donors (n=3) of lnASCs, obASCs, or were cultured without ASCs. The breast cancer cells were irradiated after 96 hours of co-culture using a cesium-source irradiator at doses of 0, 2, 5, 10 Gy and further incubated 24 hours.

Results: The ER+ breast cancer has an increased survival after therapeutic doses of radiation after co-culture with obASCs. A significant increase in IL-6 expression levels was observed in ER+ breast cancer cells co-cultured with obASCs. IL-6 has been shown to play a protective role in resistance to radiation. We then treated ER+ breast cancer cells with recombinant humanized IL-6 and saw comparable survival benefits to obASC co-culture. Finally, MCF7 cells were co-cultured with obASCs and an IL-6 neutralizing antibody. We found that neutralizing IL-6 abrogated the pro-survival effects of obASC co-culture. Here we demonstrate obASCs enhance the survival of ER+ breast cancer cells after exposure to radiation. This study sheds new light on ASCs ability to promote breast cancer development, which has important clinical implications on the worse outcomes for obese women who develop breast cancer.

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ADIPOSE-DERIVED STEM CELLS PROTECT SKIN FLAPS AGAINST ISCHEMIA/REPERFUSION INJURY VIA IL-6 EXPRESSION

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Flap necrosis is the most frequent postoperative complication encountered in reconstructive surgery. We elucidated whether adipose-derived stem cells (ADSCs) and their derivatives might induce neovascularization and protect skin flaps during ischemia/reperfusion (I/R) injury. Flaps were subjected to 3 hours of ischemia by ligating long thoracic vessels and then to blood reperfusion. Q-tracker-labeled ADSCs, ADSCs in conditioned medium (ADSC-CM), or ADSC exosomes (ADSC-Exo) were injected into the flaps. These treatments led to significantly increased flap survival and capillary density compared with I/R on postoperative day 5. IL-6 levels in the cell lysates or in conditioned medium were significantly higher in ADSCs than in Hs68 fibroblasts. ADSC-CM and ADSC-Exo increased tube formation. This result was corroborated by a strong decrease in skin repair after adding IL-6 neutralizing antibodies or small interfering RNA for IL-6 ADSCs. ADSC transplantation also increased flap recovery in I/R injury of IL-6 knockout mice. This result may provide a new strategy in rescuing the falling flap in the future.

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A UNIQUE APPROACH TO TREATING CATASTROPHIC DISTAL-LIMB WOUNDS WITH ADIPOSE STEM CELLS, PLATELET-RICH-PLASMA, AND VETAP-17 (SM-1997)

Presenter: Kaylen M. Capps, MS (USA)
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Trinity Research Institute (TRI) uses the horse as the animal model of distal-limb wounds in combat veterans. Adipose-derived mesenchymal stem cells (ASC's) and platelet-rich-plasma (PRP) enhance skin repair. The positive trophic effects of SM-1997, presented at IFATS in 2017, on the in vitro proliferation of Human Umbilical derived mesenchymal stem cells (HUC-MSC's) in a 3-D wound model, became the impetus to combine ASC's, PRP and SM-1997 to treat distal-limb wounds in vivo. This case represents a typical distal-limb wound in the horse which, without access to ASC's, PRP, and SM-1997, would have been euthanized. Euthanasia is not an option for combat-wounded veterans, and amputation is common. "Sully," a 14-year-old gelding sustained a full thickness (severed extensor muscles and tendons), de-gloving wound of the left distal leg and was enrolled in a compassionate care regenerative medicine program through TRI after the horse developed gangrene in the non-healing wound. ASC's, PRP, and SM-1997 were added as adjunct therapies to traditional wound care protocols. Antibiotics and anti-inflammatory agents were discontinued. Wound debridement included chemical, physical, and surgical methods. Anthropomorphic data, photos and functional evaluation of the limb were recorded pre and post treatments. Punch biopsies were used to determine the degree and quality of healing. With addition of ASC's, PRP, and SM-1997, the wound began to heal. The periosteum was restored. A healthy granulation bed was established within days and has been maintained for months over the course of 97 bandage changes in the absence of antibiotics. Within six weeks the horse was weight-bearing and able to walk and trot on the limb. Currently, the leg is re-vascularizing with minimal lymphedema and full thickness re-epithelialization sans-scaring. In this case, the use of ASC's and PRP parallels numerous similar catastrophic distal-limb wound cases treated by TRI. Addition of SM-1997 allowed proficient, scar free, fully haired re-epithelialization. The horse has regained use of the limb as resected tendons continue to heal. Combining ASC's, PRP, and SM-1997 with conventional surgical wound care techniques suggests an improved method to treat of distal-limb wounds in combat-wounded veterans.

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IN VITRO AND IN VIVO EVALUATION OF A BIOENGINEERED NERVE CONDUIT COMBINING TOPOGRAPHICAL CUES AND ADIPOSE TISSUE-DERIVED SUPPORT CELLS

Presenter: Suzanne E. Thomson, BSc, MBChB, MRCSEd, PhD (United Kingdom)
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Background: Nerve injury is common with significant cost to the individual and society. Autologous adipose tissue-derived support cells may be used to augment nerve regeneration. The ability of adipose stem cells (ADSCs) to be differentiated towards a Schwann cell-like lineage (dADSCs) and support neurite outgrowth has been demonstrated. In this study, we investigated the effects of combining support cells, either stromal vascular fraction (SVF) or dADSCs, with topographical cues in vitro. Using this approach, a nerve conduit was fabricated and used to reconstruct a critical size nerve gap in vivo.

Methods: Biodegradable scaffolds with refined topographical features were fabricated and their biocompatibility assessed in 2 and 3D in vitro culture models. Autologous SVF and ADSCs were isolated and cultured on the material. The stem cells were differentiated towards a Schwann cell-like lineage and the impact of topography on the differentiation was evaluated using immunocytochemistry, qRT-PCR and quantitative In-Cell Western and ELISA. A 15mm rat sciatic nerve gap model was used to study nerve regeneration. There were five study groups (n = 10 per group): 1) empty conduit, 2) conduit seeded with SVF 3) conduit seeded with dADSCs 4) autologous nerve graft (current gold standard) 5) no repair. A comprehensive suite of outcome measures was employed, including functional and electrophysiological analyses, immunohistochemistry and high-res 3D microCT imaging. Statistical analyses were performed using GraphPadPrism software.

Results: In vitro work demonstrated that dADSCs maintain their differentiated state on topography and anisotropic linear cues enhance the differentiation process. The bioengineered nerve conduit supported nerve regeneration across a critical size nerve gap in vivo and the addition of either SVF or dADSCs enhanced regeneration. Electrophysiology demonstrated a benefit of cell differentiation. Outcomes using autologous nerve graft remained superior across the majority of outcome measures.

Conclusion: This combinational approach demonstrates the potential of tissue engineered nerve conduits pre-seeded with SVF or dADSCs to improve outcomes following surgical repair of nerve injury.

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IN VITRO AND CLINICAL STUDIES WITH LONGITUDINAL ANALYSIS OF FUNCTIONAL ADIPOSE TISSUE REGENERATION USING ADIPOSE ALLOGRAFT MATRIX

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Introduction: Allograft adipose extracellular matrix has shown great promise in vitro and in animal studies as an off-the-shelf adipogenic matrix for permanent volume replacement. In this study, we report analyses of adipose tissue regeneration, first in-vitro using human adipose stromal cells seeded and cultured on allograft adipose matrix (AAM) and subsequently clinically, in a prospective single-center study in which 120cc of total AAM was grafted into 6 sites of the pannus of 10 pre-surgical abdominoplasty patients. The overall goals for these studies were to longitudinally evaluate the body's innate response to AAM.

Methods: In-vitro - Passage 3 human adipose stromal cells (7.5x10^5) in 75µl AAM were cultured in DMEM+5% FBS and adipogenesis was measured through morphology by confocal microscopy, triglyceride content normalized to DNA, and RNA expression of adipogenic genes (LPL, CEBPA, PPARG, FABP4, ADIPOQ) at 1, 2, and 3 weeks. Clinical - 10 healthy subjects undergoing elective abdominoplasty were recruited to receive AAM either 3 or 6 months prior to surgery. Subjects were monitored for local and adverse events in addition to undergoing optional serial biopsies at 1 and 2 months. Representative biopsy samples were stained with Masson's trichrome for collagen, perilipin for lipid accumulation, elastin for skin quality, and CD34 for angiogenesis and adipose progenitor cells.

Results: In vitro outcomes suggested that AAM contains endogenous adipogenic components that support adipose stromal cell differentiation toward mature adipocytes without exogenous stimuli. Such response was not observed in allograft matrices derived from non-adipose tissues such as dermis. Clinically, all patients tolerated AAM well with no unanticipated or serious adverse events reported. Perilipin staining demonstrated the presence of mature fat cells within the acellular matrix by 1 month with extensive remodeling and regeneration of adipose tissue evident at 3 and 6 months. Histologic observations of matrix replacement with adipose tissue paralleled clinical assessments that AAM softened over time and integrated into adipose tissue.

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CLINICAL EXPERIENCE WITH ALLOGRAFT ADIPOSE MATRIX GRAFTING IN THE PEDIATRIC PATIENT

Presenter: Kevin Hopkins, MD, FACS (USA)
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Introduction: Autologous fat grafting has been successful in soft tissue augmentation and contouring primarily in the adult population. It is also a viable tool in restoring soft tissue in the pediatric patient for congenital and traumatic defects but there are inherent issues in this population such as the accessibility and amount of available autologous fat. Recent FDA approval of allograft adipose matrix (AAM) provides a viable alternative tool for correcting soft tissue congenital and traumatic defects in the pediatric patient. This paper recounts our recent experience using AAM in the pediatric population.

Methods: 27patients (9 female, 18 male); ages 1-16 years (average age 10.3) presented with 23 congenital defects (17 cleft lip/palate, 6 craniofacial soft tissue deficits and 4 traumatic defects (3 craniofacial and 1 trunk with follow up time ranging from 2 weeks to 18 months. The cleft lip and palate defects include palatal fistula with severe scarring and fibrosis (1); velopharyngeal insufficiency (9); a asymmetric soft tissue volume (7) Congenital defects were hemifacial microsomia (1), hemifacial atrophy (1), and frontonasal dysplasia (1). The traumatic deformities involved the face (3), trunk (1). Five patients underwent serial AAM grafting. Dehydrated allograft adipose matrix was reconstituted with sterile 0.9% saline. The volume of AAM transferred ranged from 0.9 ml to 15 ml per site using Coleman cannulas and modified standard spinal needles to facilitate the intraoral delivery of AAM to the contours of the palate

Results and Conclusions: Allograft adipose matrix may be safely used and effectively grafted to correct contour deformities in children. Direct observation and serial photographs demonstrate increased soft tissue volume and enhanced tissue quality. There is improvement in all patients with VPI following AAM grafting.

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STRUCTURAL ANALYSIS AND CYTOCOMPATIBILITY OF HUMAN DECELLULARIZED ADIPOSE TISSUE DERIVED HYDROGEL

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Introduction: Decellularized tissue-based scaffolds are useful tools for tissue engineering. Adipose tissue, due to its extensive availability, is an attractive candidate as a biological scaffold. Several recent studies have shown that decellularized adipose tissue (DAT) can be used for adipose tissue engineering, wound healing and as a filler after lumpectomy. The goal of the current study was to convert DAT into an injectable hydrogel that allows easy encapsulation of cells and growth factors, while retaining its extracellular matrix (ECM) characteristics.

