IFATS
International Federation for Adipose Therapeutics and Science

20th Annual IFATS Conference





THERE'S ONLY ONE IFATS

October 5-7, 2023

Omni Shoreham Hotel, Washington, DC

Presidential Note

On behalf of the 2023 IFATS Program Committee and Board of Directors, it is a great honor to welcome you to the annual IFATS meeting in Washington DC.

The International Federation for Adipose Therapeutics and Science (IFATS) is the premier, global scientific society focused on promoting research on adipose biology and adipose-derived therapeutics. The annual conference, which began in 2003, has a rich tradition in being multi-perspective and features innovations in basic science, translational research, clinical and surgical practice, and industry-led initiatives. Annual features of the conference include regulatory and legal issues pertinent to regenerative therapeutics, clinician-driven therapeutic translation, basic science investigations in therapeutic mechanisms of action, and industry-academia commercialization partnerships.

This year's IFATS program committee dedicated our efforts to achieving a 3-day conference embedded with inclusivity and diversity, including in our geographic reach, clinical expertise, career stage, and our racial and ethnic background. Toward these goals, we are excited to present three exciting days of scientific discussion and expert panels focused on unique avenues for improving patient care and therapeutic innovation translation, the impact of diversity in research translation and health equity, and new frontiers in adipose therapeutics.

A secondary goal for this year's IFATS conference is increasing junior trainee accessibility and engagement. While enabling student and trainee opportunities has always been a pillar of the IFATS mission, this year we aimed to further increase the educational value of the meeting curriculum through a new program component called IFATS Academy. In these sessions, expert faculty provide fundamental knowledge on the neurobiology of pain, etiology of obesity and lipidemia, fat grafting clinical fundamentals, and academic career development, to enhance student understanding, promote attendee engagement, and encourage camaraderie. As the field of adipose science is still in its infancy, we hope that this novel program will inspire scientists and clinicians at pivotal career points to undertake research exploring mechanisms through which biologics, including adipose therapeutics, modulate tissue pathophysiology.

As we gather in this collaborative space, it is imperative that we remain mindful of the responsibility that accompanies scientific discovery. We are not only advancing the frontiers of knowledge but also impacting the lives of individuals seeking hope and healing. To this end, we have invited Graham Parker, PhD, of Wayne State University and Editor-in-Chief at Mary Ann Liebert, Inc., to lead us in discussions on ethical considerations, safety, and patient-centered care. These must remain at the forefront of our discussions, guiding us toward responsible and effective use of these exciting new therapies and discoveries.

Our conference is not just a platform for scientific exchange; it is a catalyst for change and a call to action. The discoveries made here have the potential to transform the way we approach patient care, to enhance the quality of life for millions. Together, we have the opportunity to bring science to the bedside, to make a tangible difference in the lives of those who need it most. I encourage you all to actively engage in the discussions, to collaborate, to challenge existing paradigms, and to foster innovation. The synergy of ideas and perspectives within this diverse gathering is our greatest asset. Let us harness the collective intelligence of this assembly to unlock the full potential of adipose biologics for the betterment of humanity.

Lauren Kokai, PhD
IFATS President

Executive Committee - Board of Directors

Executive Committee

William Futrell, MD
Pittsburgh, PA, USA

Adam J. Katz, MD
Past President 2005
Winston-Salem, NC, USA

Ramon Llull, MD, PhD
Past President 2003
Winston-Salem, NC, USA

Ricardo Rodriguez, MD
Past President 2016
Baltimore, MD, USA

J. Peter Rubin, MD
Past President 2004
Pittsburgh, PA, USA

Board of Directors

Lauren Kokai, PhD
President 2023
Pittsburg, PA, USA

Torsten Blunk, PhD
Past President 2022
Wuerzburg, Germany

Ivona Percec, MD, PhD
Past President 2020-2021
Bryn Mawr, PA, USA

Guy Magalon, MD
Past President 2019
Marseille, France

Kotaro Yoshimura, MD
Past President 2018
Shimotsuke, Japan

Bruce A. Bunnell, PhD
Past President 2015
New Orleans, LA, USA

Marco N. Helder, PhD
Past President 2014
Amsterdam, Netherlands

Kacey Marra, PhD
Past Co-President 2013
Pittsburgh, PA, USA

Sydney Coleman, MD
Past Co-President 2013
New York, NY, USA

Julie Fradette, PhD
Past President 2012
Quebec, QC, Canada

Stuart K. Williams, PhD
Past President 2011
Louisville, KY, USA

Louis Casteilla, PhD
Past President 2008
Toulouse, France

Keith March, MD, PhD
Past President 2007
Gainesville, FL, USA

Jeffrey M. Gimble, MD, PhD
Past President 2006
New Orleans, LA, USA

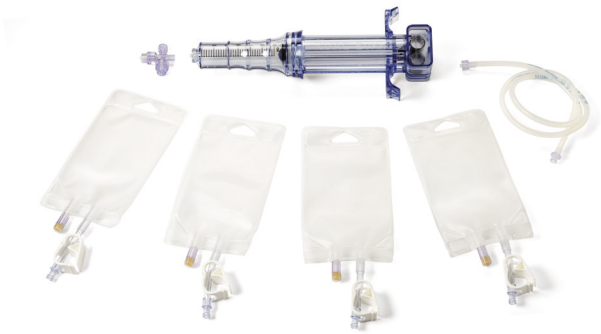
renuva®

Still You, Only Better.

The first and only
off-the-shelf
allograft alternative
to small-volume
fat transfer

lipograft®

A comprehensive, closed, and efficient
fat transfer solution for
cell-survivability and
predictable results



mtfbiologics
Plastic & Reconstructive Surgery

Learn more at **mtfbiologics.org**.

Scientific Program Committee

Lauren Kokai, PhD – *President*

Susanna Miettinen, PhD
Trivia Frazier, PhD, MBA
Summer E. Hanson, MD, PhD
Frederik Kolle, MD, PhD

Invited Speakers & Session Moderators

Rosalyn D. Abbotm PhD
Sara Al-Ghadban, PhD
Vence L. Bonham, Jr., JD
Sherry Collawn, MD, PhD
Thomas A. Davis, PhD
Julie Fradette, PhD
Trivia Frazier, PhD, MBA
Paul Gatenholm, PhD
Jeffrey M. Gimble, MD, PhD
Blaine Hamilton
Summer E. Hanson, MD, PhD
Selwyn Jayakar, PhD
Hyungtaek Jeon
Adam J. Katz, MD
Stephen W. P. Kemp, PhD
Francesco Klinger, MD
Lauren Kokai, PhD
Frederik Kolle, MD, PhD
Mark Long, PhD
Ramon Lull, MD, PhD
Guy Magalon, MD
Keith L. March, MD, PhD
Peter Marks, MD, PhD
Miguel Medina, MD
Susanna Miettinen, PhD
Graham Parker, PhD
Kirsi Pietilainen, MD
Kun (Mark) Qian, MD
Nicole Redmond, MD, PhD, MPH
Julio A. Rivera, PhD
Ricardo Rodriguez, MD
J. Peter Rubin, MD
Antonio Salgado, PhD
Issam Saliba, MD, FRCSC
Cecilia Sanchez, PhD
Deniz Sarhaddi, MD
Dmitry Traktuev, PhD
Ian Valerio, Cpt, MD, MS, MBA
Mari van de Vyver, PhD
Kamakshi R. Zeidler, MD
Yinan Zheng

Abstract Reviewers

Rosalyn D. Abbott
Carnegie Mellon University

Petra Bauer-Kreisel, PhD
University of Wuerzburg

Torsen Blunk, PhD
University of Wuerzburg

Bruce A. Bunnell, PhD
University of North Texas Health Science Center at Fort Worth

Evangelia Charni, PhD
MTF Biologics

Bryan Choi, MD
Advanced Biologics

Sherry Collawn, MD, PhD
University of Alabama at Birmingham

Julie Fradette, PhD
LOEX-Universite Laval

Susanna Kauhanen, MD, PhD
Helsinki University Hospital

Paul Kingham, PhD
Umeå University

Lauren Kokai, PhD
University of Pittsburgh

Kacey Marra, PhD
University of Pittsburgh

Susanna Miettinen, PhD
University of Tampere

Sugii Shigeki, PhD
Singapore Bioimaging Consortium / Duke-NUS Graduate Medical School

Dmitry Traktuev, PhD
University of Florida College of Medicine

Free Paper Presenters

Derek Banyard, MD, MS, MBA
Megan Campbell Benz
Courtney Brock
Emily Budziszewski
R. Brannon Claytor, MD
Sweelin Chew, PhD
Sherry Collawn, MD, PhD
Eray H. Copcu, MD
Patrick S. Cottler, PhD
Franziska Dusi
Amr Elmeanaway, MD
Julie Fradette, PhD
Rachel Louise Furmidge
Pietro Gentile, MD, PhD
Summer Hanson, MD, PhD
Joshua Harrison, MD
Katherine L. Hebert
Ki Yong Hong, MD, PhD
Elizabeth Kaleigh Johnston
Miia Juntunen, PhD
Nimesh Kabaria, MS
Susanna Cecilia Kauhanen, PhD
Frederik Kolle, MD, PhD
Chen Lei, MD
Hong-Wei Liu, PhD
Michelle Maartens
Guy Magalon, PhD
Sophie Menkes, MD
Carola Niesler, PhD
Eleni Priglinger
Chi-Ming Pu, MD
Caroline Rinderle, MS
Julio A. Rivera, PhD
Nicolas Serratrice, MD
Yi Ru Su, MD
Dmitry Traktuev, PhD
Chloe Trotzier
Klaus Ueberreiter, MD
Marlene Wahlmueller, MSc
Eddy Hsi Chun Wang
Alma Yrjänäinen, MSc

WEDNESDAY - OCTOBER 4

5:30 -7:00 pm	**IFATS EXECUTIVE BOARD MEETING**	*Capitol Room*

THURSDAY - OCTOBER 5 - Improving Patient Care and Innovation Translation

Blue Room

8:30 - 9:00 am	**Continental Breakfast in Exhibit Hall**	
9:00 - 9:10 am	**Welcome Remarks and Overview** Lauren Kokai, PhD - IFATS President	
9:15 - 10:00 am	**OPENING KEYNOTE SPEAKER:** **Unmet Surgical Challenges in War Wounded, An Urgent Need for Regenerative Therapeutics** Ian Valerio, Cpt, MD, MS, MBA *Dr. Valerio is a military captain and a leader in reconstructive, regenerative and restorative surgery, microsurgery and peripheral nerve surgery* *Boston, MA, USA* Introduced by J. Peter Rubin	
10:00 - 10:30 am	**Coffee Break in Exhibit Hall**	*Blue Prefunction*
10:30 - 11:15 am	**Regenerative Medical Advances in Military Medicine and Surgery Based on the Work Ongoing at USUHS, Walter Reed and Bethesda Naval Medical Centers** Introduced by Jeffrey M. Gimble, MD, PhD **Patient Outcomes and Complications after OPRA Osseointegration Surgery for Patients with Transfemoral Amputations** Julio A. Rivera, PhD *Scientific Director, DoD Limb Optimization and Osseointegration Program, Assistant Professor of Surgery, USU Walter Reed Surgery and Rehabilitation, Bethesda, MD, USA* **Trauma Beyond the Injury Site** Thomas A. Davis, PhD *Vice Chair of Research, professor USU Walter Reed Surgery, Bethesda, MD, USA*	*Blue Room*
11:20 - 12:30 pm	**Free Papers 1 - Pain & Wound Healing Indications** Moderator: Summer Hanson, MD, PhD	*Blue Room*
11:20	(p.17) - **Stromal Vascular Fraction (SVF) Relieves Symptoms of Carpometacarpal I Osteoartrosis (OA) - Preliminary Interim Analysis of Randomized Control Trial (RCT)** Presenter: Susanna Cecilia Kauhanen, PhD - Finland Affiliation: Helsinki University Hospital Authors: Susanna Cecilia Kauhanen, Jussi Kosola, Samuli Aspinen	
11:31	(p.18) - **Combination Therapy with Adipose Fat Grafting for Hypertrophic Burn Scars** Presenter: Sherry Collawn, MD, PhD - USA Affiliation: University of Alabama Authors: Sherry Collawn	
11:42	(p.18) - **Outcomes and Complications after OPRA Osseointegration Surgery for Patients with Transfemoral Amputations** Presenter: Julio A. Rivera, PhD - USA Affiliation: Henry M. Jackson Foundation for the Advancement of Military Medicine Authors: Julio A. Rivera, Benjamin K. Potter, Ashley B. Anderson, Angelica Melendez-Munoz; Jason M. Souza, Jonathan A. Forsberg	
11:53	(p.19) - **Preclinical Volume Retention of Fat Grafts Processed with the REVOLVE™ ENVI Filtration-Based System or Decantation Methods in Irradiated and Nonirradiated Wounds** Presenter: Patrick S. Cottler, PhD - USA Affiliation: Allergan Aesthetics, an AbbVie Company Authors: Christopher A. Campbell, Patrick S. Cottler, Graham M. Grogan, Nimesh Kabaria, Maryellen Sandor	