Methods: Native adipose tissue (NAT) was acquired from human donors undergoing elective lipectomy. NAT was decellularized using an enzyme and detergent based protocol. Decellularized adipose tissue (DAT) was then digested in a pepsin/HCl solution for 2 days to produce a pre-hydrogel form of DAT. ASCs were seeded on DAT derived hydrogel at a concentration of 1 million cells/mL; cell viability and proliferation were analyzed over time using calcein-AM and alamar blue staining respectively. Structural arrangement of ECM proteins in hydrogel was compared with NAT and DAT using hematoxylin & eosin (H&E), picrosirius red (PR) and Masson's trichrome (MT) staining.

Results: The pre-hydrogel when neutralized and incubated at 37oC converted into a solid hydrogel. The gelation time of the hydrogel was found to be 18±2 minutes. The calcein-AM stain showed viable cells (green) spread across the hydrogel after 7 days of cell culture. The alamar blue assay indicated a 450% increase in cell density inside the hydrogel by day 12. H&E stain displayed that proteins had reassembled in the hydrogel to form a matrix, however the structure appeared to be less organized in comparison to native ECM. PR and MT stains presented cross-linked collagen fibrils in the form of a meshwork. H&E and MT also confirmed the attachment of cells to hydrogel matrix.

Conclusions: Quick gelation time at physiological temperature and cytocompatibility of DAT derived hydrogel, allows for its development as an injectable scaffold. This could be beneficial for promoting regeneration of damaged body tissues in a minimally invasive manner. In the future, this hydrogel can be tested in vivo for the regeneration of soft and hard tissues.

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KEY ROLE OF ADIPOSE STEM CELLS FOR OSTEOGENESIS IN A SCAFFOLD-FREE GRAFT FOR LARGE CRITICAL SIZE BONE DEFECT

Presenter: Sophie Veriter, PhD (Belgium)
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Large critical size bone defect is one of the most challenging pathologies in orthopaedic surgery. The direct application of adipose stem cells (ASCs) remains limited in vivo by a low homing efficiency associated to a low survival rate at the implantation site. This study aims to demonstrate the role of the ASCs function in a scaffold-free approach in terms of in vivo osteogenesis.

Before transplantation, the molecular characterization (for skeletal development/ angiogenesis) of the osteogenic human ASCs was performed on the fresh and decellularized 3D scaffold-free grafts. The bioactivity of the ASCs/matrix of the scaffold-free graft was then in vivo studied in 2 nude rat models: (i) the comparison of fresh and decellularized grafts in term of angiogenesis promotion after transplantation (up to 1 month) in a fibrotic tissue (cauterized muscular pocket,n=20); (ii) the in vivo osteogenicity of the scaffold-free graft (in comparison to HA/bTCP bone substitute) at 1/2/3 months post-implantation, in an irreversible femoral critical size bone defect (n=28). Angiogenesis was investigated by histomorphometry, cellular engraftment by HLA-I staining, the mineralization by micro-CTscan and the osteogenic genes expression by qRT-PCR on graft explants.

The decellularization of the graft was confirmed by the loss of key osteogenic/ angiogenic genes in comparison to fresh grafts. After intra-muscular transplantation, the stability (with no resorption) of both fresh and decellularized grafts was found at 1 month with a similar level of mineralization and revascularization while the presence of human ASCs (with major osteogenic genes expression) was determined in the implantation site of the fresh grafts. A complete integration and bone fusion were found (at 4/8 weeks post-implantation in the femoral defect) for the 3D graft in comparison to the bone substitute alone which revealed a lack of tissue remodelling and osteogenesis. Interestingly, a delay of 4 weeks was determined in term of the osteogenic genes overexpression for explants with bone substitutes in comparison to the graft made of ASCs.

In conclusion, the ASCs (included in a scaffold-free graft) play a major role for osteogenesis in a fibrotic environment and to recover a bone fusion in a critical-sized bone defect

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DEVELOPMENT OF XENO-FREE EPITHELIAL DIFFERENTIATION MEDIA FOR ADHERENT, NON-EXPANDED ADIPOSE STROMAL VASCULAR CELL CULTURES

Presenter: Manisha K. Shah, PhD (USA)
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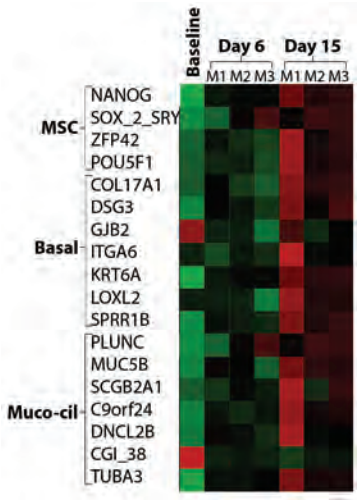
Introduction: Reconstruction of respiratory epithelium is critical for the fabrication of bioengineered airway implants. Epithelial differentiation is typically achieved using bovine pituitary extract (BPE). Due to the xenogenic nature and undefined composition of BPE, an alternative for human applications, devoid of BPE, must be developed. The goal of this study was to develop two BPE-free media, with and without select pituitary hormones (PH), M3 and M2, respectively, which could initiate epithelial differentiation for use in human implantation.

Methods: The ability of the two BPE-free media to initiate epithelial differentiation of adherent, non-expanded stromal-vascular cells grown on porcine small intestinal submucosa was compared to traditional BPE-containing media (M1). Nanostring® was used to measure differences in gene expression of stemness (MSC), basal cell (basal), and ciliated markers (muco-cil), and staining was performed support the gene data.

Results: Compared to baseline, both BPE-free media upregulated epithelial and stemness genes, however this was to a lower degree than BPE-containing media (Fig 1). In general, the expression of basal cell markers (COL17A1, DSG3, ITGA6, KRT6A, LOXL2) and secreted mucous proteins (PLUNC, MUC5B, SCGB2A1) was upregulated. Expression of ciliated markers C9orf24, TUBA3 and DNCL2B were upregulated, indicating that mucus-secreting cell differentiation occurs more rapidly than ciliogenesis. The ability of the adherent stromal vascular cells to upregulate gene expression of both epithelial and stemness markers suggests maintenance of the self-renewal capacity of undifferentiated and/or basal cell-like cells contributing to proliferation and ensuring a persisting source of cells for regenerative medicine applications.

Conclusion: This study provides the initial step to defining a BPE-free epithelial differentiation medium for clinical translation. Thus, either of the proposed BPE-free medium are viable alternatives to BPE-containing medium for partial epithelial differentiation for human translational applications.

Fig 1. Heat map of gene expression by time in culture. BPE-containing M1 showed the greatest overall increase, followed by BPE-free M3 medium, with PH. Red: greater gene expression; green: lower.



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OIL AND WATER: A RANDOMIZED, BLINDED, PLACEBO-CONTROLLED STUDY OF AUTOLOGOUS FAT GRAFTING FOR SCAR PREVENTION AND REMODELING

Presenter: Adam J. Katz, MD (USA)
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Background: It is widely accepted that autologous fat transfer (AFT) is able to alter the appearance and quality of overlying skin and scar tissue. However, the majority of supporting literature is either retrospective or anecdotal; and, those studies that do provide objective and quantitative analyses are limited in scope by their measurement methods and statistics. We performed a multi-center, double-blinded, randomized placebo controlled trial to subjectively and objectively evaluate the effect of AFT on overlying scar tissue.

Methods: Subjects with cutaneous scars were enrolled in the study, with one site randomized to treatment with experimental therapy (AFT) and one site to treatment with saline (control). Outcome metrics were measured at baseline (pre-treatment), 6 months, and 12 months post-treatment. Scars were evaluated using: subjective scar quality assessment (POSAS), hardness (durometer), elasticity (cutometer), color/pigment (colorimeter) and histological analysis. Graft samples were analyzed for cellular quality. Statistics were completed using SPSS.

Results: Although AFT demonstrated a few statistically significant benefits in treated scars over time, these changes were not significantly different than scars treated with saline.

Conclusion: Although many in our specialty endorse and promote the therapeutic effects of fat grafting, our placebo controlled study results suggest that any putative improvements in scar quality related to fat grafting are also achieved using saline. We will discuss limitations of our study as well as potential mechanisms that may explain our findings. Further objective, randomized trials including a control treatment group are required to confirm the therapeutic effects of autologous fat grafting for scar remodeling.

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FAT ON A CHIP MODEL OF HUMAN SUBCUTANEOUS ADIPOSE TISSUE

Presenter: Michelle McCarthy, MS (USA)
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Introduction: Obesity has increased considerably in incidence and frequency both within the United States and globally. Commonly utilized in vitro obesity models employ human or mouse pre-adipocyte cell lines, in a 2-dimensional (2-D) format. Due to the structural, biochemical, and biological limitations of these models, increased attention has been placed on "organ on a chip" technologies for 3-dimensional (3-D) culture.

Methods: Herein we describe a superior culture method employing cryopreserved primary human stromal vascular fraction (SVF) cells and a human blood product derived biological scaffold, Obagel, to create a 3-D adipose depot in vitro. The "fat on a chip" has been validated relative to 2-D cultures based on proliferation, flow cytometry, adipogenic differentiation, confocal microscopy/immunofluorescence, functional assays (adipokine secretion, glucose uptake, lipolysis), and functional response to AMPK inhibitors.

Results: "Fat on a chip" cultures exhibited maintenance of SVF heterogeneity that more closely resembled freshly harvested cells, and increased functionality based on expression of adiponectin, leptin, 2-DG uptake, glycerol secretion, and ability to form fat in vivo. Furthermore, the 3-D cultures were induced selectively to display biomarkers associated with either beige/brown (BAT) or white (WAT) adipose tissue depots, respectively.

Conclusions: The current study validates the utility of Obagel and SVF cells as an in vitro human subcutaneous adipose depot model capable of modeling response to metformin and isoproterenol. Further studies are needed to establish pharmacokinetic and pharmacodynamic profiles in the adipose tissue model. Future studies include using SVF cells isolated from adipose depots in the viscera, omentum, and around vital organs to model multiple anatomical depots.

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A SYSTEMATIC REVIEW OF AUTOLOGOUS PLATELET-RICH PLASMA AND FAT GRAFT PREPARATION METHODS

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NOT PRESENTED

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THE ROUTE BY WHICH INTRANASALLY DELIVERED STEM CELLS ENTER THE CENTRAL NERVOUS SYSTEM

Presenter: Peter Edenhoffer, MD (USA)
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NOT PRESENTED

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REGENERATIVE MEDICINE AND WRIST OSTEOARTHRITIS: INTRA-ARTICULAR INJECTION TREATMENT OF A MIXTURE OF AUTOLOGOUS MICROFAT ASSOCIATED WITH AUTOLOGOUS PLASMA-ENRICHED PLATELETS

Presenter: Guy Magalon, MD (France)
Affiliation: Culture and Cell Therapy Unit INSERM CBT1409
Authors: Eraud JE, Kachouh NK, Curvale CC, Iniesta AI, Mayoly AM, Casanova DC, Sabatier FS, Veran JV, Magalon JM, Legre RL

Introduction: The management of osteoarthritis of the wrist resistant to medical treatment involves stiffening and non-conservative surgery. The search for a minimally invasive therapeutic alternative represents a medical-surgical challenge in the management of this pathology. Intra-articular injection of autologous microfat with autologous platelets rich plasma (PRP) may be a promising alternative. We present the results of the intra-articular injection of an autologous Microfat and PRP mixture in the osteoarthritis wrist at 6 months of follow-up.

Method: AMIPREP is a prospective, single-center, non-comparative phase I-IIa open-label clinical trial. Included patients have Kellgren and Lawrence's Grade 3 or 4 wrist osteoarthritis, which is resistant to medical treatment and pain> 40 mm on the Visual Analogue Scale (VAS).