12:04	(p.19) - **Mechanical Processing of Human Lipoaspirate with a Fluidic Device System Enhances Recovery of Mesenchymal Stem Cells and Promotes Wound Healing Through Hydrodynamic Shear Flow** Presenter: Derek Banyard, MD, MS, MBA - USA Affiliation: Sayenza Biosciences Authors: Derek A. Banyard, Alexandria M. Sorensen, Mary Zeigler, Pisrut Phummirat, David Zalazar, Alan D. Widgerow, Jered B. Haun	
12:15	**TBD** Presenter: Kamakshi R. Zeidler, MD - USA Affiliation: Aesthetx Authors: Kamakshi R. Zeidler	
12:30 - 1:30 pm	**Lunch**	*Blue Prefunction and Terrace*
12:30 - 1:30 pm	**IFATS ACADEMY - Neurobiology of Chronic Pain** Selwyn Jayakar, PhD	*Capitol Room*
1:30 - 2:30 pm	**SPECIAL PRESENTATION BY PETER MARKS, MD, PhD:** **Adipose Stem Cells: Turning the Hype into High-End Medical Products** Peter Marks, MD, PhD *Director, Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, Silver Springs, MD, USA* Introduced by Keith March, MD, PhD	*Blue Room*
2:30 - 3:55 pm	**PANEL: Adipose Therapeutics for Pain: Demystifying Avenues of Medical Intervention** Introduced by Antonio Salgado, PhD **Fat Grafting to Enhance Peripheral Nerve Regeneration and Attenuate Neuropathic Pain** Stephen W. P. Kemp, PhD *Director, Neuromuscular Lab, Associate Editor, Muscle & Nerve, Associate Professor, University of Michigan, Section of Plastic Surgery, Department of Surgery, Department of Biomedical Engineering, Michigan Neuroscience Institute Affiliate, Ann Arbor, MI, USA* **A Systems Pharmacology Approach to Analgesic Development** Selwyn Jayakar, PhD *Fellow F.M. Kirby Neurobiology Center, Department of Neurology, Boston Children's Hospital and Harvard Medical School, Boston, MA, USA* **Cerebral Organoids to Study Central Mechanisms of Pain: The Effect of Stem Cell Secretome on Opioid Receptors and Neuroplasticity** Antonio Salgado, PhD *Coordinating Investigator and Vice-dean for Research at the School of Medicine, Life and Health Sciences Research Institute (ICVS), University of Minho Portugal, Spain* **Fat Grafting as Treatment in Pain Syndromes** Francesco Klinger, MD *Reconstructive and Aesthetic Plastic Surgery School, Department of Medical Biotechnology and Translational Medicine (BIOMETRA), University of Milan, Plastic Surgery Unit, Humanitas Research Hospital, Milan, Italy*	
4:00 - 4:55 pm	**Free Papers 2 - Head and Neck** Moderator: J. Peter Rubin, MD	*Blue Room*
4:00	(p.20) - **Nanofat Graft in Treatment of Infraorbital Dark Circles** Presenter: Yi Ru Su, MD - Taiwan Affiliation: Cathay General Hospital Authors: Yi Ru Su, Chi-Ming Pu	
4:11	(p.20) - **Nanofat as a Rescue for Peri Oral Rejuvenation Following Aggressive CO2 Laser and Microneedling Treatment** Presenter: R. Brannon Claytor, MD - USA Authors: R. Brannon Claytor	
4:22	(p.21) - **Oil Cysts Formation after Lower Blepharoplasty with Fat Graft** Presenter: Chi-Ming Pu, MD - Taiwan Affiliation: Cathay General Hospital Authors: Chi-Ming Pu	
4:33	**Corneal Regeneration Using Human Adipose Stem/stromal Cells and Bioprinting** Presenter: Susanna Miettinen, PhD - Finland Affiliation: Tampere University Authors: Paula Puistola, Anni Mörö, Heli Skottman Heli	

4:44	**Fat Grafting: The Perfect Adjunct to Facial Rejuvenation Surgery** Presenter: Deniz Sarhaddi, MD - USA Affiliation: Deniz Sarhaddi Plastic Surgeon Authors: Deniz Sarhaddi	
5:00 - 5:45 pm	**KEYNOTE SPEAKER:** **Hyaluronic Acid Fat Graft Myringoplasty** Issam Saliba, MD, FRCSC *Professor, Otorhinolaryngology - Head & Neck Surgery , University of Montreal - School of Medicine, Otology, Neurotology & Skull Base Surgery, Chief Department of ORL-HNS - University of Montreal Health Center (CHUM), Chair, Division of Otorhinolaryngology - Head & Neck Surgery, University of Montreal, Director of Fellowship - Division ORL-HNS, University of Montreal, Director of Research - Division ORL-HNS, University of Montreal, Medical Director - Polyclinique Centre-Ville ORL & Spécialités Médicales* Introduced by Lauren Kokai, PhD	*Blue Room*
5:45 pm	**Meeting Adjourns for the Day**	

▪ FRIDAY - OCTOBER 6 - Global Health Equity

Blue Room

8:00 - 9:00 am	**IFATS ACADEMY - Obesity and Lipedema: Etiology and Therapeutics** Susanna Mittinen, PhD and Sara Al Ghadban, PhD	*Capitol Room*
8:30 - 9:00 am	**Continental Breakfast in Exhibit Hall**	*Blue Prefunction*
9:00 - 10:00 am	**OPENING KEYNOTE SPEAKER:** **Expanding Patient Demographic Diversity to Improve Translation of Regenerative Medicine Therapeutics** Mari van de Vyver, PhD *Senior Researcher Stellenbosch University| SUN · Department of Medicine PhD Physiological Sciences, South Africa* Introduced by Lauren Kokai, PhD	*Blue Room*
10:00 - 11:15 am	**PANEL: Research Diversity Impact and Global Health Equity** Introduced by Trivia Frazier, MD, MBA **Lack of Diversity in Genomic Databases is a Barrier to Translating Precision Medicine Research Into Practice** Vence L. Bonham, Jr. JD *Acting Deputy Director, Office of the Director, Associate Investigator, Social and Behavioral Research Branch, National Human Genome Research Institute, National Institutes of Health* **The Impact of Biologic Diversity on Measured Research Outcomes** Kun (Mark) Qian, MD *Director Advanced Research L'Oreal Research and Innovation* **Optimizing Inclusion: Challenges in Policy and Practice** Nicole Redmond, MD, PhD, MPH *Applications and Prevention Branch (CAPB), Division of Cardiovascular Sciences (DCVS), National Heart, Lung, and Blood Institute (NHLBI)* **Incorporating Patient Diversity within Adipose Tissue Models for Metabolic Disease Screening** Cecilia Sanchez, PhD *Obatala Sciences, Inc.*	*Blue Room* *Panel Sponsored by:* L'ORÉAL RESEARCH & INNOVATION
11:15 - 11:30 am	**Coffee Break in Exhibit Hall**	*Blue Prefunction*
11:30 - 12:35 pm	**Free Papers 3 - Adipose-derived Cell Therapeutics** Moderator: Ricardo Rodriguez, MD	*Blue Room*
11:30	(p.21) - **Use of Autologous Adipose-Derived Mesenchymal Stem Cells for Ovarian Rejuvenation Poor Responder IVF Patients: A Phase 1 Randomised Placebo Controlled Double Blind Crossover Study** Presenter: Carola Niesler, PhD - South Africa Affiliation: University of KwaZulu-Natal Authors: T. Mohamed, J.K. Adam, C. Niesler, A. Chikandiwa	

11:41	(p.22) - **Definitive Results of the Preclinical Study Conducted in Rodents to Determine the Neuroprotective and Neurotrophic Effects of the Autologous Fat-derived Stromal Vascular Fraction (SVF) in the Acute Management of Spinal Cord Contusions** Presenter: Nicolas Serratrice, MD - France Affiliation: Neurosurgeon, Spine & Spinal Cord Surgeon, Associate Researcher Author: Nicholas Serratrice	
11:52	(p.22) - **Age Does not Seem to Affect ASC Stemness and Pro-angiogenic Potential** Presenter: Chloe Trotzier - France Affiliation: L'Oreal Research & Innovation Authors: Chloe Trotzier, Kun Qian, Celine Auxenfans, Ali Mojallal	
12:03	(p.23) - **Proteomic analysis: The Effect of Antioxidant Supplementation on Bone Marrow Derived Mesenchymal Stem Cells in Diabetes** Presenter: Michelle Maartens - South Africa Affiliation: Division of Clinical Pharmacology, Faculty of Medicine and Health Sciences, Stellenbosch University Authors: Michelle Maartens, Mare Vlok, C Smith, Mari van de Vyver	
12:14	**Breast Enlargement and Implant Replacement with Ex Vivo Expanded Stem Cell Enriched Fat Grafting** Presenter: Fred Koelle, MD, PhD - Denmark Affiliation: Stem Medical Authors: Fred Koelle	
12:45 - 1:45 pm	**Lunch and Learn with IFATS Key Opinion Leaders and Industry**	*Blue Prefunction and Terrace*
12:45 - 1:45 pm	**IFATS ACADEMY - Career Development: How to Get Your Work Published - an Editor's Perspective AND Decision Making for Academic Success -** Graham Parker, PhD	*Capitol Room*
1:45 - 3:00 pm	**PANEL: Adipose Health Disorders: Obesity and Lipedema** Introduced by Susanna Miettinen, PhD and Sara Al-Ghadban, PhD **Adipose Tissue Metabolism in Obesity** Kirsi Pietiläinen, MD, PhD *Professor in Clinical Metabolism, Programme Director, Research Programme for Clinical and Molecular Metabolism, Faculty of Medicine, University of Helsinki, Chief Physician, Obesity Center, Helsinki University Central Hospital, Helsinki, Finland* **Effects of Obesity on Adipose Stem/Stromal Cells** Susanna Miettinen, PhD *Professor of Cell and Tissue Technology, Adult Stem Cells Group, Faculty of Medicine and Health Technology, Tampere University, Tampere, Finland* **Characterization of Estrogen Receptors (ERs) and Estrogen Metabolizing Enzymes in Lipedema and Non-lipedema Adipose-derived Stem Cells (ASCs) in 2D Monolayer and 3D Cultures** Sara Al-Ghadban, PhD *Research Scientist, Dept. of Microbiology, Immunology & Genetics, University of North Texas Health Science Center, Denton, TX, USA* **A Comparison Study of Potential Translational Screening Tools for Lipedema** Yinan Zheng, MD Candidate *Vanderbilt University School of Medicine, Nashville, TN, USA*	*Blue Room*
3:05 - 3:50 pm	**Free Papers 4 - Adipose in Health** Moderator: Dmitry Traktuev, PhD	*Blue Room*
3:05	(p.23) - **Leptin Signaling Drives Tumor Growth in Triple Negative Breast Cancer** Presenter: Courtney Brock - USA Affiliation: Tulane University School of Medicine Author: Courtney Brock	
3:16	(p.24) - **Stromal Vascular Fraction and Blood-derived Extracellular Vesicle miRNAs as Novel Biomarker for Lipedema** Presenter: Eleni Priglinger - Austria Affiliation: Johannes Kepler University Medical Faculty Department for Orthopedics and Traumatology Authors: Eleni Priglinger, Karin Strohmeier, Sarah Moussa, Susanna Skalicky, Johannes Oesterreicher, Marlene Wahlmueller, Wolfgang Holnthoner, Matthias Sandhofer, Martin Barsch, Matthias Hackl, Susanne Wolbank	

3:27	(p.24) - **Adipose Tissue Contains Extracellular Lipids Associated with Regions of Collagen** Presenter: Elizabeth Kaleigh Johnston - USA Affiliation: Carnegie Mellon University Authors: Elizabeth K. Johnston, Megan DeBari, Qijia Zhou, Phil Campbell, Rosalyn Abbott	
3:38	(p.27) - **Novel Kinase Inhibitor Screening for Inhibition of Continuation of Adipogenic Differentiation in Adipose-derived Stem Cells** Presenter: Caroline Rinderle, M.S. - USA Affiliation: The University of North Texas Health Science Center at Fort Worth Authors: Bruce Bunnell, Caroline Rinderle	
3:55 - 4:40 pm	**Free Papers 5 - Adipose Modeling for Disease Research** Moderator: Julie Fradette, PhD	*Blue Room*
3:55	(p.28) - **ERK5 Characterization in a Novel Adipose-Based Breast Cancer Microphysiological System** Presenter: Katherine L. Hebert - USA Affiliation: Tulane University School of Medicine Authors: Katherine Hebert, Thomas Cheng, Jack Elliott, Van Barnes, Frank Lau, Elizabeth Martin, Matthew Burow	
4:06	(p.28) - **In Vitro Tissue Reconstruction Using Stromal Cells from Adipose Tissue of Healthy or Obese Donors: Impact on 3D Cell Differentiation and Extracellular Matrix** Presenter: Julie Fradette, PhD - Canada Affiliation: LOEX-Universite Laval Authors: Julie Fradette, Luis Sorroza-Martinez, Nabil Amraoui, Léa Gagné, Viviane Séguin, Marie-Frédérique Gauthier, Giada Ostinelli, André Tchernof	
4:17	(p.29) - **Comparison of Adipocyte Like Spheroids from Human Vascular Fraction and Adipose Stromal/stem Cells in Various Culture Conditions** Presenter: Miia Juntunen, PhD - Finland Affiliation: Tampere Univeristy Authors: Miia Juntunen, Niklas Lostedt, Alma Yrjänäinen	
4:28	(p.29) - **A Novel Barrier-free, Open-top Microfluidic Chip for Generating Merged 3D Vascular Networks** Presenter: Alma Yrjänäinen, MSc - Finland Affiliation: Tampere University Authors: Alma Yrjanainen, Elina Kalke, Ella Lampela1, Jose Kreutzer, Jorma Vihinen, Jorma Vihinen, Kaisa Tornberg, Hanna Vuorenpää, Susanna Miettinen, Pasi Kallio and Antti-Juhana Mäki	
4:40 - 5:00 pm	**Break and Visit Exhibits**	*Blue Prefunction*
5:00 - 5:45 pm	**KEYNOTE SPEAKER:** **3D Bioprinting of Living Human Adipose Tissue for Grafting and as Model to Study Obesity** Paul Gatenholm, PhD *CEO CELLHEAL, Sweden* Introduced by Rosalyn D. Abbott, PhD	*Blue Room*
5:45 pm	**Meeting Adjourns for the Day**	

▪ SATURDAY - OCTOBER 7 - Next Frontiers in Adipose Therapeutics — *Blue Room*

8:00 - 8:45 am	**Continental Breakfast in Exhibit Hall**	*Blue Prefunction*
8:00 - 8:50 am	**IFATS Members Meeting**	*Blue Room*
9:00 - 11:00 am	**Best Papers** Moderators: Adam J. Katz, MD and Mari van de Vyver, PhD	*Blue Room*
9:00	**Basic Science - Student** (p.30) - **3D Adipose Tissue Model with Tunable Triglyceride Content Using Melt Electrowriting (MEW) Scaffolds Seeded with Multicellular Spheroids** Presenter: Franziska Dusi - Germany Affiliation: University Hospital Wuerzburg Authors: Tamara Weidemeier, Martin Watzling, Hannes Horder, Torsten Blunk, Petra Bauer-Kreisel	

9:13	**Basic Science - PI** (p.30) - **Acquisition of Myofibroblast Phenotype by Adipose Stromal Cells in Inflammatory Environments Depends upon Autocrine Activin A Activity** Presenter: Dmitry Traktuev, PhD - USA Affiliation: University of Florida Authors: Stephanie Merfeld-Clauss, Keith L. March, Dmitry O. Traktuev	
9:26	**Translational - Student** (p.31) - **Stress-Induced Premature Senescence and Senolytic Intervention in the Adipose Stromal Vascular Niche** Presenter: Marlene Wahlmueller, MSc - Austria Affiliation: Ludwig Boltzmann Institute for Traumatology Authors: M. Wahlmueller, MS Narzt, K. Missfeldt, V. Arminger, A. Krasensky, I. Lämmermann, B. Schaedl, M. Mairhofer, S. Suessner, S. Wolbank, E. Priglinger	
9:39	**Discussion**	
9:45	**Clinical Science - Student** (p.31) - **Molecular Evaluation of Microfragmented Adipose Tissue Correlated to Clinical Outcomes in Patients Undergoing Treatment for Knee Osteoarthritis** Presenter: Joshua Harrison, MD - USA Affiliation: University of New Mexico, School of Medicine Authors: Joshua Harrison, Melody Sun, Erin Milligan, Anil Shetty, Dustin Richter	
9:58	**Clinical Science - PI** (p.32) - **Assessment and Outlook for the Treatment of Scleroderma 2009-2023** Presenter: Guy Magalon, PhD - France Affiliation: Aix Marseille Universite France Authors: Guy Magalon, Jeremy Magalon, Florence Sabatier, Aurélie Daumas, Brigitte Granel	
10:11	**Translational - PI** (p.32) - **Modeling Hormone-Sensitive Breast Cancer Using a Novel Three-Dimensional Microphysiological System** Presenter: Megan Campbell Benz - USA Affiliation: Tulane University Authors: Megan C. Benz, Katherine L. Hebert, Elizabeth D. Martin, Frank H. Lau, Matthew E. Burow	
10:30 - 10:45 am	**Coffee Break in Exhibit Hall**	*Blue Prefunction*
10:45 - 11:30 am	**KEYNOTE SPEAKER:** **Ethics in Regenerative Medicine** Graham Parker, PhD *Assistant Professor, Wayne State University* *Editor-in-Chief at Mary Ann Liebert, Inc., Integrative Health Science Facility Core, CURES NIEHS P30, Detroit, MI, USA* Introduced by Ricardo Rodriguez, MD	*Blue Room*
11:30 - 12:10 pm	**Industry Showcase**	
11:30	**MFT Biologics** **Allograft Adipose Matrix – Latest Clinical Applications & Evidence** Marc Long, PhD *EVP R&D, Clinical & Medical Affairs, Strategy and Business Development – MTF Biologics*	
11:40	**Sientra** **Enhanced Viability Fat Transfer with Viality™** Miguel Medina, MD	
11:50	**Tissue and Cell Technologies** **Redefining the Fat Transfer Patient Journey with Fat Banking** Blaine Hamilton *Vice President, Commercial Operations*	
12:00	**XCell Therapeutics Inc.** **Acheiving a Seamless and Adaptable Shift from Serum to Chemically Defined Media-based Cultures** Hyungtaek Jeon	
12:10 - 1:00 pm	**Lunch and Learn with IFATS Key Opinion Leaders and Industry**	*Blue Prefunction and Terrace*
12:00 - 1:00 pm	**IFATS ACADEMY - Fat Grafting Fundamentals** Fred Koelle, MD, PhD and Summer Hanson, MD, PhD	*Capitol Room*
1:00 - 2:05 pm	**Free Papers 6 - Adipose Tissue Processing** Moderator: Ramon Lull, MD, PhD	*Blue Room*

1:00	(p.33) - **Millifat, Microfat, Stromal Vascular Tissue: Mechanical Preparation, Lipoconcentrate Gel, Topical Washing Buffer...Which Product for Which Application** Presenter: Sophie Menkes, MD - Switzerland Affiliation: Clinique Nescensd Authors: Sophie Menkes
1:11	(p.33) - **Impact of Preparation Methods on the Extracellular Matrix Components of Different Fat Grafts** Presenter: Eddy Hsi Chun Wang - USA Affiliation: L'Oreal Research & Innovation Authors: Eddy Hsi Chun Wang, Chloe Trotzier, Clement Bellanger, Wan-Yi Yen Sweelin Chew, I-Chien Liao, Ying Chen, Qian Zheng, Charbel Bouez, Kun Qian
1:22	(p.34) - **Fat Graft Processing Using the REVOLVE™ System Versus LipoGrafter and Decantation: In Vitro Properties and Tissue Quality** Presenter: Nimesh Kabaria, MS - USA Affiliation: Allergan Aesthetics, an AbbVie Company Authors: Sachin Shridharani, Nimesh Kabaria, Carrie Fang, Jared Lombardi, Eric Stec, Li-Ting Huang, Hui Li, Maryellen Sandor
1:33	(p.34) - **Whole Proteomic Analysis of Skin Regenerative Factors in Coleman-Fat, Nanofat, and SVF-Gel** Presenter: Sweelin Chew, PhD - China Affiliation: L'Oreal (China) Research & Innovation Authors: Sweelin Chew, Wan-yi Yen, Eddy Hsi Chun Wang, I-Chien Liao, Ying Chen, Qian Zheng, Nan Huang, Charbel Bouez, Kun Qian
1:44	(p.35) - **Activated Fat Grafting: A Novel Approach for Enhanced Fat Graft Retention and Natural Long-Term Results** Presenter: Eray H. Copcu, MD - Turkey Affiliation: Mest Health Services Inc. Authors: Eray H. Copcu, Sule, Sule Oztan
1:55	(p.35) - **Examining Long-Term Responses of Diverse Human Body Systems and Disorders to Mechanically Obtained Fat-Derived Stromal Cells** Presenter: Eray H. Copcu, MD - Turkey Affiliation: Mest Health Services Inc. Authors: Eray Copcu, Sule Oztan
2:10 - 3:05 pm	**Free Papers 7 - Fat Grafting Retention & Mechanisms** *Blue Room* Moderator: Sherry Collawn, MD
2:10	(p.36) - **Improving Fat Graft Volume Retention with Vitamin D3** Presenter: Amr Elmeanawy, MD - Egypt Affiliation: University of Pittsburgh Authors: A. Elmeanawy, S. Loder, A. Vagonis, B. Bengur, V. Nerone, R. Ricketts, Y. Villalvazo, Y. Surucu, P. Humar, J. Arellano, H. Malekzadeh, B. Shaaban, D. Ramkumar, A. Gavrilescu, PLL Lee, J. Rubin, L. Kokai
2:21	(p.37) - **Long Time Results After Breast Augmentation by Fat Graft** Presenter: Dr. Klaus Ueberreiter - Germany Affiliation: Park-Klinik Birkenwerder Authors: Klaus Ueberreiter, Charlotte Ueberreiter
2:32	(p.37) - **Optimizing Adipose Stem Cell Therapy through Cell Supplemented Engineered Grafts** Presenter: Summer Hanson, MD, PhD - USA Affiliation: University of Chicago Medicine and Biological Sciences Authors: Summer Hanson, Miguel Gonzalez, Luke Zhang
2:43	(p.38) - **Multiple Administrations of Adipose-derived Stromal Cells Concurrent with Fat Grafting** Presenter: Ki Yong Hong, MD, PhD - Korea Affiliation: Seoul National University Hospital - Korea Authors: Ki Yong Hong, Hak Chang