Four milliliters of a MicroFat-PRP mixture are injected into the radiocarpal joint under local anesthesia in the operating room. The tolerance assessed by the occurrence of adverse events up to one month post-injection is the primary endpoint. The Pain-VAS, the DASH and PRWE functional scores, the strength and the joint amplitudes are also evaluated at each control visit up to 12 months of follow-up. Cartilage regeneration is evaluated at 12 months by the variation of the cartilage section surface measured on a high resolution 3T MRI.

Results: Twelve patients were included and treated between June 2017 and February 2018. No serious adverse events were identified during follow-up. At 6 months of follow-up, all patients had a reduction of pain ≥ 20 mm according to the VAS and 80% of the patients showed a functional improvement with a significant decrease (≥ 10 points) of the DASH and PRWE scores. Measurements of strength and range of motion were not significantly improved.

Conclusion: Intra-articular injection of a mixture of autologous Microfat and PRP is an innovative, simple and minimally invasive procedure that could be a therapeutic alternative to heavy and non-conservative surgeries in the management of osteoarthritis of the resistant wrist medical treatment.

73

DEVELOPMENT OF A HUMAN-DERIVED ADIPOSE ACELLULAR ALLOGENIC FLAP (AAFS) USING PERFUSION DECELLULARIZATION: TOWARDS UNIVERSAL, SHELF-READY FLAPS?

Presenter: Giorgio Giatsidis, MD (USA)
Affiliation: Brigham and Women s Hospital - Harvard Medical School
Authors: Giatsidis G, Orgill DP, Guyette J, Ott HC

Adipose flaps are routinely used in reconstructive surgery to repair large soft tissue defects caused by surgery, trauma, chronic diseases, or malformations. As procurement of autologous flaps causes secondary donor site morbidity in patients, novel solutions are needed. Unfortunately, tissue-engineered biomaterials are currently unable to repair clinically-relevant, large-volume defects. Allogenic flaps could provide a ready-to-use biological alternative if treated with methods to avoid the immune-rejection of the donor's cells. Here, we describe the successful decellularization of a large (> 800 cc) human-derived adipose flap through a perfusion apparatus; we demonstrate the complete removal of the immunogenic cellular components of the flap with the retention of its structural components and vascular network. Our work aims at obtaining a universally-compatible, off-the-shelf acellular allogenic flap (AAF) that could be recellularized with cells from recipient patients and provide an alternative for reconstruction of large-volume soft-tissue defects.

74

CONSTRUCTION OF VASCULARIZED TISSUE ENGINEERING BLADDER WITH AUTOLOGOUS ADIPOSE DERIVED STROMAL VASCULAR FRACTION COMBINED WITH BLADDER ACELLULAR MATRIX

Presenter: Rui-Peng Jia, MD, PhD (China)
Affiliation: Nanjing First Hospital
Author: Jia RP

Introduction: The formation of an effective vascular network can promote peripheral angiogenesis, ensuring effective blood, oxygen and nutrient supply of the engineered bladder, which is important for bladder tissue engineering. Adipose tissue derived stromal vascular fraction (ad-SVF) has been verified to promote vascularization and improve the function of injured tissues. In this study, ad-SVF was introduced as an angiogenic cell source, and seeded into the bladder acellular matrix (BAM) to construct ad-SVF-BAM complex for bladder reconstruction. The morphological regeneration and functional restoration of the engineered bladder were evaluated. In addition, we also explored the role of the Wnt5a/sFlt-1, one of the non-canonical Wnt signaling pathway, in regulating angiogenesis of ad-SVF cells, as well as in maintaining the rational differentiation ability of ad-SVF into vasculature in regenerated tissues.

Methods: Rat tissue engineering bladders were constructed using ad-SVF seeded BAM scaffolds (ad-SVF-BAM) or BAM alone. After 4 weeks and 12 weeks, the tissue regeneration was observed, while the bladder function was evaluated. Different doses of recombinant Wnt5a protein were added to ad-SVF cultured in vitro, and their angiogenesis regulation was explored.

Results: Histological assessment indicated that the ad-SVF-BAM complex was more effective in promoting smooth muscle, vascular and nerve regeneration than the BAM alone, which subsequently led to restoration of bladder volume and bladder compliance. Moreover, exogenous Wnt5a was able to enhance angiogenesis by increasing the activity of VEGFR2, MMP2, and tie-2. Simultaneously, the expression of sFlt-1 was also increased, which inhibited the ad-SVF angiogenesis, therefore, the angiogenic capacity of ad-SVF was stable.

Conclusion: These results demonstrated that ad-SVF may be a potential cell source for tissue-engineered bladder, and the Wnt5a/sFlt-1 pathway was involved in the regulation of ad-SVF autologous vascular formation. Therefore, rational regulation of this pathway can promote neo-microvascularization of tissue-engineered bladder.

1195 **75**

PEDAL FAT GRAFTING: CORRELATING ADIPOSE TISSUE CHARACTERISTICS TO CLINICAL OUTCOMES AND VOLUME RETENTION

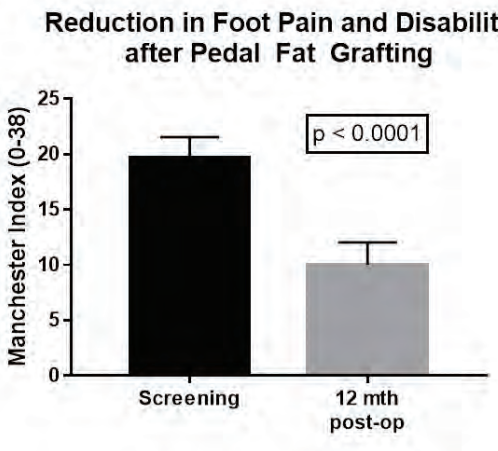
Presenter: Sheri Wang, BS (USA)
Affiliation: University of Pittsburgh
Authors: Wang S, DiBernardo G, James I, Minteer D, Zhang W, Gusenoff B, Marra K, Kokai L, Gusenoff J

Introduction: Pedal fat pad atrophy alters foot pressure distribution, causes debilitating pain and reduces quality of life. Fat grafting is a promising solution to pedal fat pad atrophy but is limited by unpredictable volume retention. Researchers have investigated the relationship between fat characteristics and fat retention in hopes of better predicting outcomes. Studies have demonstrated in mice that high-density fat is associated with increased graft retention. Previous work by our lab demonstrated that CD34+ adipose stem cells (ASCs) are predictive of fat graft retention in mice. We aim to assess the relationship between molecular characteristics of fat, patient factors, and clinical outcomes.

Method: 30 nondiabetic and 6 well-controlled diabetic patients were enrolled in 2 IRB approved prospective, randomized crossover clinical trials. The patients were randomized into either the standard of care or autologous fat grafting. Fat was harvested by manual liposuction, processed by Coleman technique, and injected into the forefoot. Manchester Foot Pain and Disability Index (MFPDI) was used to assess clinical outcomes. Ultrasound was used to assess submetatarsal tissue thickness at baseline, 6, 12, and 24mos. Processed lipoaspirate was returned to the lab for stromal vascular fraction (SVF) isolation, flow cytometry, and collagen assessment.

Result: Mean age was 63.3±7.8 years. Mean BMI was 26.6±5.3. Patients experienced a 9.6-point improvement in the MFPDI at 12mos vs baseline ($p<0.0001$). Tissue thickness retention percentage was correlated to improved total and component MFPDI at 12, 18, and 24mos ($p<0.05$). The SVF harvested per ml lipoaspirate was positively correlated with tissue thickness at 6 ($p=0.01$), 12 ($p=0.006$), and 24mos ($p=0.004$). The correlation between proportion of CD34+ ASCs and tissue thickness did not reach statistical significance. Collagen 1 content is negatively correlated with percent CD34+ ASCs ($p<0.001$) and SVF viability ($p=0.023$).

Conclusion: Predicting fat graft volume retention remains a challenge. The correlation between SVF viability and increased volume retention warrants further investigation. These discoveries allow us to better predict fat graft retention and clinical outcomes, leading to higher patient satisfaction.



POSTER PRESENTATIONS

1P

A 10-YEAR JOURNEY: TRENDS IN FAT GRAFTING ACROSS THE MAJOR PLASTIC SURGERY JOURNALS

Presenter: Alexandra Conde-Green, MD (USA)
Affiliation: Rutgers New Jersey Medical School
Authors: Conde-Green A, Liu FL, Gala ZG, Hasbun SH, Arbelaez JA, Mitchell BM, Cansancao AC

NOT PRESENTED

2P

SYSTEMATIC REVIEW OF THE EFFICACY OF FAT GRAFTING AND PLATELET-RICH PLASMA FOR WOUND HEALING

Presenter: Oliver J. Smith, MBChB, MRCS (United Kingdom)
Affiliation: Royal Free Hospital
Authors: Smith OJ, Kanapathy M, Hachach-Haram N, Mann H, Khajuria A, Mosahebi A

NOT PRESENTED

3P

GLUTEOPLASTY WITH IMPLANTS AND LIPO TRANSFERENCE

Presenter: Aristides Arellano, MD (Mexico)
Affiliation: Clinica Dermatologica y Cirugia Estetica de Puebla
Author: Arellano A

Gluteoplasty (gloutὸs from the greek, grupa + plassein, to shape) denotes the plastic surgery and the liposuction procedures for the correction of the congenital, traumatic, and acquired defects and deformities of the buttocks and the anatomy of the gluteal region; and for the aesthetic enhancement (by augmentation or by reduction) of the contour of the buttocks.

The corrective procedures for buttock augmentation and buttock repair include the surgical emplacement of a gluteal implant (buttock prosthesis); liposculpture (fat transfer and liposuction); and body contouring (surgery and liposculpture) to resolve the patient's particular defect or deformity of the gluteal region. Also, in the praxis of sexual reassignment surgery, the prosthetic and liposculpture augmentation of the buttocks can be performed on transsexual and transgender women to enhance the anatomic curvature of the gluteal region in order to establish the markedly feminine buttocks and hips that project more (to the rear and to the side) than masculine hips.

The functional purpose of the buttocks musculature is to establish a stable gait (balanced walk) for the man or the woman who requires the surgical correction of either a defect or a deformity of the gluteal region; therefore, the restoration of anatomic functionality is the therapeutic consideration that determines which gluteoplasty procedure will effectively correct the damaged muscles of the buttocks. The applicable techniques for surgical and correction include the surgical emplacement of gluteal implants; autologous tissue-flaps; the excision, (cutting and removal) of damaged tissues; lipoinjection augmentation; and liposuction reduction to correct the defect or deformity caused by a traumatic injury (blunt, penetrating, blast) to the buttocks muscles (gluteus maximus, gluteus medius, gluteus minimus), and any deformation of the anatomic contour of the buttocks. Likewise, the corrective techniques apply to correcting the sagging skin of the body, and the muscle and bone deformities presented by a formerly obese patient, after a massive weight loss (MWL) or bariatric surgery procedure; and for correcting congenital defects and deformities of the gluteal region.