2:54	(p.38) - **Oil Droplets in Apoptotic Uniocular Adipocytes: A Double-edged Sword in Determining Macrophage Phenotype and Its Implications on Fat Grafting** Presenter: Chen Lei, MD - China Affiliation: The First Affiliated Hospital of Fujian Medical University Authors: Songyu Wang, Jong Ye, Meishui Wang, Feng Lu, Biao Wang	
3:05 - 3:15 pm	**Coffee Break in Exhibit Hall**	*Blue Prefunction*
3:15 - 4:00 pm	**Free Papers 8 - Adipose Tissue Engineering** Moderator: Julie Fradette, PhD	*Blue Room*
3:15	(p.39) - **Porous Poly(glycerol sebacate)-based Scaffolds For Enhancing Adipose Tissue Regeneration** Presenter: Rachel Louise Furmidge - United Kingdom Affiliation: The University of Sheffield Authors: Rachel L Furmidge, Victoria Workman, Victoria Giblin, Frederik Claeyssens, Vanessa Hearnden	
3:26	(p.39) - **A Biopolymer Scaffold for Improved Fat Graft Viability and Volume Retention** Presenter: Emily Budziszewski - USA Affiliation: InSoma Bio Authors: Emily Budziszewski, Stefan Roberts	
3:37	(p.40) - **Xenograft-decellularized Adipose Tissue Derived from Humans and Rabbits Supports Adipose Remodeling in Rabbit Mode** Presenter: Hong-Wei Lui, PhD - China Affiliation: The First Affiliated Hospital Authors: Hong-Wei Liu, Hong-Yin Huang	
3:48	(p.40) - **Fat Graft Enriched with Adipose-Derived Stem Cells for Breast Augmentation and Reconstruction: Clinical, Histological, and Instrumental Evaluation** Presenter: Pietro Gentile, MD, PhD - Italy Affiliation: Associate Professor of Plastic and Reconstructive Surgery, University of Rome Author: Pietro Gentile	
4:05 - 4:50 pm	**KEYNOTE PRESENTATION:** **Scenescience** Ramon Llull, MD, PhD *Associate Professor, Plastic and Reconstructive Surgery, Wake Forest Univeristy, School of Medicine, Winston-Salem, NC - USA* Introduced by Guy Magalon, MD	*Blue Room*
4:50 - 5:00 pm	**AWARD ANNOUNCEMENTS** 2024 President Announcement and Presentation	*Blue Room*
5:30 pm	**Meeting Adjourns**	
6:00 pm	**Cocktail Reception** (Pre-registration required)	*Blue Prefunction*

Synopsis of Conference Panels

Regenerative Medical Advances in Military Medicine and Surgery Based on the Work Ongoing at USUHS, Walter Reed and Bethesda Naval Medical Centers

Thursday, October 5, 2023 9:15 – 10:00 am
Introduced by Jeffery M. Gimble, MD, PhD

This panel focuses on problems and complications following combat-related blast injuries and the need for new regenerative solutions in the wound healing and recovery process.

Patient Outcomes and Complications after OPRA Osseointegration Surgery for Patients with Transfemoral Amputations Rosalyn D. Abbott, PhD
Julio A. Rivera, PhD
Scientific Director, DoD Limb Optimization and Osseointegration Program, Assistant Professor of Surgery, USU Walter Reed Surgery and Rehabilitation
Bethesda, Maryland

Trauma Beyond the Injury Site
Thomas A. Davis, PhD
Vice Chair of Research, Professor USU Walter Reed Surgery
Bethesda, Maryland

Adipose Therapeutics for Pain: Demystifying Avenues of Medical Intervention

Thursday, October 5, 2023 1:30 – 2:45 pm
Introduced by Antonio Salgado, PhD

Though surgeons have utilized adipose for both structural and regenerative effects for over 30 years, more recent clinical evidence that adipose may also ameliorate pain provides new and exciting avenues for fat grafting use. In this panel, our speakers will provide medical and scientific expert knowledge on chronic pain etiology and mechanistic research findings on mechanisms through which adipose therapeutics mitigate inflammation, fibrosis, and chronic and debilitating pain.

Fat Grafting to Enhance Peripheral Nerve Regeneration and Attenuate Neuropathic Pain
Stephen W. P. Kemp, PhD
Director, Neuromuscular Lab
Associate Editor, Muscle & Nerve, Associate Professor, University of Michigan, Section of Plastic Surgery, Department of Surgery, Department of Biomedical Engineering, Michigan Neuroscience Institute Affiliate
Ann Arbor, Michigan

A Systems Pharmacology Approach to Analgesic Development
Selwyn Jayakar, PhD
Fellow F.M. Kirby Neurobiology Center
Department of Neurology, Boston Children's Hospital and Harvard Medical School,
Boston, Massachusettes

Cerebral Organoids to Study Central Mechanisms of Pain: The Effect of Stem Cell Secretome on Opioid Receptors and Neuroplasticity
Antonio Salgado, PhD
Coordinating Investigator and Vice-dean for Research at the School of Medicine, Life and Health Sciences Research Institute (ICVS), University of Minho
Braga, Portugal

Fat Grafting as Treatment in Pain Syndromes
Francesco Klinger, MD
Reconstructive and Aesthetic Plastic Surgery School, Department of Medical Biotechnology and Translational Medicine (BIOMETRA), University of Milan, Plastic Surgery Unit, Humanitas Research Hospital
Milan, Italy

Research Diversity Impact and Global Health Equity

Friday, October 6, 2023 10:00 – 11:15 am
Introduced by Trivia Frazier, PhD

The IFATS community is comprised of clinicians, basic scientists and industry representatives with significant interest in translating regenerative medicine research outcomes to practice. As such, our organization strongly supports efforts to increase diversity in research and to better understand the impact of research inclusivity on health equity. This panel will discuss how policy and practice can be used to increase diversity in research outcomes.

Lack Of Diversity In Genomic Databases Is A Barrier To Translating Precision Medicine Research Into Practice
Vence L. Bonham, Jr. JD
Acting Deputy Director National Human Genome Research Institute
Bethesda, Maryland

The Impact of Biologic Diversity on Measured Research Outcomes
Kun (Mark) Qian, MD
Director Advanced Research, L'Oreal Research and Innovation
Clark, New Jersey

Optimizing Inclusion: Challenges in Policy and Practice
Nicole Redmond, MD, PhD, MPH
Chief, Clinical Applications and Prevention Branch (CAPB)
Division of Cardiovascular Sciences (DCVS)
National Heart, Lung, and Blood Institute (NHLBI)
Washington, District of Columbia

Incorporating Patient Diversity within Adipose Tissue Models for Metabolic Disease Screening
Cecelia Sanchez, PhD
Obatala Sciences Inc.
New Orleans, Louisiana

Adipose Health Disorders: Obesity and Lipedema

Friday, October 6, 2023 1:45 – 3:00 pm
Introduced by Susanna Miettinen, PhD and Sara Al-Ghadban, PhD

Global epidemic of obesity and its multiple metabolic consequences have triggered an increasing need for understanding the functions of human adipose tissue (AT) in health and disease. Obesity may alter the cellular content of AT and affect their functions, which may have implications on utilization of AT and its derivatives as therapeutics. Lipedema is a painful AT disorder that is often confused with obesity and lymphedema. As the AT is the primary affected tissue in patients, defining the role of adipose stem cells (ASCs) in the disease-associated processes will provide insights into the pathophysiology of lipedema and will help researchers develop potential treatment for the disease.

The 2023 IFATS panel on Adipose Health Disorders: Obesity and Lipedema is designed to provide an overview on the recent developments in the field of obesity and lipedema research and provide a platform to discuss about the special features of obesity and lipedema and how they should be considered when therapies are planned.will discuss how policy and practice can be used to increase diversity in research outcomes.

Adipose Tissue Metabolism in Obesity
Kirsi Pietiläinen, MD, PhD
Professor in Clinical Metabolism, Programme Director, Research Programme for Clinical and Molecular Metabolism, Faculty of Medicine, University of Helsinki, Chief Physician, Obesity Center, Helsinki University Central Hospital
Helsinki, Finland

Effects of Obesity on Adipose Stem/Stromal Cells
Susanna Miettinen, PhD
Professor of Cell and Tissue Technology, Adult Stem Cells Group, Faculty of Medicine and Health Technology, Tampere University
Tampere, Finland

Characterization of Estrogen Receptors (ERs) and Estrogen Metabolizing Enzymes in Lipedema and Non-lipedema Adipose-derived Stem Cells (ASCs) in 2D Monolayer and 3D Cultures
Sara Al-Ghadban, PhD
Research Scientist, Dept. of Microbiology, Immunology & Genetics, University of North Texas Health Science Center
Denton, Texas

A Comparison Study of Potential Translational Screening Tools for Lipedema
Yinan Zheng, MD Candidate
Vanderbilt University School of Medicine
Nashville, Tennessee

CELEBRATING

10

YEARS

REVOLVE™

Advanced Adipose System

A DECADE AGO, WE BROUGHT YOU SOMETHING NEW.

NOW, WE'RE GETTING READY TO DO IT AGAIN.

REVOLVE ENVI™

Advanced Adipose System 600

COMING SOON!

RVE157936 09/22

Abstracts

THURSDAY, OCTOBER 5, 2023
FREE PAPER SESSION #1: Pain and Wound Healing Indications

Stromal Vascular Fraction (SVF) Relieves Symptoms of Carpometacarpal I Osteoartrosis (OA) - Preliminary Interim Analysis of Randomized Control Trial (RCT)

Presenter: Susanna Cecilia Kauhanen, PhD - Finland
Affiliation: Helsinki University Hospital
Authors: Susanna Cecilia Kauhanen, Jussi Kosola, Samuli Aspinen

INTRODUCTION: OA of the carpometacarpal (CMC) joint of the thumb causes pain, disability, decreased quality of life. For persistent symptoms not responding to conservative treatment surgery of variable invasiveness and efficacy prevail. SVF contains e.g mesenchymal stem cells, endothelial progenitor cells and stromal components. The purpose of this RCT is to delineate outcome after thumb carpometacarpal injection with SVF derived from adipose tissue. SVF injection with thumb splinting and splinting alone are compared.

METHODS: Our study is an open label RCT with 1:1 arms aiming at 30 + 30 patients 40-70 years of age with thumb OA (Eaton Littler II). Exclusion criteria are post-traumatic OA, relevant comorbidities, inflammatory joint disease, corticosteroid use, <6 mo from other hand surgery. Patients randomized into the SVF arm undergo liposuction in local anesthesia in a outpatient clinic setting. SVF is produced as validated for the Q-Graft system (Humanmed, Germany). SVF is injected into the CMC joint (appr 1 ml) under sterile conditions. Outcomes; pain on a visual analogue (VAS) scale and a Patient-Rated Wrist Evaluation (PRWE) questionnaire, global improvement (5-step likert scale), grip and pinch strength and Mental Health Quotient (MHQ) questionnaire. Complications are also recorded. Follow-up:1 mo (phone)3 and 6 months, and long term 1 year and 5 years.

RESULTS: Patients were operated under local anestesia without sedation. Sick-leave was 2 days. One patient had discomfort due to hematoma at the fatharvest site. Interim results of the first 12 patients in the SVF group are shown in the tables below.
Limitations of the study: low number of study subjects and short follow-up time. The lack of a sham- liposuction procedure in the "splinting alone" arm of the RCT, (limited financial research resources) is acknowledged.

CONCLUSION: We describe short term pain relief and functional improvement (PRWE, VAS) in CMC I OA patients receiving intra-articular SVF in a feasible outpatient setting. Adipose derived stem cells secrete cytokines and growth factors redirecting inflammation towards regeneration. Whether the positive effect of SVF on thumb OA is due to the cells injected into the joint or to splinting as such remains to be shown in our ongoing RCT.

Demographics	
Male/Female	1/11
Age	55 (42-66)
Symptom duration	9 mo (4-15mo)
BMI	28.3 (19.8-38.9)
ASA	1-2
Working/unemployed/retired	10/1/1

VAS (pain at rest)	Pre-op	1 mo	3 mo	6 mo
Mean, min-max	48 (30-80)	31 (0-60)	23 (0-60)	13 (0-50)

Pain-VAS MCID 16-19 p.

PRWE	Pre-op	3 mo	6 mo
Pain score	33.6 (8.5 SD)	21.5 (13.5)	22.6 (14.0 SD)
Function score	41.5 (21.0 SD)	33.1 (28.0)	29.5 (26.0)
Total score	75.1 (27.0 SD)	56.5 (41.0)	54.1 (25.5)

PRWE MCID 12-16 p.

Global rating	1 mo	3 mo	6 mo
Much worse (-2)	-	-	-
Worse (-1)	-	-	-
No difference (0)	3	1	1
Better (+1)	5	6	5
Much better (+2)	5	5	4

Combination Therapy with Adipose Fat Grafting for Hypertrophic Burn Scars

Presenter: Sherry Collawn, MD, PhD - USA
Affiliation: University of Alabama
Author: Sherry Collawn

INTRODUCTION: Hypertrophic scarring following burns can result in a painful debilitating scar condition. This data will demonstrate that adipose grafting combined with platelet rich plasma (PRP) as well as injection of 5-fluorouracil (5-FU) and triamcinolone can result in dramatic improvement in skin texture with decreased pain and scarring, and improved range of motion.

METHODS: This prospective study follows 9 patients with hypertrophic burn scars that were all injected with the above 4 materials. Fat/PRP was mixed at a ratio of 0.8/0.2. Three syringes of 5-fluorouracil and triamcinolone were injected per session into multiple areas of scarring.

RESULTS: Patient's demonstrate excellent improvement after 1 session of treatment. In figure 1 the patient only had one treatment session of her hypertrophic skin graft left knee with significant scar flattening. The other treated area not shown in the photo is the left foot.
The patient in figure 2 is shown after two sessions of injection of right cheek, ear, neck and submental hypertrophic and keloid burn scars. He has had significant scar flattening with decreased pain and increased neck range of motion. Other treated areas not shown in the photo are the right axilla and shoulder.

CONCLUSION: Patients have had successful results with scar improvement with this quadrivalent injection therapy.

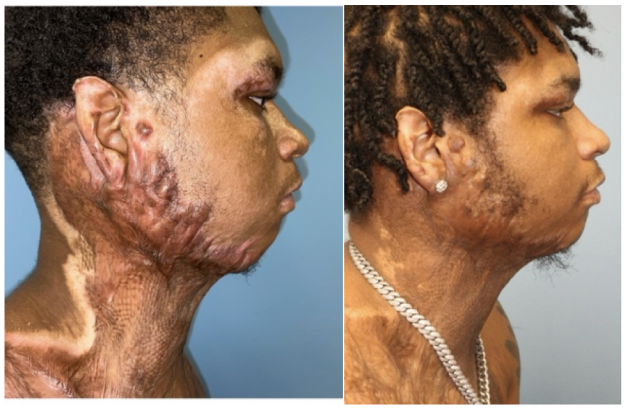


Figure 1. The left figure is pretreatment and the right figure is 7 weeks after one treatment.

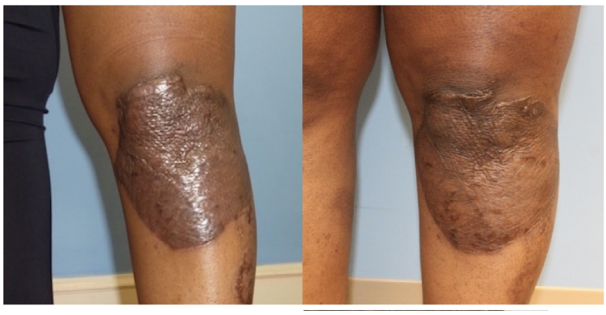


Figure 2. The left figure is pretreatment and the right figure is 11 months after two treatments.

Outcomes and Complications after OPRA Osseointegration Surgery for Patients with Transfemoral Amputations

Presenter: Julio A. Rivera, PhD - USA
Affiliation: Henry M. Jackson Foundation for the Advancement of Military Medicine
Authors: Julio A. Rivera, Benjamin K. Potter, Ashley B. Anderson, Angelica Melendez-Munoz, Jason M. Souza, Jonathan A. Forsberg

INTRODUCTION: Most individuals with transfemoral amputations experience difficulties with conventional socket wear. Osseointegration (OI) allows for the direct, transdermal skeletal attachment of external prostheses helping mitigate many challenges. Therefore, the purpose of this study was to (1) evaluate "before and after" changes in functional ability and pain and (2) evaluate the frequency and severity of complications with OI in service members and beneficiaries with transfemoral amputations (TFA).

METHODS: We conducted this prospective study in 41 TFA patients, initially as part of an FDA HDE study, and later continuing following PMA approval of the OPRA device for transfemoral amputations. Patient reported outcome measures including PROMIS and the Q-TFA were given at pre-op, 3, 6, 12, and 24-months after surgery. Incidence of soft and deep tissue complications were recorded to determine the propensity of infections at the skin penetration site. We used t-tests to evaluate the change in outcome measures from baseline to the 24-month follow-up.

RESULTS: All 41 enrolled TFA patients underwent OI surgery. There were 13 patients with bilateral TFA, for total of 54 implants. As of May 2023, 39 participants (95%) have reached the 24-month follow-up, showing significant improvements in most outcome measure domains. Twenty-three of the 54 implants (42%) developed superficial infection and were treated successfully with oral antibiotics and four implants (7%) developed deep infections.

CONCLUSION: We demonstrated significantly improved functional results for TFA ossoeintegration in a US patient population. Rates of superficial and deep infection were modestly improved compared to prior studies. Long-term functional and patient reported outcomes will be prospectively followed for the duration of the implant in order to determine the frequency of long-term complications such as loosening, fracture, stress shielding or chronic osteomyelitis.

Preclinical Volume Retention of Fat Grafts Processed with the REVOLVE™ ENVI Filtration-Based System or Decantation Methods in Irradiated and Nonirradiated Wounds

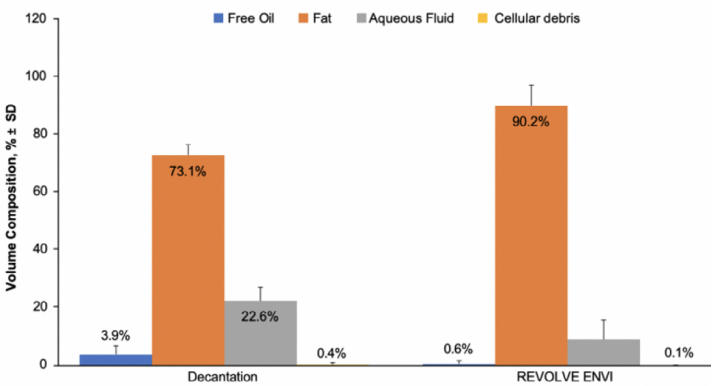
Presenter: Patrick S. Cottler, PhD - USA
Affiliation: Allergan Aesthetics an AbbVie Company
Authors: Christopher A. Campbell, Patrick S. Cottler, Graham M. Grogan, Nimesh Kabaria, Maryellen Sandor

INTRODUCTION: The processing of harvested fat for transplantation is critical to fat graft performance in vivo. In breast reconstruction, fat grafting may involve implantation adjacent to tissue damaged by radiation treatment. This preclinical animal study evaluated the effects of radiation on retention volume and quality of fat grafts after processing by decantation or the REVOLVE™ ENVI system (Allergan Aesthetics, an AbbVie Company), a filtration-based device that can process up to 600 cc of lipoaspirate.

METHODS: Lipoaspirate was collected from individual human donors (n=6), processed using either REVOLVE ENVI or decantation methods, and implanted (0.5 cc) into 60 athymic mice for 4 weeks. Animal dorsal implant sites had been either irradiated with a single 35-Gy dose 12 weeks before implantation or remained nonirradiated and aged 12 weeks. Assessments included volume retention of explanted grafts measured by magnetic resonance imaging (MRI) and weight-based methods, as well as volume composition of grafts before implantation (free oil, fat, aqueous fluid, cellular debris) measured in vitro.

RESULTS: MRI-based volume retention analysis demonstrated higher mean (SD) percent retention with REVOLVE ENVI than decantation: 94% (6%) vs 84% (7%) in nonirradiated sites ($p<0.01$) and 91% (7%) vs 85% (8%) in irradiated sites ($p=0.70$), respectively. Weight-based volume retention analysis revealed higher mean (SD) percent retention with REVOLVE ENVI than decantation: 102% (11%) vs 79% (13%) in nonirradiated sites ($p<0.01$) and 98% (18%) vs 76% (9%) in irradiated sites ($p<0.01$), respectively. Volume composition analysis demonstrated higher fat content and lower aqueous fluid and free oil content with REVOLVE ENVI than with decantation, with similarly minimal cellular debris content (Figure).

CONCLUSION: REVOLVE ENVI-processed grafts, whether implanted in irradiated or nonirradiated sites, demonstrated significantly greater volume retention by weight than decanted grafts in a preclinical mouse model. Similar results were observed by MRI, except in nonirradiated sites, for which volume retention was similar for both processing methods. Graftable fat content was also greater with REVOLVE ENVI. Results suggest better early volume retention and quality of fat grafts with REVOLVE ENVI than decantation alone, in both healthy and radiation-treated surgical sites.



Mechanical Processing of Human Lipoaspirate with a Fluidic Device System Enhances Recovery of Mesenchymal Stem Cells and Promotes Wound Healing Through Hydrodynamic Shear Flow

Presenter: Derek Banyard, MD, MS, MBA - USA
Affiliation: Sayenza Biosciences
Authors: Derek A. Banyard, Alexandria M. Sorensen, Mary Zeigler, Pisrut Phummirat, David Zalazar, Alan D. Widgerow, Jered B. Haun

INTRODUCTION: Adipose tissue is an easily accessible source of stem and progenitor cells that offers exciting promise as an injectable autologous therapeutic for regenerative applications. Mechanical processing is preferred over enzymatic digestion, and the most common method involves shuffling lipoaspirate between syringes and filtering to produce nanofat. Although traditional nanofat (NF) has shown exciting clinical results, we hypothesized that optimization of fluid dynamics principles, integration, and automation of new device designs could enhance and standardize recovery of stem/progenitor cells, and potentially, augment the regenerative capacity of this non-enzymatic stromal vascular fraction (NESVF™) via shear-induced mechanotransduction.

METHODS: The authors designed and fabricated the emulsification and micronization device (EMD) and filtration device (FD) to replace traditional nanofat procedures. An Activation Device (AD) was added downstream to further enhance sheer stress. Human lipoaspirate was used to optimize EMD and FD processing parameters and compared to traditional nanofat using standard ex vivo measurement assays. Samples were subsequently processed with the AD at different flow rates. Results were compared to collagenase digestion and NF methods both immediately and after 24 hour culture. Finally, expression of genes related to wound healing and functional angiogenic capacity were assessed.

RESULTS: Lipoaspirate processing with EMD and FD was superior to NF in terms of both recovered cell percentages (>1.5-fold) and numbers (two- to three-fold). Differences were statistically significant for total mesenchymal stem cells and a DPP4+/CD55+ subpopulation. MSC recovery and viability were not significantly affected by the AD, but EPCs were enriched in a shear stress-dependent manner. Culturing samples did not alter cell numbers substantially but did reveal changes in transcriptional programs linked to wound healing, particularly for immune priming, matrix remodeling, and angiogenesis. These responses were consistently stronger for our device platform than NF, and differences were statistically significant for CXCL1, IL1β, IL6, CSF3, and COL1A2. Notably, vessel sprouting was significantly improved for our devices compared to NF.

CONCLUSION: Mechanical processing of adipose tissue with a three-device technology platform resulted in enhanced enrichment of stem and progenitor cells, the activation of genes implicated in wound healing, and the induction of angiogenic sprouting when compared to traditional nanofat.