1105 **4P**

REGENERATIVE MEDICINE OF MESENCHYMAL STEM CELLS: A PROMISING TREATMENT OF FRACTURE, PARALYSIS AND WOUND OF ANIMALS

Presenter: Kamlesh K. Bajwa, MSc (India)
Affiliation: National Dairy Research Institute
Authors: Bajwa KK, Saini S, N Malik H, Sharma V, Kumar D, Kumar S, Kumar S

Advances in mesenchymal stem cells (MSCs) research have opened new perspectives for regenerative and reproductive medicine in human being and animals. Mastitis and massive wound are the most expensive dairy disease as the animals are suffering long time and rendering them useless and unproductive. MSCs can be differentiated in osteocytes, chondrocytes, adipocytes, neurone like cells and sperms and oocytes which has immense application in regenerative medicine and reproductive biology. Here we report the treatment of massive wound and mastitis of cattle and buffaloes and paralysis and fracture of dogs that can be cured completely with adipose tissue derived MSCs. Adipose tissues were isolated aseptically from tail head region fat pad of cattle and buffalo by liposuction methods. These adipose tissues were processed aseptically and digested with collagenase enzyme for 2 h in CO2 incubator. MSCs were passed through 47 µm filter after collagenase digestion and cultured in medium containing DMEM/F12, 10% FCS and 10 µl/ml FGF growth factor. The cultured MSCs were characterized with alkaline phosphatase, molecular markers like CD105, CD44, CD90 and CD34 positive expression whereas CD34 and CD45 markers negative expression in cattle, buffalo and dog. Immunostaining of MSCs was also carried out with anti-antibody of CD90, CD105 and CD44 observing positive expression. MSCs were cryopreserved using DMEM + 10% serum and 10% DMSO cryoprotectant into 2 ml cryovial and kept into liquid nitrogen. MSCs were injected around @ 1-5 million cells/site of injury of animal. We had treated massive wounded 400 cattle, 60 buffaloes and 28 bulls and 50 paralyzed, 135 massive wounded, 15 fractured of dogs using in vitro cultured MSCs. All the suffering animals were cured completely and permanently one an average 30 days. Surprisingly, we observed new skin and hair gradually covered the wound in all the animals. In conclusion, MSCs for regenerative medicine therapy can cure chronic incurable massive wound, mastitis, of cattle, buffaloes and paralysis and fracture dogs completely. In the present extensive study in animal models, we postulate that MSCs can also be cured in human diseases like, wound, fracture, paralysis, leprosy, diabetes, cancer, Alzheimer, Parkinson in near future.

1105 **4P**

REGENERATIVE MEDICINE OF MESENCHYMAL STEM CELLS: A PROMISING TREATMENT OF FRACTURE, PARALYSIS AND WOUND OF ANIMALS

Presenter: Kamlesh K. Bajwa, MSc (India)
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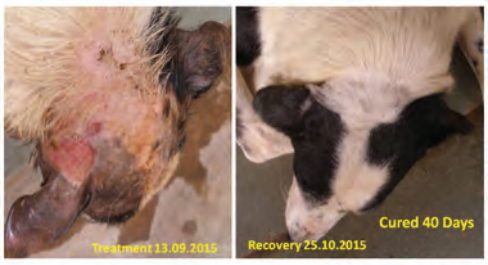
Authors: Bajwa KK, Saini S, N Malik H, Sharma V, Kumar D, Kumar S, Kumar S



5P

BREAST AUGMENTATION USING LOOPS AND LIPOFILLING: HOW I DO IT?

Presenter: Marwan H. Abboud, MD (Belgium)
Affiliation: Chu Tivoli
Authors: Abboud MH, El Hajj H, Abboud NM

WITHDRAWN

6P

VALIDATION OF PORCINE ADIPOSE-DERIVED STROMAL/STEM CELLS FOR WOUND HEALING STUDY

Presenter: Joanna Bukowska, PhD (Poland)
Affiliation: Institute of Animal Reproduction and Food Research
Authors: Bukowska J, Walendzik K, Kopcewicz M, Gawronska-Kozak B

Introduction: Adipose derived stromal/stem cells (ASCs) are promising strategy for damaged tissue. The growing interest in human ASCs application in skin wounds became a part of a therapy that significantly improve healing. The use of ASCs in regenerative medicine routinely employs human donors whereas their equivalents that derive from domestic animals have received minimal attention. Since variety of pig organs and tissues reveal multiple similarities to their human counterpart, investigating pig ASCs (pASCs) is valuable for the evaluation of their efficacy in wound healing in human. Hence, the present study assesses functional features of pASCs and bioactivity of pASCs conditioned media (pASCs-CM) that might provide alternative cues for skin wound healing.

Methods: Porcine (Sus scrofa domestica) stromal vascular fraction (SVF) cells were isolated and cultured to expand to ASCs using standard protocol. Conditional medium (pASCs-CM) was collected from subconfluent cells. ASCs phenotype was confirmed through assessment of (i) the levels of mesenchymal stem cells markers (MSC): CD29, CD73, CD90, CD105 and (ii) clonogenicity (CFU-F) assay. Furthermore, metabolic activity of pASC as well as the effect of pASCs-CM on dermal fibroblasts (DFs): (i) viability, (ii) migration, (iii) pro-fibrotic markers expression (collagen type 1, 3 (col1, col3) were examined.

Results: Porcine ASCs showed the expression of MSC markers (CD29, CD73, CD90, CD105) at the levels comparable to those observed in bone marrow MSC (used as positive control), and created colonies when seeded in clonal densities. Moreover, pASCs-CM reduced DFs metabolic activity within 24h and 48h. Likewise, wound healing in vitro assay revealed inhibitory effect of pASC on DFs motility when compared to control media-treated cells. Furthermore, the administration of pASCs-CM downregulated the mRNA levels of pro-fibrotic markers: Col1 and Col3.

Conclusions: Pig ASCs fulfill minimal criteria for cultured MSCs. The inhibitory effect of pASCs-CM on DFs cellular characteristic underlines the role of pASC secretome and thus suggests that pASCs might act in paracrine manner. The in vitro data indicates pASC as attractive candidates for future transplantation study.

7P

FACIAL REJUVENATION WITH ADIPOSED DERIVED STEM CELLS ASSISTED LIPOTRANSFER

Presenter: Chao-Chuan Wu, MD (Taiwan)
Affiliation: Chai-Yen Plastic and Aesthetic Clinic
Author: Wu CC

Introduction: Since 2013 I began to performe cell-assisted lipotransfer for facial rejuvenation for female and male patients.

Method: I used ultrasound-assisted liposuction for fat collection. We washed the fat to remove the blood cells and connective tissue waste. Then 40 cc of the washed fat was digested with collagenase and processed for about 90 minutes. Then the final product, the SVF was added to the other part of washed fat.

Fat injection to the face was performed with 1 cc syringe with a blunt cannula mannually. The amount of fat injected ranged from 30 to 50 cc per face according to the patient's individual condition. The total time of operation took about 4-5 hours, and preventive antibiotics was used in every patient. Intravenous sedation was performed by an anesthesiologist for every patient.

Result: The graft take is good and the skin texture and skin turgor also improve after injection.

Conclusion: Cell-assisted lipotransfer of the face can improve the survival rate of graft take and even improve the skin texture and skin turgor. However strict strict aseptics must be followed to avoid infection. Patient safety is the primary issue, anesthesiologist, washoff the collagenase, blunt cannula to prevent intrvasation, and the amount of fat injected, are all important factors for a successful and safe procedure of cell-assisted lipotransfer in the face for rejuvenation.

8P

ENRICHMENT OF HUMAN AMNIOTIC MEMBRANE WITH ADIPOSE-DERIVED MESENCHYMAL STEM CELLS: FUTURE IN WOUND CARE

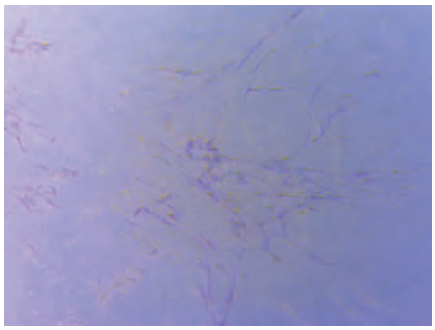
Presenter: Angelica Schettino, MD (Brazil)
Affiliation: Marcilio Dias Naval Hospital
Authors: Schettino A, Fusco MA, Franco D, Bueno DF, Pinheiro C, Sant'Ana L, Fonseca AC, Gregorio ML

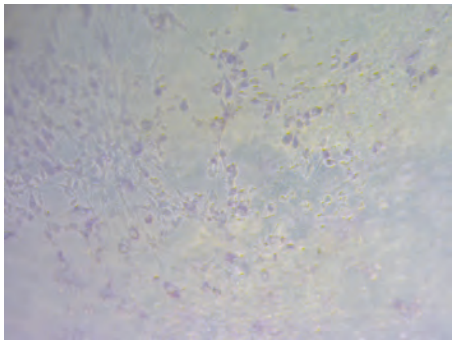
Introduction: The search for more advanced dressings for the different types of wounds has been tireless throughout the world. Recently, Adipose-Derived Mesenchymal Stem Cells (ADSCs) have been gaining attention, especially in the field of Regenerative Medicine, mostly due to its multipotent properties (Rigotti, 2009) which allow its use in a variety of clinical conditions, including wound healing. On the other hand, the use of human amniotic membrane (HAM) as a biological dressing dates back to 1910 (Davis, 1910). HAM is still considered an ideal dressing today due to the presence of different growth factors and cytokines of great importance to the healing process (Herndon et al., 2017). Thus, the use of HAM added with ADSCs could act synergistically in the healing of wounds.

Methods: To achieve this goal, HAM collected at Marcílio Dias Naval Hospital (HNMD) was used as substratum to culture 105 Passage-3 ADSCs (Zuk, 2001) collected from lipoaspiration at Marcílio Dias Naval Hospital (HNMD). For better adhesion of ADSCs, HAM was previously stored for 28 days at 4°C to achieve amniotic epithelial cells death (Hennerbichler et al., 2007) and then treated for 30 seconds with 0,5M NaOH for amniotic epithelial cells removal and basement membrane exposure (Saghizadeh et al., 2013). Also, Petri dishes were treated overnight with 16% BFS to prevent adhesion of the cells to the plaque.

Results: After four days, 1% toluidine blue was added to the dishes for 5 minutes in order to successfully visualize ADSCs added to the previously denuded HAM, using an inverted microscope.

Conclusion: To our knowledge, this is the first time ADSCs were seeded in HAM. The use of a powerful scaffold added to high plasticity cells makes HAM-ADSC complex a very promising alternative for the treatment of wounds of difficult healing and should be the subject of further studies.





9P

THREE-DIMENSIONAL EVALUATION OF BREAST VOLUMES: A NOVEL APPROACH TO ASSESS FAT GRAFTING OUTCOMES

Presenter: Carlo M. Oranges, MD (Switzerland)
Affiliation: Basel University Hospital
Authors: Oranges CM, Harder Y, Haug M, Kalbermatten DF, Schaefer DJ, Thieringer FM

Three-dimensional photography is becoming crucial to assess surgical changes of breast volume, tissue distribution and projection. However, the majority of methods available are still expensive or not accurate. Based on a recent work from our group, we aim to present an innovative, simple and inexpensive three-dimensional assessment procedure used to evaluate breast volume augmentation after fat grafting [1].

The three-dimensional scanning process is performed using the Structure Sensor 3D scanner (Occipital, Inc., Boulder, Colo.) connected to an iPad Pro (Apple, Inc., Cupertino, Calif.). The device is a structured/infrared light handheld scanner that measures 11.92 (width) × 2.9 (height) × 2.8 (depth) cm, has a weight of 95 g, and is available at a price of $379. Preoperative and postoperative three-dimensional scans are obtained from patients undergoing fat grafting to treat breast surgery sequelae, such as contracted scars or contour deformities. MeshLab 2016, a three-dimensional mesh-processing application available as open-source software, is used to elaborate the three-dimensional images, clean the raw data, and calculate breast volumes. The total breast volumes are assessed at baseline and at postoperative follow-up visits to estimate percent augmentation. The influence of the body mass index (BMI) is excluded at each step. Results coherent with the volume of transplanted fat are obtained demonstrating the accuracy of the volume estimation process.

This novel three-dimensional technology allows objective evaluation of breast volume and morphology changes, which represent an important outcome for procedures such as fat grafting. This approach could easily become part of the everyday plastic surgery practice, not just in the academic setting but even in private, because of the very limited dimensions and cost of the device and its simple handling [1].

1. Oranges CM, Thieringer FM, Kalbermatten DF, Haug M, Schaefer DJ. The Evolution of Photography and Three-Dimensional Imaging in Plastic Surgery. Plast Reconstr Surg. 2018 Jan;141(1):196e-197e.

10P

ENHANCING THE RESULTS OF LOWER BLEPHAROPLASTY WITH FAT TRANSPLANTATION

Presenter: Yu-Hsiu Yen, MD, PhD (Taiwan)
Affiliation: Cathay General Hospital
Authors: Yen YH, Pu CM, Lu SY

The aesthetic goals of lower blepharoplasty include not only tightening the loose lower eyelid skin, reducing the herniated orbital fat but also improving the deep nasojugal groove or tear trough. We corrected the loose lower eyelid by removal of estimated excess skin. Capsulopalpebral fascia tightening and minimal herniated orbital fat removal were carried out to correct the budging orbital fat. Furthermore, arcus marginalis release was also performed at the same time to improve nasojugal groove. Even we used all of the above procedures to restore the young appearance of lower eyelid but deep tear trough deformity persisted in most severe cases. Fat grafting is a powerful weapon for plastic surgeons to correct the deformed or depressed contour. For correcting the deep nasojugal groove after lower blepharoplasty, we harvested autologous fat from abdominal wall and transplanted it into sub-orbicularis oculi space to blend the lid-cheek junction by micro-autologous fat transplantation (MAFT) gun. This report summarizes the author's personal surgical techniques and results, which prove a real benefit from lower blepharoplasty in conjunction with autologous fat transplantation to enhance the result of lower blepharoplasty.

11P

TRENDING FAT GRAFTING ACROSS THE WORLD: ANALYSIS OF THREE ANNUAL MAJOR PLASTIC SURGERY MEETINGS

Presenter: Farrah C. Liu, BS (USA)
Affiliation: Rutgers New Jersey Medical School
Authors: Liu FC, Arbelaez JA, Gala ZG, Hasbun SH, Cansancao AC, Conde-Green AC

Purpose: Fat grafting has seen a recent surge in both reconstructive and aesthetic endeavors. Clinical research has explored the applicability of adipose stem cells beyond traditional boundaries. Despite rising international interest in the regenerative outcomes, no methodological standardization exists. This study analyzes the literature on fat grafting techniques during the experimental and clinical stages to show that more funding and emphasis on fat-grafting can unlock its true potential.

Methods: A systematic review of all program presentations in plastic surgery conferences (ISAPS, ASPS, ASPS) for the years 2006 to 2016 was performed. Programs from the annual conferences were obtained on the websites or via hard copy archives that were shipped directly to Newark, NJ. Independent reviewers classified each itinerary listed, and filtered for the relevant fat-grafting presentation. The data was further divided by congress, year, country of publication, subject, results, and area of the body.

Results: The review yielded a total of 628 presentations, with 218 (34.7%) from ISAPS, 213 (33.9%) from ASAPS, and 197 (31.4%) from ASPS. Abstracts consisted of 29.9% of the total, while big session presentation consisted of 41.1%, and 28.8% were master classes. Basic science research made up 21.1%, while the rest were human studies (78.9%). Pre-operative assessment was studied in 6.4%, and the majority (61.9%) addressed clinical outcomes. Complications, harvesting, processing, techniques, and future uses made up the remaining investigations. Aesthetic presentations made up 59.7% while reconstructive purposes were 5.6%, and the remaining projects addressed both Facial regions were the most common area, closely followed by breast, and gluteal region.

Conclusion: To our knowledge, this is the first study of this magnitude to inclusively analyze prior trends in fat grafting, its origins, current research, and future implications. Fat grafting is becoming increasingly widespread in clinical practice, yet a lack of standardization and an absence of basic science and clinical evidence in certain aspects prevents its vast potential. We hope this review will provide some insight in the evolution of fat grafting, and emphasize the facets that can undergo investigation.

12P

A SIMPLE METHOD FOR CONCENTRATING NANOFAT GRAFT BY CENTRIFUGATION AND NEGATIVE PRESSURE

Presenter: Hongwei Liu, MD, PhD (China)
Affiliation: The First Affiliated Hospital of Jinan University
Authors: Liu H, Wu YD

NOT PRESENTED

13P

THE EFFECTS OF INTRAVENOUS INSULIN ADMINISTRATION ON THE INCREASE IN SVF CELL DENSITY

Presenter: Agus Budi, MD (Indonesia)
Affiliation: Faculty of Medicine Airlangga University
Author: Budi A

Background: The amount of adipose cells harvested during liposuction is an important factor in SVF processing. Diabetic patients tend to have thinner fat layer which in turn will limit the amount of adipose cells collected during the procedure. Therefore, an intervention is needed to acquire the desired amount of good quality adipose cells. A blood glucose level of >200mg/dl will hamper wound healing and insulin administration is invariably needed to control its level. This leads us to the question: Will intravenous insulin also affect the quantity and quality of adipose cells?

Objectives: The purpose of this study is to determine whether insulin administration increases the amount of SVF cells as a product of lipoaspirate processing.

Results: We studied 5 patients who were subjected to lipoaspiration. Three of these patients receive intravenous insulin before the procedure. In each of these 3 patients, we harvested more than 4 million cells with >97% viability and only less than 4 million cells with <85% viability was harvested from the other two patients who did not receive insulin.

Conclusion: There is a proven benefit of insulin administration before liposuction in increasing the quantity and viability of cells harvested.

Keyword: Diabetes, Insulin, SVF, Cell Viability

14P
CLINICAL USE OF CRYOPRESERVED WHOLE ADIPOSE TISSUE

Presenter: Michael Badowski, PhD (USA)
Affiliation: Celebration Stem Cell Center
Authors: Badowski M, Harris DT, Muise A

Introduction: Autologous fat grafting has now been used extensively and successfully for more than two decades. Although most adipose grafts and adipose-derived MSC therapies are done with fresh tissue, cryopreservation of tissue allows much greater flexibility of use.

Methods: Over the course of five years, 250 cryopreserved adipose samples were thawed and returned to the collecting physician for subsequent autologous applications. Samples were stored with the mean cryogenic storage time of 10 months with some samples being stored as long as 46 months. The volumes of tissue stored varied from 12 cc to as large as 1440 cc.

Results: Upon thaw the volume of recovered whole adipose tissue averaged 67% of the amount stored. This recovery yield ranged from a low of 46% for some patients to a high of 100%. Recovery yield was not found to be a function of patient age, collection volume, amount of tissue thawed, or length of time in cryopreservation. Viability of thawed cells remained high with a mean value of 91%.

Conclusions: While an average recovery of 67% of volume frozen indicates that the use of banked and thawed tissue requires a larger amount of sample be taken from the patient initially, this requirement is easily accomplished by an experienced clinician. As cryopreservation of adipose tissue becomes more commonplace physicians will find it helpful to know what will be the likely amount of tissue that will be available after thaw procedures.

15P
PURIFICATION OF EXOSOMES FROM ADIPOSE-DERIVED CONDITIONED MEDIA

Presenter: Sherry Collawn, MD, PhD (USA)
Affiliation: UAB
Authors: Collawn S, Banerjee NS, Chow LT

Introduction: There is considerable interest on the role of secreted membrane vesicles such as exosomes in mediating communication amongst cells and in influencing cell migration. We tested whether exosomes were present in the adipose-derived stromal cell- conditioned (ADSC-CM) using exoquick preparations with nanosight evaluations and findings are consistent with the presence of exosomes. Addition of these vesicle exoquick preparations that have been further purified with size exclusion columns accelerate migration in scratch assays of submerged cultures of primary human keratinocytes.

Methods: Cell culture media from ADSC-CM is centrifuged to remove detached cells and debris. The manufacturers recommended aliquot of ExoQuick-TC polymer is added to the conditioned media. The resulting pellet is resuspended in PBS. For purification, size exclusion columns (IZON Science) are used and fractions collected. Fractions 7, 8, and 9 contain most of the exosomes. Scratch assays of submerged cultures of primary human keratinocytes are performed by seeding neonatal keratinocytes into 24-well plates and allowing them to grow 2 days. At confluence the cells are scratched with a pipette. The time course of cell migration is followed with photos taken with the Nikon SMZ18 microscope.

Results: We have now purified our exosomes with IZON column purification and Nanosight evaluations are reported in figure 1 below. Results are consistent with the presence of exosomes.

Figure 1. Nanosight evaluations of exosomes obtained from ASC (ADSC)-conditioned media using Exoquick (System Biosciences) followed by IZON size exclusion columns. The left figure demonstrates the vesicle profile for 5 runs of the sample. The right figure is an average of the 5 runs (standard error bars in red). These exosome preparations enhance cell migration in keratinocyte scratch assays (Table 2).

Conclusions: We have demonstrated the presence of exosomes in the ADSC-CM. The addition of ADSC-CM exosomes accelerated migration in keratinocyte scratch assays in comparison with controls. Our future goal is to determine the specific factors in the ADSC exosomes that accelerate migration.

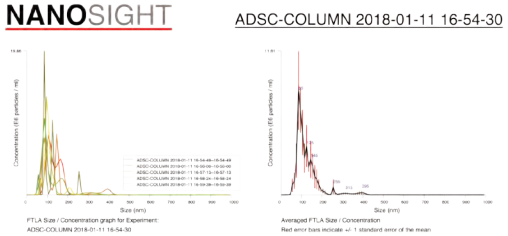


Figure 1. Nanosight evaluations of exosomes obtained from ASC (ADSC)-conditioned media using Exoquick (System Biosciences) followed by IZON size exclusion columns. The left figure demonstrates the vesicle profile for 5 runs of the sample. The right figure is an average of the 5 runs (standard error bars in red).

Experiment	Time Zero (wells 1,2,3) Scratches in microns	12 hours (wells 1,2,3) Scratches in microns	24 hours (wells 1,2,3) Scratches in microns
ADSC exosome izon column eluate (fractions 7,8,9)	1121,1127,986	629,468,572	294,0,0
ADSC conc cm	1119,1322,1247	562,741,586	328,377,407
Regular Media	1291,1330,1265,1186,1213	1171,1129,629,870,985	451,873,671,662,682

Table 2A: The wound gaps immediately after the scratch (Time Zero) and 12 and 24 hours after the scratch in submerged cultures of primary human keratinocytes are measured in microns. The numbers are paired such that the first number in each column is the same well at time zero then 12 and 24 hours later. Narrower gaps indicate more rapid healing upon the addition of purified exosome preparations (exoquick followed by IZON column chromatography) from cultured primary ADSC-CM, or with ADSC-CM. Column purified exosomes (fractions 7,8,9) contain the purified exosomes. Regular media is the control.

16P

ADIPOSE-DERIVED STEM CELLS ATTENUATE ATOPIC DERMATITIS-LIKE SKIN LESIONS IN NC/NGA MICE

Presenter: Ji-Ung Park, MD (Soth Korea)
Affiliation: Seoul National University Boramae Hospital
Authors: Park JU, Park HS, Son YS, Hong HS, Kim SD

Introduction: There is an unmet need in novel therapeutics for atopic dermatitis (AD). Recently, adipose-derived stem cells (ADSCs) showed a potential to ameliorate AD in both human and animals. We examined the effect of ADSCs for the treatment of AD-like skin lesions in NC/Nga mice and compared it to that of conditioned medium of adipose-derived stem cells (ADSC-CM).