THURSDAY, OCTOBER 5, 2023
FREE PAPER SESSION# 2: Head and Neck

Nanofat Graft in Treatment of Infraorbital Dark Circles

Presenter: Yi Ru Su - Taiwan
Affiliation: Cathay General Hospital
Authors: Yi Ru Su, Chi-Ming Pu

INTRODUCTION: Infraorbital dark circle (IDC) refers to visible darkness of the periorbital areas. There are several clinical causes of IDC. Lasers, topical therapies, chemical peels, carboxytherapy, normobaric oxygen therapy, fillers, platelet-rich plasma and surgery are all been reported as treatment options. Nanofat is an ultra-purified adipose tissue-derived product that emulsified to 400 to 600 μm parcel. It can regulate neovascularization and tissue regeneration through paracrine effects. A wide range of improvements were seen in wrinkles, discolorations, and scars in previous research.

We present a case series of IDC treated with nanofat grafting with and without combination of microfat graft, and review the current literature, to address the utility of nanofat graft in periocular rejuvenation.

METHODS: A retrospective review was performed of all patients who underwent nanofat grafting for treatment of IDC at the authors' institution between January 2021 and June 2023, and follow-ups for more than 3 months were included. Patient's preoperative data, intraoperative and post-operative outcomes were retrieved from the institution`s prospective database. Series preoperative and postoperative photography were taken for the outcome evaluation.

RESULTS: Ten women were included, 6 cases were treated with nanofat graft and 4 were treated with nanofat combined with microfat graft. The results showed nanofat graft can be a good option for improvement of infraorbital dark circle.

CONCLUSION: This report of 10 cases highlights the curative effect of nanofat graft transplantation in treatment of IDC. Proper diagnosis of underlying etiology is crucial during treatment planning. Besides, patients often require multiple treatments to achieve satisfying improvement. Even though nanofat graft theoretically has multiple effects target on most of the mechanism of IDC, combined treatment with surgery should always keep in mind as a choice.

Nanofat as a Rescue for Peri Oral Rejuvenation Following Aggressive CO2 Laser and Microneedling Treatment

Presenter: R. Brannon Claytor, MD - USA
Affiliation: Claytor Noone Plastic Surgery
Authors: R. Brannon Claytor

INTRODUCTION: Treating facial aging with CO2 lasering combined with microneedling are cornerstones of facial rejuvenation. Combining thermal injury with mechanical injury at the same treatment has traditionally been considered too injurious for practical usage with concerns about scarring or excessively long and painful recovery. Introducing nanofat as a rescue is a novel technique which we have demonstrated not only accelerates recovery but also dramatically reduces post procedure pain.

METHODS:23 patients were treated with CO2 laser with 2 passes. The first pass was a minimal surface area with very deep penetration down to the reticular dermis. The second pass was high percentage surface area with a shallow tissue penetration which only partially vaporizes the epidermal layer. Immediately following the CO2 laser treatment the skin was treated with microndeeling to a depth of 2.5 mm. During the microneedling treatment, nanofat was liberally deposited on the skin in small aliquots. The nanofat was absorbed into the skin through the microneedling pores.

RESULTS: All patients reported no pain on the Numerical Rating System 0-10. This was recorded in follow up phone calls the evening of the procedure and the next day. Patients were seen at 5 days post op and again recorded 0 pain on the Numerical Rating System. Additionally patients were able to out in public attending to activities of daily living as early as 5 days post procedure demonstrating rapid recovery.

CONCLUSION: Therapy with thermal CO2 remodeling and mechanical penetration with microneedling have the potential for more complete treatment of perioral rhytids, however, the injury from these treatments has the potential to have scarring and prolonged painful recovery times. Introducing triple therapy with the addition of nanofat accelerates healing and minimizes perineural inflammation which reduces pain.

Oil Cysts Formation after Lower Blepharoplasty with Fat Graft

Presenter: Chi-Ming Pu, MD - Taiwan
Affiliation: Cathay General Hospital
Authors: Chi-Ming Pu

INTRODUCTION: Oil cysts are pseudocysts, owing to their lack of epithelium or endothelium. An oil cyst is caused by central fat necrosis due to microenvironments around the fat drop that did not properly improve during the first three days after surgery. Clinically, oil cyst or fat necrosis presents as a palpable, discrete, and persistent subcutaneous firmness found by clinical examination. A recent systematic review of complications after breast augmentation with fat grafting showed that palpable cysts occurred in 2.0% of cases. However, no studies have been conducted to evaluate the complication rate of oil cyst formation occurring after lower blepharoplasty or total blepharoplasty with autologous fat grafting.

METHODS: IA retrospective review was performed of all patients who underwent lower or total blepharoplasty combined with fat graft at the authors' institution between January 2018 and June 2020. Complication rates were observed, and associations between preoperative variables and outcomes were assessed to evaluate the complication rate of oil cyst formation.

RESULTS: A total of 119 patients were included in the series. The average patient age was 54.88±11.94 years, and the average grafted fat was 1.88±1.0 ml. On a per-eyelid basis for all patients, the complication rate of oil cyst formation was 6.72 percent (16 of 238 eyelids). The average age of patients with oil cysts formation was 56.38±9.96 years. The occurrence of oil cyst formation was not associated with age (p-value = 0.784), gender (p-value = 0.317), surgical type (p-value = 0.091), or fat volume (p-value = 0.215). The mean interval between the fat graft procedure and oil cyst noted was 236.5±118.9 days.

CONCLUSION: Lower blepharoplasty or total blepharoplasty combined with fat graft is an effective treatment of an aged eyelid. The complication rate of oil cyst formation is low and can be managed easily. Reduce surgical trauma might decrease the complication rate of oil cyst formation.

ABSTRACTS - FRIDAY, OCTOBER 6, 2023
FREE PAPER SESSION# 3: Adipose-derived Cell Therapeutics

Use of Autologous Adipose-Derived Mesenchymal Stem Cells for Ovarian Rejuvenationin Poor Responder IVF Patients: A Phase 1 Randomised Placebo Controlled Double Blind Crossover Study

Presenter: Carola Niesler, PhD - South Africa
Affiliation: University of KwaZulu-Natal
Authors: T. Mohamed, J.K. Adam, C. Niesler, A. Chikandiwa

INTRODUCTION: Despite the application of various methods to augment ovarian responsiveness, the management of poor ovarian responders remains challenging and pregnancy rates following in vitro fertilisation (IVF) are poor. Advances in adult stem cell research and their clinical application has prompted interest in their use in assisted reproduction. We report the first double blind, randomised, placebo-controlled clinical study using autologous human stromal vascular fraction (SVF)containing adipose-derived stem cells (ADSCs) for ovarian rejuvenation.

METHODS: Thirty patients were recruited. Twenty-one had lower-than-expected reserves for their age and nine had premature ovarian insufficiency (POI). Patients were randomized into a placebo group (10) and into an intervention group (20). SVF was obtained from adipose tissue following abdominal liposuction; the ADSC component was characterised using flow cytometry. Three equal insertions, adjusted based on ovarian volume, were performed at monthly intervals via an ultrasound-guided transvaginal needle puncture. The SVF was not cultured prior to transplantation. Those in the placebo group were then crossed over to the intervention group and received a single SVF (maximally concentrated) insertion (crossover group).

RESULTS: The median viable SVF cell number inserted per patient over three months, and the % MSC (mesenchymal stem cells) thereof, was 1.6 x106 and 13.2% respectively. Resulting AMH changes were variable over the treatment course with a notable placebo effect. Patients with POI showed no change in AMH, both to intervention and placebo. Despite this, a temporary return of menses was noted in a third of patients while on treatment. Patients with low reserves for age showed an increase in AMH, although not statistically significant when compared to placebo. In the crossover group, insertions were limited to one intervention comprising all cells; here a significantly higher median of 3.4 x 106 SVF cells were injected containing an average of 16.9% MSCs. No significant change in AMH was noted. To date 12 patients have undergone ovarian stimulation and IVF post stem cell therapy; of these nine have had embryo transfers with a resulting pregnancy rate of 33%. There were also 2 spontaneous pregnancies.

CONCLUSION: Although the application of SVF-derived adipose-derived stem cells for ovarian rejuvenation remains experimental, the current study provides further support for the safety of this approach and presents encouraging results as to its efficacy in assisted reproduction.

Definitive Results of the Preclinical Study Conducted in Rodents to Determine the Neuroprotective and Neurotrophic Effects of the Autologous Fat-derived Stromal Vascular Fraction (SVF) in the Acute Management of Spinal Cord Contusions

Presenter: Nicolas Serratrice, MD - France
Affiliation: Neurosurgeon, Spine & Spinal Cord Surgeon, Associate Researcher
Authors: Nicolas Serratrice

INTRODUCTION: Spinal cord injuries (SCI) lead to functional alteration with important consequences such as motor and sensory disorders. The repair strategies developed to date remain ineffective. The autologous adipose tissue-derived stromal vascular fraction (SVF) is composed of a "cocktail" of mesenchymal and hematopoietic stem cells with trophic, pro-angiogenic and immunomodulatory effects. Numerous therapeutic benefits have been shown for tissue regeneration, peripheral neuropathies as well as in the context of certain neurodegenerative diseases, but never in the context of SCI.

METHODS: Our strategy is based on the very early injection of the autologous SVF after spinal contusions. To verify our hypothesis, we conducted a preclinical study in adult male rats (300 g). Spinal cord contusions are performed at the T10 thoracic level using a dedicated impactor; thus all animals are rendered paraplegic. The epididymal fat is removed in a second operation, then the autologous SVF cells are purified (>90% viability), before being injected directly into the spinal cord lesion within 4 hours after the trauma (1 million cells, maximum dose obtainable in rats for their age). The same work was then repeated after intensive training of the animals on a treadmill.

RESULTS: Autologous SVF implantation promotes 1) locomotor recovery (BBB test, Ladder rung walking test, Catwalk), 2) H-reflex normalization, and ventilatory frequency adjustment to an isometric exercise. 3) In vivo 7T MRI, shows signs of regeneration and revascularization. We also identified a biomarker for the following of the inflammation. These results were confirmed by 4) immunohistological stainings (angiogenesis with CD31, number of neurons with MAP2 and axonal regeneration with GAP43), and by 5) studying proinfammatory cytokines (IL-1, IL-6, TNF-) by ELISA. 6) Finally, intensive training significantly potentiates the regenerative effects of SVF.

CONCLUSION: These very encouraging results obtained in rats demonstrate, in addition to an immediate neuroprotective effect, significant revascularization and signs of bone marrow regeneration after implantation of the autologous SVF cells. The work is currently being carried out in pigs before moving on to humans.

Age Does Not Seem to Affect ASC Stemness and Pro-angiogenic Potential

Presenter: Chloe Trotzier - France
Affiliation: L'Oreal Research & Innovation
Authors: Chloe Trotzier, Kun QIAN, Celine Auxenfans, Ali Mojallal

INTRODUCTION: Aging is a progressive decrease in the regenerative abilities to maintain tissue homeostasis, such as vascularization or stem cell potential. Autologous fat grafting is widely used in reconstructive and plastic surgeries for its volume correction effects as well as its skin rejuvenation outcomes. However, the resorption rate of the graft is still unpredictable, and the skin rejuvenation mechanism is not well defined. Among factors that influence graft survival and skin rejuvenation, Adipose-derived Stem/Stromal Cells (ASC) has been postulated to be the key player due to their potential to differentiate into endothelial cells and pro-angiogenic factors containing secretome. In this study we aim to investigate how age affects ASC differentiation, stemness and pro-angiogenic potential.

METHODS: Freshly extracted ASC from liposuction of 6 young (< 30yo) and 6 old (>50yo) female donors were assessed for differentiation potential, colonies forming efficiency and pro-angiogenic activity. In the Cytodex beads based pro-angiogenic assay, ASC were cultured on top of the fibrin gel containing human dermal endothelial cells until sprouting. Sprouts were imaged using confocal microscope and analyzed using Sprout Morphology plugin of ImageJ. Total network length of each condition was quantified.

RESULTS: Proportion of ASC colonies forming efficiency between young and old ASC show no statistical difference. Neutral lipid content and mineralization concentration show no statistical difference between young and old ASC, indicating that ASC differentiation potential does not change with age. ASC induced significantly longer total network length compared to fibroblasts, however, total network length between young and old ASC donor exhibits no statistical difference.