Method: AD-like skin lesions were induced in NC/Nga mice by 2,4-dinitrochlorobenzene (DNCB) application. Autologous ADSCs and conditioned medium Adipose-derived stem cells were harvested and injected intralesionally three times whereupon mice were sacrificed on day 53 (4 days after the last injection). Clinical severity, histopathologic findings, as well as the results of immunohistochemistry, immunofluorescence, and enzyme-linked immunosorbent assay experiments were compared between the following groups: sham naïve control (A, n = 3), saline-treated (B, n = 6), ADSC-treated (C, n = 6), ADSC-CM-treated (D, n = 6), and 2.5% cortisone lotion-applied (E, n = 6).

Results: Groups C, D, and E demonstrated significantly lower severity index compared to that of group B on day 53 ($P = 0.000$). Skin thickness measured by a calliper was significantly thinner ($P = 0.000$) and the numbers of mast cells were significantly lower in those groups ($P < 0.001$). Expression levels of thymic stromal lymphopoietin ($P < 0.001$), CD45 ($P < 0.001$), and chemoattractant receptor-homologous molecule ($P < 0.001$) were also significantly decreased. Serum immunoglobulin E levels elevated by DNCB application were slightly decreased in groups C–E. In contrast, immunoglobulin E level was further elevated in group B. Tissue levels of interferon-gamma and serum levels of interleukin-33 decreased in groups C–E ($P=0.003$, $P=0.048$, and $P=0.006$, respectively). Serum level of interleukin-4 was significantly decreased only in group D ($P < 0.001$). In addition, serum level of interleukin-13 was also significantly decreased in groups C and E ($P < 0.05$)

Conclusions: Autologous ADSCs and their conditioned culture medium demonstrated immunomodulatory effects and improved DNCB-induced AD-like skin lesions in NC/Nga mice by reducing inflammation associated with Th2 immune response. Injection therapy using autologous ADSCs or their condition

17P

CUTANEOUS WOUND HEALING EFFECTS OF MESENCHYMAL STEM CELLS AND THEIR SHEETS OVEREXPRESSING PLATELET-DERIVED GROWTH FACTOR IN DOGS

Presenter: Namyul Kim, DVM (South Korea)
Affiliation: Seoul National University
Author: Kim N

Introduction: Platelet-derived growth factor (PDGF) is one of the growth factors that play a key role in each stage of the wound healing and the first approved cytoactive factor by the U.S. FDA for wound healing. Various approach for stem cell delivery have attempted to increase wound healing. I compared PDGF-overexpressed adipose derived mesenchymal stem cells (PDGF-MSCs), its cell sheet (PDGF-CS), undifferentiated MSC sheet (UCS) and undifferentiated MSCs (U-MSCs) on cutaneous wound model in dogs.

Materials and Methods: Six square full-thickness wounds (1.5 x 1.5 cm) were created on the either side of dorsal thoracic region in 8 dogs. Cell sheets (PDGF-CS or UCS) were carefully placed and covered in entire wound beds and stem cells (PDGF-MSCs or U-MCS) was injected intradermally around wound area. After 5 and 10 days, wounds were harvested and evaluated macroscopically and histopathologically.

Result: On gross examinations of day 5 and 10, the rate of epithelialization was significantly higher in PDGF-CS**, UCS*, PDGF-MSCs** and MSCs* groups than in the control groups (*$P<0.05$, **$P<0.01$). On contraction and total healing rate, stem cell* and sheet groups** had significantly higher than control groups at day 10 (*$P<0.05$, **$P<0.01$). Histopathologically, all experimental groups had longer and thicker regenerated epithelium than control groups and rete ridge-like structure were significantly identified on PDGF-CS, PDGF-MSCs. More proliferative keratinocytes (Ki67) were detected in PDGF-CS, PDGF-MSCs than other groups at day 10. In granulation tissue, PDGF-CS, UCS groups are significantly higher than control groups on histological score (*$P<0.05$) and collagen deposition (**$P<0.01$) at day 5 and 10. Activated fibroblasts (FAP α) were more detected in experimental groups than control groups and the most activated fibroblasts were detected in PDGF-CS group. PDGF-CS and PDGF-MSCs groups showed more numerous number of blood vessels although significant difference was not found among experimental groups.

Conclusion: PDGF-CS, UCS, PDGF-MSCs and U-MSCs accelerated cutaneous wound healing. PDGF groups (PDGF-MSCs and PDGF-CS) groups increased blood vessels on wound bed and epithelium proliferation and cell sheets groups (PDGF-CS, UCS) improved quantity and quality of granulation tissue.

18P

ADIPOSE-DERIVED STEM CELL INDUCED ENDOTHELIAL PROGENITOR CELL SALVAGE ISCHEMIC SKIN FLAP BY PROMOTING ANGIOGENESIS

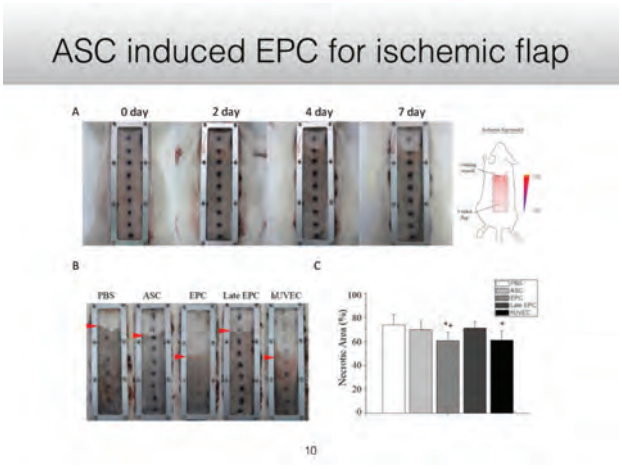
Presenter: Yuan-Yu Hsueh, MD, PhD (Taiwan)
Affiliation: National Cheng Kung University Hospital
Authors: Hsueh YY, Wang D, Chang Y, Lin S, Wu C

Purpose: To facilitate the survival of ischemic skin flap by endothelial progenitor cell induced from adipose-derived stem cells (ASC).

Materials and Methods: ASCs were harvested and processed from lipoaspirate from human liposuction surgery and treated in endothelial growth medium for 3 days to induce early endothelial progenitor cell (EPC). Laminar shear stress was then given in continued flow system to induce late EPC. The in vitro phenotype of endothelial cell function was investigated with tube formation assay in 3D Matrigel. Therapeutic cells (1x106 cells) were injected equally into the hypodermis of skin flap 3 days before surgery. Ischemic dorsal skin flap (10x3 cm) was then created on back of Sprague-Dawley rats (250~300 g) with special designed skin flap chamber to obstruct collateral circulation from the adjacent skin. Seven days after surgery, the skin flaps were harvest to analyze the survival and tissue PCR.

Results: To analyze the in vitro endothelial function of the therapeutic cells, the tube formation assay in Matrigel revealed better tube formation ability in LSS and hUVEC cells after 3 hours. The EPC cells remained viable with minimal cellular extension, as comparted to ASC cells. After the therapeutic cells were injected and the dorsal ischemic flaps were created for 7 days, large area of flap necrosis was seen in PBS group. In EPC and hUVEC groups, the ischemic skin flap could be significantly rescued, with reduced cell necrosis. Tissue PCR of survived flaps revealed significantly increased PECAM signals in both EPC and hUVEC groups.

Conclusion: Using this unique ischemic flap chamber, we clearly demonstrate the therapeutic effect of induced early EPC from ASC to improve the skin flap survival, facilitating enhancing signals of angiogenesis. This preliminary result supports the clinical feasibility to apply autologous cell therapy using ASC cells for clinical ischemic disease.



19P

A PAPER-SUPPORTED APTASENSOR BASED ON UPCONVERSION LUMINESCENCE RESONANCE ENERGY TRANSFER FOR THE ACCESSIBLE DETERMINATION OF EXOSOMES

Presenter: Xiaosong Chen, MD, PHD (China)
Affiliation: Fujian Medical University Union Hospital
Author: Chen X

NOT PRESENTED

20P

OBESITY AND THE SKIN: DOES EPIDERMAL FOXN1 REGULATE DERMAL WHITE ADIPOSE TISSUE (DWAT)?

Presenter: Katarzyna Walendzik, MS (Poland)
Affiliation: Institute of Animal Reproduction and Food Research
Authors: Walendzik K, Bukowska J, Kopcewicz M, Gimble J, Gawronska-Kozak B

Skin wound healing is a dynamic and complex process involving keratinocytes, dermal fibroblasts and intradermal adipocytes (dWAT). dWAT is a unique population of fat cells actively participating in the processes of skin healing and thermoregulation. The molecular determinant regulating the wound healing process is epidermal transcription factor Foxn1 which activity is associated with scar-forming skin wound healing. Since Foxn1 deficient (nude) mice are reported to be resistant to diet induced obesity, this study explored the possible contribution of Foxn1 factor to dWAT modulation. Foxn1::Egfp transgenic mouse, in which the green fluorescent reporter mirrors Foxn1 expression, and control (B6) mice were used. Heterozygous mice possessing one wild-type Foxn1 allele and one copy of the Foxn1-eGFP fusion are phenotypically normal although the slight differences in fur coat were observed, particularly in old animals. Adult (2 months) and old (18 months old) mice were divided into two experimental groups fed: (1) a low-fat diet (LFD) and (2) a high-fat diet (HFD) for 8 weeks. Body weight and body composition were measured every week. Four (4mm diameter) excisional skin wounds were made on the back of the mice. Post-wounded skin tissues were collected at 3, 7, 14 and 21 days after wounding. Foxn1:Egfp male mice at 4 and 20 months of age fed for a period of 8 weeks with HFD gained significantly less body weight than their male B6 counterparts. The body weight gain in HFD males was the result of the increase in fat mass. However, the fat mass content at each measurement time point was lower in Foxn1:Egfp then B6 counterparts. Histological analysis of post- wounded skin tissues from Foxn1::Egfp mice confirmed the contribution of Foxn1 in the re-epithelialization process. The data also revealed a delay in the re-epithelialization in older mice, especially in the HFD group. The flow cytometry analysis of the cells isolated from post-wounded skin tissues (day 7) of Foxn1::Egfp mice revealed a decrease in the percentage of Foxn1::eGFP+ cells in older mice particularly those fed HFD. The phenotypic characteristics of cells showed accumulation of Sca1+ cells (marker of stem cells) in the Foxn1/eGFP- cell population. On the contrary, the increase in the accumulation of CD24

21P

IN VIVO AND CLINICAL EVALUATION OF THE EFFECT OF STROMAL VASCULAR FRACTION-ENHANCED FAT GRAFTING ON SOFT TISSUE AUGMENTATION

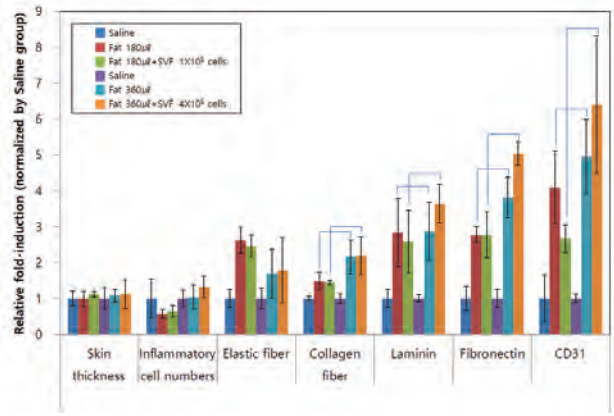
Presenter: Hyung Min Hahn, MD (South Korea)
Affiliation: Ajou University Hospital
Authors: Hahn HM, Ha N, Lee L, Yeom Y

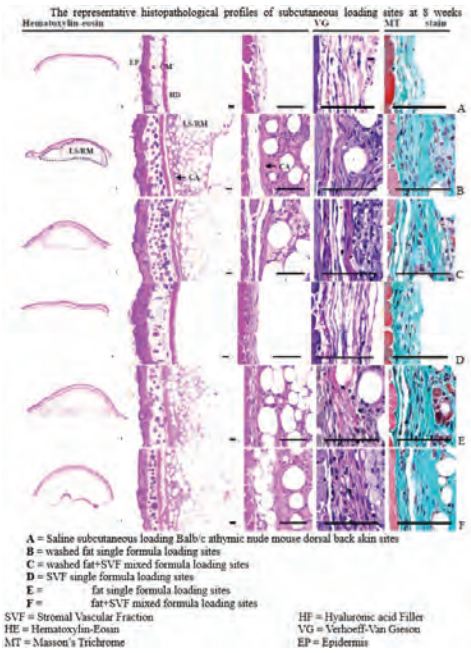
NOT PRESENTED

21P

IN VIVO AND CLINICAL EVALUATION OF THE EFFECT OF STROMAL VASCULAR FRACTION-ENHANCED FAT GRAFTING ON SOFT TISSUE AUGMENTATION

Presenter: Hyung Min Hahn, MD (South Korea)
Affiliation: Ajou University Hospital
Authors: Hahn HM, Ha N, Lee L, Yeom Y



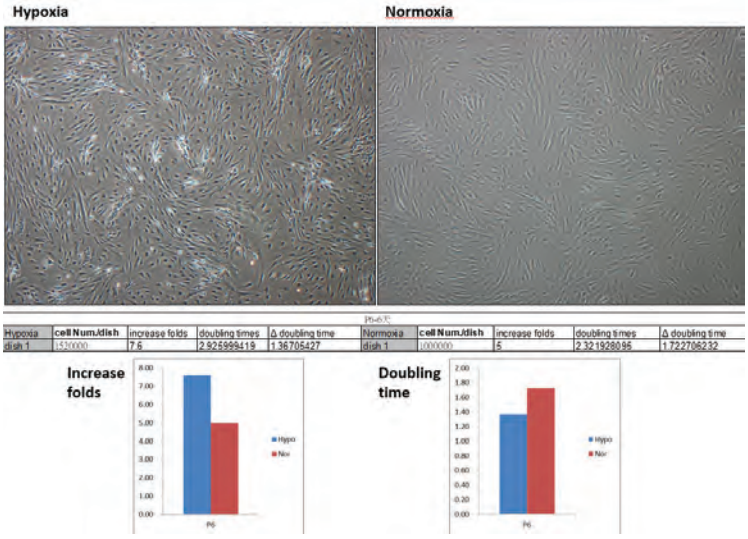


22P

STUDY FOR THE POTENTIAL OF HYPOXIA-CULTURED ASCS IN NERVE REGENERATION

Presenter: Szu-Hsien Wu, MD (Taiwan)
Affiliation: Taipei Veterans General Hospital and University of Tokyo Hospital
Authors: Wu SH, Wang J

There are still some disadvantages to use autologous nerve grafts to reconstruct the defect sites of peripheral nerve, such as limited sources of donor nerves, scar formation of sutured site may inhibit regeneration and causing morbidity to donor sites. To address the disadvantages, some nerve regeneration studies are provided as an alternative, such as conduits combined with bone marrow MSCs or ASCs. The comparison for the potential of neuroglial differentiation between BMSCs and ASCs needs to elucidate. We are also interested if ASCs increase the potential of neuroglial differentiation after expansion under hypoxic condition. The source of ASCs were from Sprague-Dawley rats. A 5-mm, critical-size segmental nerve defect was created at the right sciatic nerve in rats. A 6mm conduit was used to connect the defect area by sutures carefully placed in epineurium. 200uL of PBS without or with ASCs was injected into conduit. Rats with incisions at both sciatic nerves received an injection of hypoxic ASCs in right sciatica and normoxic ASCs in left sciatica, while those with an incision at only left sciatic nerve received an injection of PBS in both left and right sciatica. Six weeks later, the regenerated sciatic nerve within the conduits were excised for immunohistochemistry, light microscopy, myelinated fibers quantification and nerve morphometry to analyze nerve regeneration. The gastrocnemius muscles from both limbs were dissected and weighed to analyze its trophism as an indirect measurement of nerve regeneration and muscle reinnervation. Our results showed that the ASCs cultured in hypoxic condition were less senescence than that cultured in normoxic condition. From in vitro study, we also found hypoxic culture of ASCs enhanced the expression of neuronal marker expression, such as β-tubulin III, MAP2, Neu, NFL and NFM by QPCR. In conclusion, hypoxic culture may upgrade the clinical value of ASCs in nerve regeneration, improve the success rate of nerve repair, and may treat other types of peripheral neuropathy. Hypoxic ASCs maybe a better potential adjuvant treatment than normoxic ASCs.



23P

THE EFFECT OF ADIPOSE TISSUE DERIVED STEM CELLS WITH CONDITIONED MEDIA FOR THE TREATMENT OF ACNE VULGARIS SCAR ON RABBIT EAR MODEL

Presenter: Jomg-Won Rhie, MD, PhD (South Korea)
Affiliation: Catholic University of Korea Seoul St Mary Hospital
Author: Rhie JW

NOT PRESENTED

24P

EFFICACY EVALUATION OF TRANSPLANTATION OF THREE-DIMENSIONAL ADIPOSE-DERIVED STEM CELL SHEET WITH ENHANCED ANGIOGENESIS INTO ISCHEMIC VASCULAR DISEASE

Presenter: Jong-Ho Kim, PhD (South Korea)
Affiliation: Korea University College of Medicine
Authors: Kim JH, Lim I, Park C, Joo H, Hong S, Lim D

Integration of adipose-derived stem cells (ASCs) and cell sheet engineering technology has received much interest in the regenerative medicine. First of all, sphere formation of ASCs (sph-ASCs) were successfully produced by poly-2-hydroxyethyl methacrylate (poly-HEMA)-coated plates as we previously reported. Sph-ASCs showed increased expression of angiogenic growth factors and cytokine secretion compared to adherent ASCs. Significantly increased expression of HIF-1α and decreased expression of cleaved caspase-3 were detected in sph-ASCs compared to adherent ASCs. Moreover, ASC sheets were formed using thermo-responsive plates and sph-ASCs were seeded to produce ASC sheets covered with sph-ASCs (sph-ASC sheets). After 48 hrs of incubation, the cross-section of sph-ASC sheets revealed mixed and multi-layered of sph-ASCs and ASC sheets. Sph-ASC sheets showed the positive expression of HIF-1α and angiogenic markers such as FGF-2, CD31, PDGFb, and CD144, especially higher in sph-ASC-covered sites. In addition, cytokine arrays of secretome revealed that sph-ASCs and sph-ASC sheets showed augmented angiogenic potential compared to adherent ASCs. Furthermore, hind limb ischemic mouse model was induced by ligating femoral arteries of right leg, and sph-ASCs, ASC sheets, and sph-ASC sheets were transplanted. After 4 weeks, sph-ASC sheet-transplanted mice showed significantly increases in the blood flow and neovascularization in legs compared to sham, sph-ASC, and ASC sheet groups. Lastly, four groups of AMI induction only (sham), intramyocardial injection of sph-ASC, ASC sheet transplantation, and sph-ASC sheet transplantation were compared using acute myocardial infarction (AMI) rat models. After 6 weeks of transplantation, echocardiography revealed that significantly improved ejection fraction and fraction shortening in sph-ASC sheet group compared to sham, sph-ASC, and ASC sheet groups. In conclusion, transplantation of sph-ASC sheets showed enhanced neovascularization in ischemic hind limb and AMI animal models. These results indicated that the use of ASC sheets as a novel tissue engineering approach to improve the cardiac and vascular function.

25P

MOUSE ADIPOSE STEM CELLS TRANSPLANTED INTO INFARCTED MYOCARDIUM IMPROVE CARDIAC FUNCTION

Presenter: Chi-Yeon Park, PhD (South Korea)
Affiliation: Korea University College of Medicine
Authors: Park CY, Kim J, Choi J, Choi S, Joo H, Lim D

Background: Adipose stem cells (ASCs) were known to participate in the growth and remodeling of blood vessels by paracrine effects that secrete various cytokines and growth factors. Moreover, ASCs evoke only minimal immune reactivity and secrete various cytokines and growth factor to support host tissues by paracrine effects. One of the important advantages of ASCs is an easily accessible source of therapeutic cells for clinical applications.

Methods: Mouse ASCs (mASCs) were immortalized by infecting with retroviruses harboring the hTERT-IRES eGFP gene, and evaluated their stem cell properties and paracrine potential in cardiomyocyte survival during hypoxia-induced injury. Acute myocardial infarction (AMI) rats were divided into 3 groups; control, mASCs and mouse endothelial cells (mECs) groups (n=10, respectively), and 5 X 105 cells per rat were transplanted.

Results: The immortalized mASCs expressed CD29, CD44, CD106 and Sca-1, and represented multi-differentiation potential. To elucidate which paracrine factors are secreted from mASCs and mECs, conditioned medium (CM) were analyzed using mouse cytokine antibody arrays and ELISA. Dominant factors secreted from mASCs were SDF-1α and VEGF compared to mECs. In addition, mASCs exhibited significantly higher mRNA expression levels of SDF-1α and VEGF than mECs. The effect of mASC-CM on H9C2 cardiomyocyte apoptosis by CoCl2 treatment was also examined. mASC-CM significantly reduced the proportion of early apoptotic (AV+/PI-) and late apoptotic (AV+/PI+) cardiomyocytes during CoCl2-induced hypoxic injury. Futhermore, mASCs or mECs were transplanted into the peri-infarct region of AMI-induced rats to evaluate whether transplantation of mASCs or mECs improves the function of infarcted myocardium. At 1, 7, and 28 days following cell transplantation, significant improvements in ejection fraction value were observed in mASCs and mECs transplanted group compared with the control group.

Conclusion: mASC-CM increased survival and reduced apoptosis of H9C2 cardiomyocytes during CoCl2-induced hypoxic injury. mASCs transplanted into infarcted myocardium improved cardiac function in AMI rat model. mASCs are valuable sources for in vitro differentiation and in vivo regeneration studies in the cardiovascular field.

26P

EFFECT OF MATURE ADIPOCYTE-DERIVED DEDIFFERENTIATED FAT (DFAT) CELLS ON ISCHEMIC TISSUE OF NORMAL AND DIABETIC RATS

Presenter: Tsutomu Kashimura, PhD (Japan)
Affiliation: Nihon University School of Medicine
Authors: Kashimura T, Soejima K, Kikuchi Y, Kazama T, Matsumoto T, Nakazawa H

Introduction: Dedifferentiated fat (DFAT) cells, isolated from mature adipose cells, have higher proliferative potential and pluripotency compared to the mesenchymal stem cells. Here, we report the expansion of skin flap survival areas on the back of normal and diabetic rats administered with DFAT cells.

Materials and Methods: Subcutaneous adipose tissue was collected from a male Sprague-Dawley (SD) rat. The mature fat cells were cultured on the ceiling surface of the culture flask to isolate the DFAT cells. On day 7 of the culture, the flask was inverted to allow the cells to grow as a normal adherent culture. A dorsal caudal-based random pattern flap measuring 2×9 cm was raised on the normal and diabetic SD rats (SDT-fatty rat). The rats were assigned to 4 groups: normal rat control group (n=10), normal rat injection group (n=10), diabetic rat control group (n=10), and diabetic rat injection group (n=10). Rats in the injection groups were injected with DFAT cells (1×106 cells/0.1 mL) beneath the skin muscle layers 2 cm from the flap base. The flap survival areas were assessed on day 14 after the surgery.