CONCLUSION: Overall, age does not alter ASC differentiation, CFE and pro-angiogenic potential. The result of our study indicates that further studies are warranted to understand whether fat graft retention and its skin rejuvenation efficacy are linked to the ASC quantity at the recipient sites or are related to its interaction with other components of the fat graft or local microenvironment.

Proteomic Analysis: The Effect of Antioxidant Supplementation on Bone Marrow Derived Mesenchymal Stem Cells in Diabetes

Presenter: Michelle Maartens - South Africa
Affiliation: Division of Clinical Pharmacology, Faculty of Medicine and Health Sciences, Stellenbosch University
Authors: Michelle Maartens, Mare Vlok, C Smith, Mari van de Vyver

INTRODUCTION: Bone marrow resident mesenchymal stem cells (MSCs) are sensitive to changes in the micro-environment and vulnerable to glucose toxicity. Under diabetic conditions, exposure to hyperglycaemia, inflammation and oxidative stress within the micro-environment impairs the regenerative capacity of MSCs and dysregulate their immunomodulatory functions. The antioxidants N-acetylcysteine (NAC) and ascorbic acid 2-phosphate (AAP) has been shown to improve the viability and growth rate of diabetic MSCs ex vivo and suppress excessive pro-inflammatory cytokine release. The exact mechanism of action is however still unclear and needs elucidation.

METHODS: Bone marrow MSCs were isolated from obese diabetic mice (B6.Cg-lepob/J (ob/ob); >40g, 6 weeks, n=8) and the cell number expanded in culture with or without antioxidant supplementation for a period of 12 days. Antioxidant treatment consisted of 7.5mM NAC + 0.6mM AAP with media being changed every 4 days. Upon reaching 70% confluence, conditioned media was collected, and the cells lysed to harvest the intracellular protein content. Protein samples were processed using standardized procedures and analysed using label free LC-MS/MS. Statistical analysis was performed in Scaffold and functional pathway analysis and protein interactions were mapped for the differential proteins of interest ($p < 0.05$) (identified through biostatistical analysis of the LC-MS/MS data) using STRING. Zebrafish larvae was subsequently exposed to the bone marrow MSC conditioned media, and their behaviour and cognitive abilities assessed.

RESULTS & CONCLUSION Consistent with previous findings, antioxidant supplementation was able to improve the ex vivo growth rate of MSCs. LC-MS/MS identified 5602 proteins of which 747 was unique to the non-treatment group and 395 was unique to the antioxidant supplemented group. The differentially expressed proteins are known to influence biological processes such as cell structure (matrix proteins), redox homeostasis (NADH oxidase, PRDX1), and immunomodulation (MRC1, STAT1). The diabetic MSC conditioned media negatively affected zebrafish responses, whereas this effect was less pronounced in the zebrafish exposed to antioxidant treated conditioned media was collected, and the cells lysed to harvest the intracellular protein content.

ABSTRACTS - FRIDAY, OCTOBER 6, 2023
FREE PAPER SESSION# 4: Adipose in Health

Leptin Signaling Drives Tumor Growth in Triple Negative Breast Cancer

Presenter: Courtney Brock - USA
Affiliation: Tulane University School of Medicine
Authors: Courtney Brock

INTRODUCTION: Individuals with a high body mass index (BMI) have an increased risk of developing many cancers, including breast. In triple negative breast cancer (TNBC), a clinically aggressive subtype, patients who are obese have higher rates of mortality and shorter disease-free survival compared to lean patients. While these epidemiological associations are clear, the molecular underpinnings that contribute to poor outcomes for obese TNBC patients are not fully elucidated. Previous work has shown that obesity affects TNBC pathology through crosstalk between obese-imprinted adipose stem cells (ASCs) and TNBC cells. In obese individuals, ASCs have an altered secretory profile resulting in higher levels of leptin, an adipokine involved in inflammatory and wound-healing processes . Increased leptin and leptin receptor expression is associated with poor outcomes (increased mortality, increased recurrence) in many cancers, including breast. Therefore, this study seeks to examine the role of leptin signaling in triple negative breast cancer.

METHODS: This project examines the role of leptin signaling in TNBC using patient-derived cell lines and patient-derived xenografts (PDX), as well as a pharmacological inhibitor of the leptin receptor, Allo-aca (AA). To determine the effects of obesity on tumor growth in vivo, a high fat diet (HFD) was used to induce obesity in SCID/Beige mice.

RESULTS: PDX tumors implanted into HFD mice had an increased growth rate compared to tumors implanted into lean controls. Additionally, treatment with AA slowed tumor growth rate in both obese and lean animals, suggesting the role of leptin in regulating tumor growth. Exposure to conditioned media harvested from obASCs increased the percentage of TNBC cells that expressed cancer stem cell markers in vitro, whereas exposure to AA decreased the percentage of cancer stem cells. Similarly, exposure to leptin increased expression of EMT (epithelial to mesenchymal transition) genes, whereas treatment with AA reduced expression of EMT genes.

CONSLUSIONS: These molecular differences may contribute to the differences in cancer outcomes between obese and lean individuals with breast cancer, and further study of leptin signaling and its contributions to the obesity-cancer axis in TNBC is critical.

Stromal Vascular Fraction and Blood-derived Extracellular Vesicle miRNAs as Novel Biomarker for Lipedema

Presenter: Eleni Priglinger - Austria
Affiliation: Johannes Kepler University Medical Faculty
Authors: Eleni Priglinger, Karin Strohmeier, Sarah Moussa, Susanna Skalicky, Johannes Oesterreicher, Marlene Wahlmueller, Wolfgang Holnthoner, Matthias Sandhofer, Martin Barsch, Matthias Hackl, Susanne Wolbank

INTRODUCTION: Lipedema is a chronic medical condition characterized by enlargement/deposition of adipose tissue in the extremities. Due to a lack of diagnostic tests lipedema is largely under-diagnosed, urging for novel diagnostic biomarkers. Here, miRNAs have been proposed as promising biomarkers based on their controlled release from cells into biofluids, where they are found inside small extracellular vesicles (sEVs) and protein complexes. We have previously studied the relevance of stromal vascular fraction (SVF) involvement in lipedema and associated extracellular miRNA profiles where we identified for the first-time specific changes in EV-miRNAs compared to healthy controls. We extended our study to plasma samples, since non-invasive, circulating lipedema biomarkers will facilitate clinical trials.

METHODS: An unbiased quantitative analysis of small non-coding RNAs including miRNAs in sEV fractions as well as total extracellular RNA (total exRNA) was performed on platelet poor plasma samples by next generation sequencing. A proof-of-concept for the utility of miRNAs as diagnostic biomarkers was based on four different cohorts: early-stage lipedema and healthy (BMI matched), healthy obese and lipedema obese (BMI matched). In addition, a thorough characterization of isolated EV phenotypes was performed by NTA and flow cytometry to clarify their cellular origin.

RESULTS: We identified differently regulated sEV-miRNAs in peripheral blood from lipedema individuals compared to the previously identified sEV-miRNA profile derived from SVF. When comparing sEV-miRNAs derived from lipedema peripheral blood to obese, lipedema obese and healthy individuals we found several miRNAs distinctly up or downregulated. To complete the picture, a detailed and systematic investigation of the blood-derived sEVs showed significant differences in EV concentration between healthy and lipedema. The phenotypes relevant for sEV alterations in adipose tissue represented only a minority of circulating EVs (<2%). When comparing these phenotypes in the cohorts, differences could be observed in mesenchymal, blood and lymphatic endothelial and macrophage subsets.

CONCLUSION: We could show that EVs and their respective cargo can provide insight into the progression of lipedema. When corroborating the findings of this study, peripheral blood plasma EV-miRNAs could be used to identify early-stage lipedema. Readily available systems for blood-based RT-qPCR testing will accelerate translation into clinical practice.

Adipose Tissue Contains Extracellular Lipids Associated with Regions of Collagen

Presenter: Elizabeth Kaleigh Johnston - USA
Affiliation: Carnegie Mellon University
Authors: Elizabeth K. Johnston, Megan DeBari, Qijia Zhou, Phil Campbell, Rosalyn Abbott

INTRODUCTION: White adipose tissue plays a vital role in maintaining whole body homeostasis. It does so through its ability to dynamically fluctuate in size and mass. However, in a fibrotic disease state, the excessive matrix accumulation restricts these fluctuations. With limited expandability, there is potential for ectopic lipid deposition and a reduction in insulin sensitivity. Further, with apoptosis being a prevalent occurrence in other forms of fibrosis, the goal of this study is to elucidate the involvement of apoptotic bodies and other extracellular lipids (EL)s in adipose tissue pathology.

METHODS: Human subcutaneous adipose tissue was procured from UPMC's Department of Plastic Surgery from overweight/obese individuals (BMI>25). The samples were dissected, fixed, and stained with either AdipoRed or BODIPY and Phalloidin. To evaluate apoptotic origin, samples were stained with Annexin-V prior to fixation and further staining. Confocal microscopy was utilized to image intracellular and extracellular lipids alongside phalloidin and Annexin-V staining, with ImageJ being used to quantify all diameters. Multiphoton microscopy was employed to visualize collagen content via Second Harmonic Generation (SHG). The location of the EL was categorized by its proximity to collagen, with a colocalization score of 1 being assigned if touching a collagen fibril, and 0 if not.

RESULTS: All samples had ELs, determined by a positive AdipoRed staining and negative cytoskeletal staining (Figure 1A). Through quantitative analysis of 1900 ELs across 20 patient samples, the mean diameter was determined to be 7.27 μm with a standard deviation of 8.16 μm (Figure 1B). Thus, we defined a maximum diameter of 15.43 μm as an EL. In all individuals, these ELs tended to colocalize in regions of collagen, as indicated by SHG and colocalization scoring (Figure 1D, E). Results show that a portion of these ELs react with Annexin-V, indicating an apoptotic etiology (Figure 1C). Ongoing work aims to model this adipocyte-apoptotic body formation.

CONCLUSION: Adipose tissue contains ELs that present in regions of collagen. A portion of these ELs display Annexin-V around their perimeter, suggesting its potential as an apoptotic body. This indicates the involvement of adipocyte apoptosis in fibrosis, however future work aims to identify full directionality.