Results: The mean flap survival rates of the normal rat control group, normal rat injection group, diabetic rat control group, and diabetic rat injection group were 53.8±6.4%, 65.8±2.4%, 34.5±9.2%, and 48.9±10.8%, respectively. The flap survival areas were significantly smaller in the diabetic rat control group compared to the normal rat control group ($p<<0.05$). The flap survival areas were significantly expanded in the injection groups compared to their corresponding control groups ($p<<0.05$). H&E staining revealed connective tissue thickening beneath the skin muscle layer in the injection groups; the India ink staining revealed abundant neovascularization inside the thickened parts.

Conclusion: The injection of DFAT cells into the flap base promoted the expansion of survival areas. As DFAT cells can easily be collected and cultured, their broad application is expected in future in the treatment of conditions, such as ischemic ulcer and diabetic ulcer, in addition to the random pattern flap.

27P
3D BIOPRINTING THE CARDIAC PURKINJE SYSTEM USING HUMAN ADIPOGENIC MESENCHYMAL STEM CELL DERIVED PURKINJE CELLS

Presenter: Evan P. Tracy, BS (USA)
Affiliation: University of Louisville School of Medicine
Authors: Tracy EP, Gettler BC, Zakhari JS, Birla RK, Schwartz RJ, Williams SK

Introduction: Congestive Heart Failure is the leading cause of death worldwide. Demand for transplant organs and rejection risk have sparked the initiative of bioprinting a Total Bioficial Heart using autologous cell sources. One strategy suggests printing the disparate structures of the heart separately and assembling them into a functional organ. The purkinje network is part of the cardiac conduction system responsible for synchronized ventricular contraction. Human adipogenic mesenchymal stem cell derived purkinje cells in collagen were 3D bioprinted into a purkinje-like network. We hypothesize that these purkinje cells will retain structure, cellular identity, conductive function, and appropriate response to external stimuli upon culturing in a) 3D collagen matrix and b) 3D bioprinted purkinje-like network.

Methods: An anatomical image of an India Ink injected bovine left ventricular purkinje network was used to program our 3D printer. A mold was printed with pluronic F-127 and filled with varied density of purkinje cells in varied concentration of type 1 collagen. Syncytium formation over time was monitored with phase contrast microscopy. Viability, cellular identity, and conductive ability were evaluated using a live/dead assay, connexin 40 staining, and simultaneous electrical stimulation and fluorescent imaging with the membrane potential dye DiBAC4(5). Response to pacing and acetylcholine was assessed via connexin 40 relative fluorescence/localization and changes in membrane potential, respectively.

Results: The bioficial purkinje network had a 59% viability. Syncytium formed when using a collagen concentration of 1.8 mg/mL and a cellular density of 1.5 million cells per mL. Staining with connexin 40 revealed that the cells retained cellular identity when cultured in a 3D collagen matrix and when 3D bioprinted. Pacing shifted localization of connexin 40 towards connections between cell aggregates. The mean fluorescence intensity of DiBAC4(5) within purkinje cells decreased with pacing and treatment with acetylcholine.

Conclusions: The effort to print a Total Bioficial Heart must first start with the ability to print its components. The bioprinting method described is a feasible method for the creation of a purkinje network model.

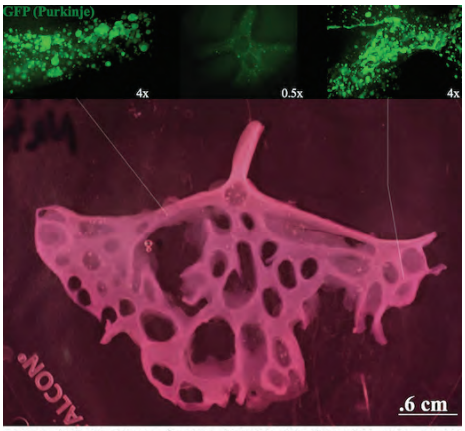


Figure: Left Ventricular Purkinje Network 3D Bioprinted with Human Adipogenic Mesenchymal Stem Cell derived Cardiac Purkinje Cells in Type 1 Collagen using the Bio Assembly Tool 3D Printer with representative GFP images.

28P
PATHOPHYSIOLOGY OF TISSUE DAMAGE AFTER RADIATION THERAPY: INFLUENCE OF RADIATION DOSE AND FRACTIONATION PROTOCOL ON ADIPOSE-DERIVED STEM CELLS IN VITRO AND IN VIVO

Presenter: Rintaro Asahi, MD (Japan)
Affiliation: Jichi Medical University
Authors: Asahi R, Shirado T, Moriya K, Yoshimura K

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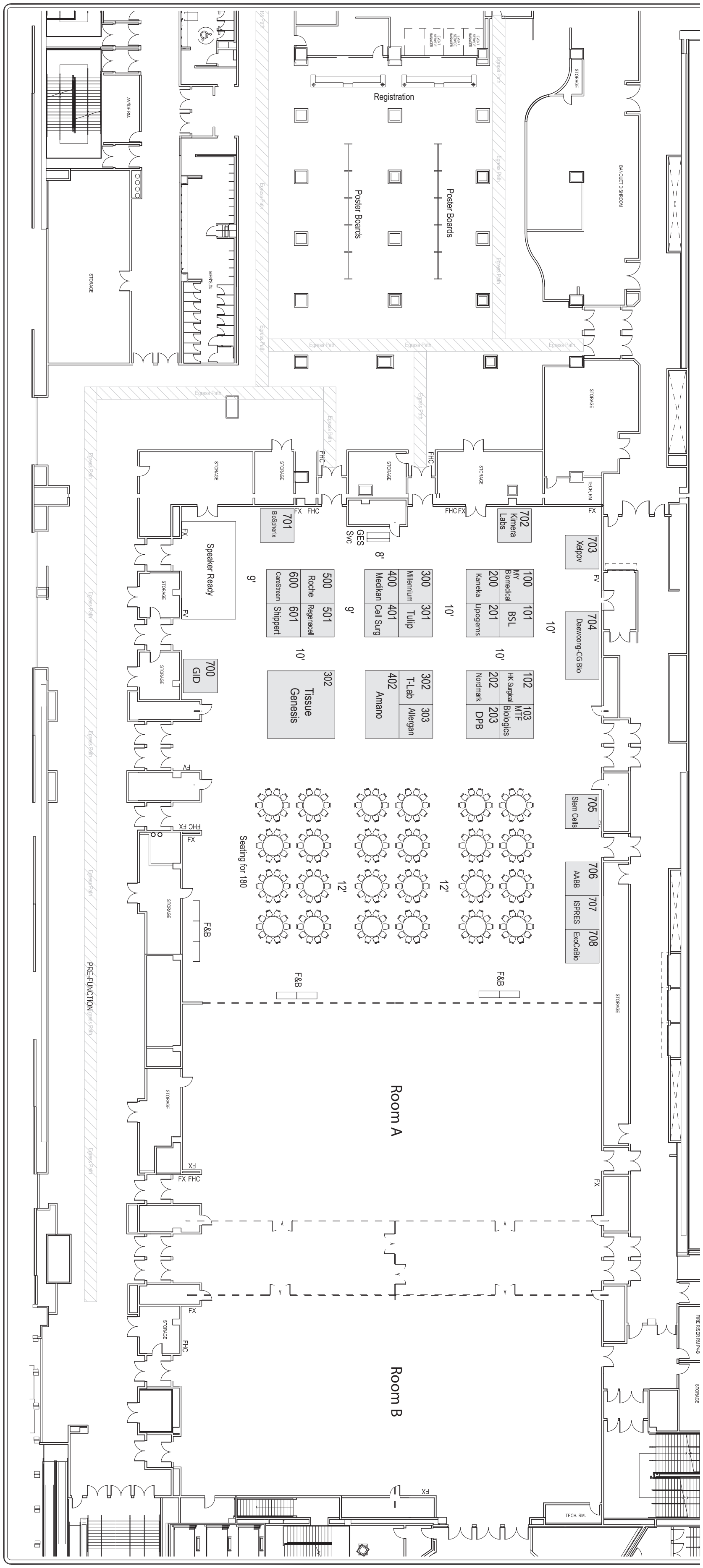

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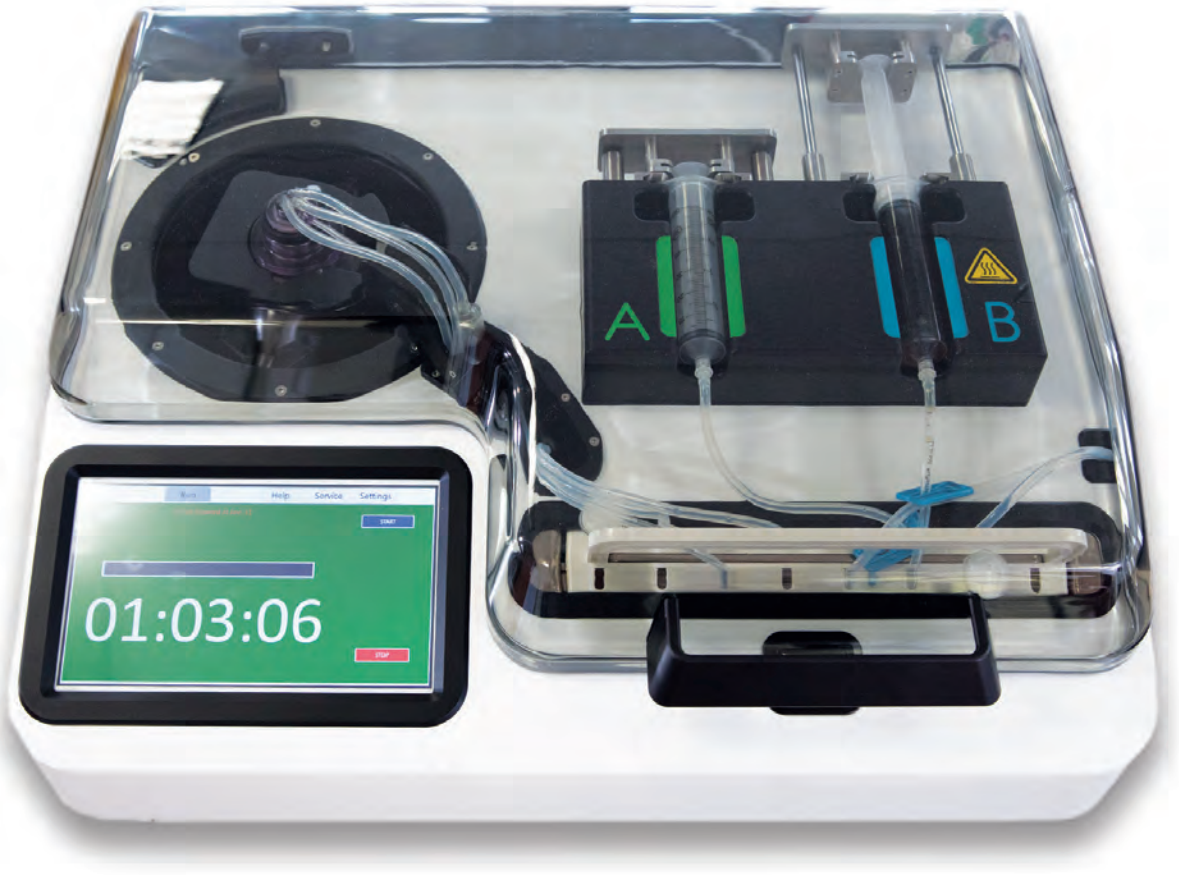

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