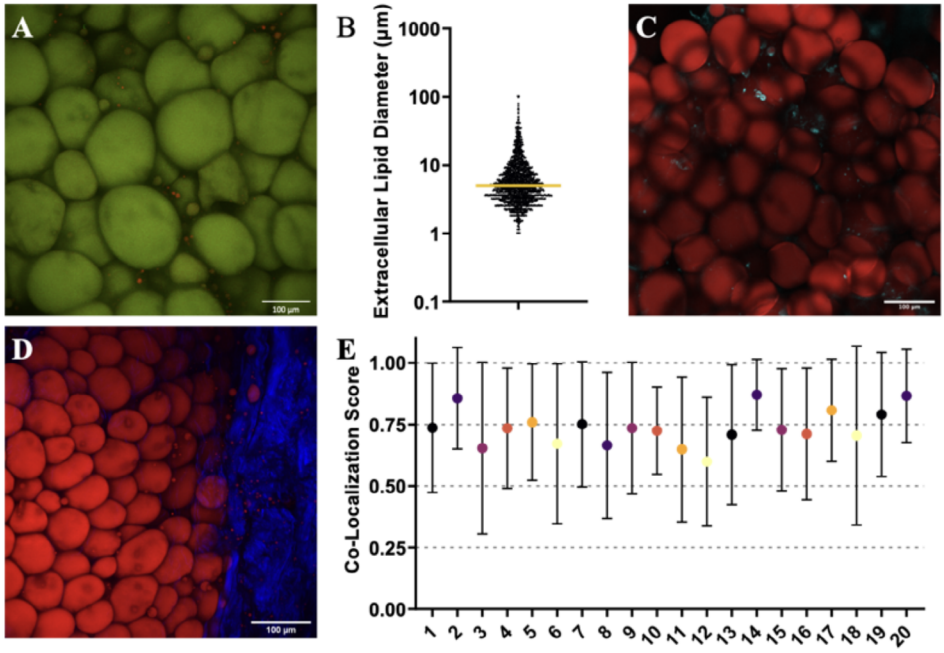
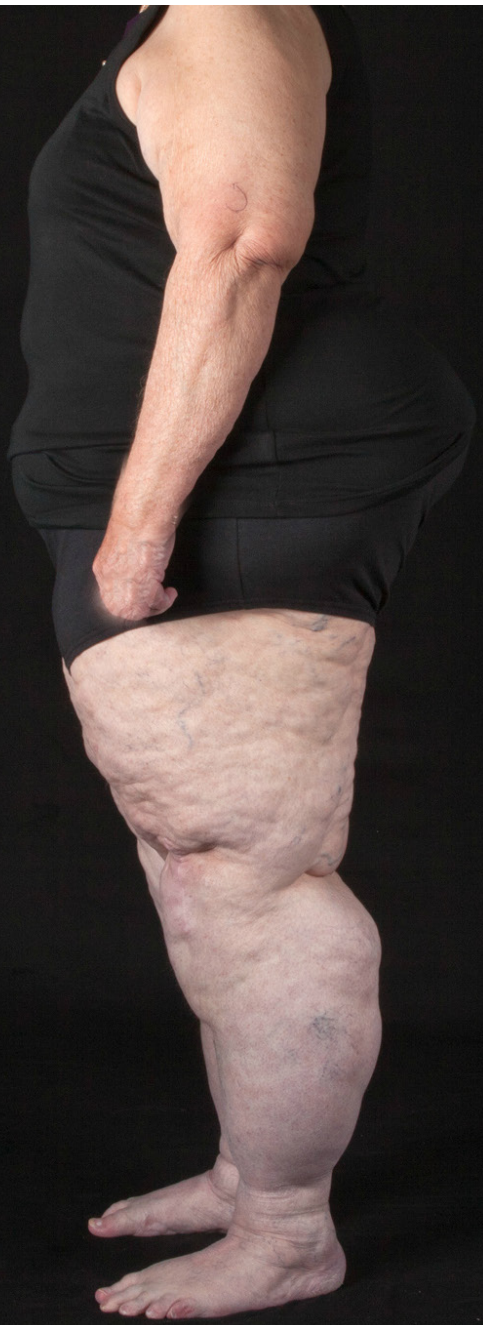


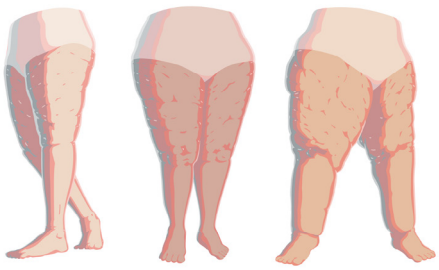
Figure 1. Adipose tissue contains extracellular lipids (red) not contained within the cytoskeleton (f-actin staining (green)) of the cell (A). Staining=AdipoRed (red) and Phalloidin (green). These extracellular lipids were defined to have a maximum diameter of 15.43 µm (mean + 1 standard deviation) based on all extracellular lipids measured (B). Bulk adipose tissue contains intracellular lipids (red) and extracellular lipids (red) that conjugate to Annexin-V (cyan) (C). Staining=BODIPY (red) and Annexin-V (cyan). Extracellular lipids (small red) tended to appear in regions of collagen (blue) (D). Staining=AdipoRed (red) and Second Harmonic Generation (blue). All individuals had a colocalization score above 0.5, indicating that in general these extracellular lipids colocalize with collagen (E). Scale bar=100 µm.

Can you recognize Lipedema in your research?



As the world's largest funder of Lipedema research, we invest in studies to **diagnose**, **define** and **treat Lipedema**.

Learn more about the research we fund:
lipedema.org/research-impact



LIPEDEMA FOUNDATION

LIPEDEMA.ORG

Novel Kinase Inhibitor Screening for Inhibition of Continuation of Adipogenic Differentiation in Adipose-derived Stem Cells

Presenter: Caroline Rinderle, M.S. - USA
Affiliation: The University of North Texas Health Science
Authors: Bruce Bunnell, Caroline Rinderle

INTRODUCTION: Obesity is characterized by excess fat accumulation and a body mass index of 30kg/m^2 or greater. Over 40% of Americans are obese, increasing the prevalence of heart disease, type 2 diabetes, and cancer. Adipose-derived stem cells (ASCs) are adult mesenchymal stem cells capable of differentiating into mature adipocytes through the process of adipogenesis. Preliminary data has shown that kinase inhibitor compounds can downregulate adipogenesis if present before the induction of differentiation. However, different kinases are likely responsible for initiating and continuing differentiation. Treatment throughout differentiation may give insight into kinases responsible for continuing adipogenesis. Suppose the differentiation of ASCs can be prevented or halted mid-differentiation via kinase inhibition. In that case, obesity may be prevented or reversed, reducing associated illness and better outcomes.

METHODS: ASCs from an obese donor were treated with 100nM of KCGS Drug Library kinase inhibitors obtained from Dr. David Drewry at the SGC at UNC Chapel Hill. Cells were treated 72 hours before induction of adipogenesis, 7 days into adipogenesis, and 14 days into adipogenesis. In one group, cells were treated with kinase inhibitor compounds in adipogenic media, which was removed and replaced with control adipogenic media after 72 hours. In another group, cells were treated with maintenance media, removed after the 72-hour treatment period, and replaced with maintenance media. The cells were differentiated for 21 days and stained with an Oil Red O lipid droplet stain. After imaging and drying overnight, the stain was removed and quantified.

RESULTS: Two kinase inhibitor compounds cause decreased differentiation when treated before induction. ASCs that differentiated for 14 days before treatment could not recover fully before the endpoint, and ASCs differentiated for 7 days before drug treatment effectively halted differentiation. However, the cells were unable to recover for the remaining 14 days.

CONCLUSION: Determining which kinases are responsible for initiating and continuing the differentiation of ASCs into mature adipocytes will give insight into potential therapeutics for preventing and curing obesity. In the future, qRT-PCR and western blots will be performed to confirm the phenotypic changes observed after kinase inhibition via gene and protein expression changes.

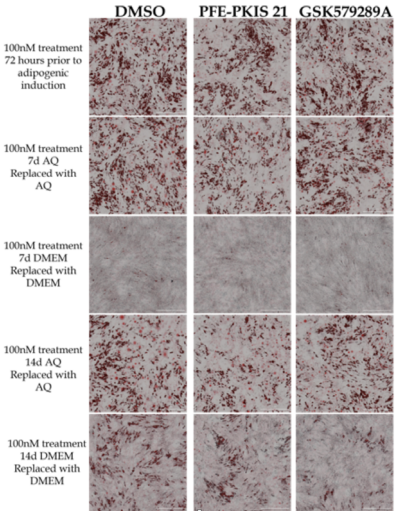


Figure 1: Oil Red O staining of ASCs treated with PFE-PKIS 29 and GSK579289A at various time points. Staining was performed 21 days after the initial induction of adipogenic differentiation.

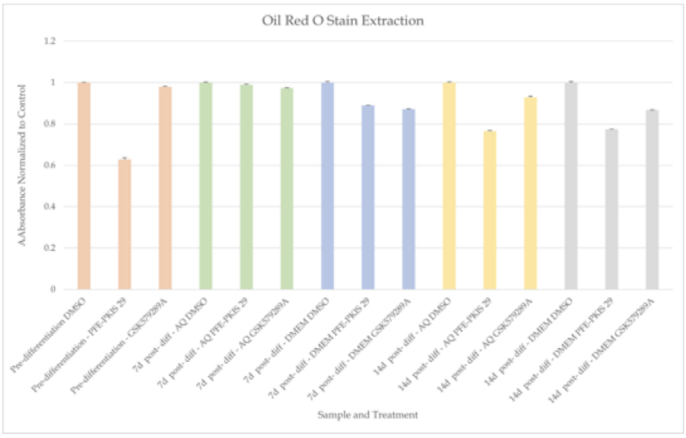


Figure 2: Oil Red O stain extraction of drug-treated ASCs from both lean and obese patients confirms the differences in stain present in the images from Figure 1.

ABSTRACTS - FRIDAY, OCTOBER 6, 2023
FREE PAPER SESSION# 5: Adipose Modeling for Disease Research

ERK5 Characterization in a Novel Adipose-Based Breast Cancer Microphysiological System

Presenter: Katherine L. Hebert - USA
Affiliation: Tulane University School of Medicine
Authors: Katherine Hebert, Thomas Cheng, Jack Elliott, Van Barnes, Frank Lau, Elizabeth Martin, Matthew Burow

INTRODUCTION: Breast Cancer is the second leading cause of cancer death in women and incidence rates are increasing 0.5% per year. Triple negative breast cancer (TNBC), which is classified by negative hormone receptors (HR-) and human epidermal growth factor receptor 2 (HER2) negative, is the most aggressive subtype and occurs more often in younger Black and Hispanic women. Kinases in the MEK5/ERK5 pathway, part of the mitogen-activated protein kinase (MAPK) family, regulate proliferation, cell survival, differentiation, and apoptosis. In TNBC ERK5 signaling is linked to drug resistance and metastatic progression. ERK5 interacts with the tumor micro-environment (TME) to promote extracellular matrix (ECM) factors. Therefore, ERK5 should be further characterized in a 3D system that recapitulates the cell-to-tissue interaction.

Compared to 2D models, microphysiological systems and other 3D systems are more relevant to human biology while also encompassing complex environments. The Breast Cancer-Microphysiological System (BC-MPS) described here utilizes human breast tissue (HBT) to generate a more native environment to culture cancer cells.

METHODS: In this study, we distinguish ERK5 characterization in 2D systems versus our 3D BC-MPS model. We demonstrate ERK5-induced phenotypic changes in our established TNBC cell line, MDA-MB-231. We further assessed the effects of ERK5 expression on collagen content in HBT after being cultured in BC-MPS for 5 days through Maison's Trichrome stain.

RESULTS: Our findings show that expression of inflammation, integrin, and pro-angiogenic factorsdiffer in 2D culture compared to 3D culture. In addition, we demonstrate how HBT can modulate tumor heterogeneity through the use of multiple patient donors, observed through differences in inflammation markers in lean and obese donors in our 3D microphysiology system. In addition, activated NFkB protein expression varied in 2D culture compared to 3D. ERK5 expression increased collagen content in HBT, and ERK5-knockout cells had decreased collagen content compared to parental control cells.

CONCLUSION: In conclusion, our results in 2D culture compared to 3D culture show ERK5 interaction with the TME can vary based on individual patient factors; however, ERK5, in the presence of HBT plays a role in cancer proliferation. Overall, these data suggest that ERK5 is a potential target for therapies.

In Vitro Tissue Reconstruction Using Stromal Cells from Adipose Tissue of Healthy or Obese Donors: Impact on 3D Cell Differentiation and Extracellular Matrix

Presenter: Julie Fradette, PhD - Canada
Affiliation: LOEX-Universite Laval
Authors: Julie Fradette, Luis Sorroza-Martinez, Nabil Amraoui, Léa Gagné, Viviane Séguin, Marie-Frédérique Gauthier, Giada Ostinelli, André Tchernof

INTRODUCTION: The impact of obesity on the performance of human adipose-derived stromal/stem cells (ASCs) in regenerative medicine is still poorly understood, especially for tissue reconstruction strategies such as the cell sheet technology. This study aimed to determine the impact of obesity on the proliferation rate of ASCs, as well as their adipogenic and osteogenic potential in presence of endogenously derived matrix components.

METHODS: ASC were isolated from subcutaneous adipose tissue samples of seven non-obese donors (ASC-nOb), with an average body mass index (BMI) of 23.6 kg/m2, and of eight obese donors (ASC-Ob), with an average BMI of 44.7 kg/m2. The extracted cells were amplified in culture, and the proliferation ratio was calculated over seven passages. Connective tissues were then engineered according to the self-assembly approach, leading to cell sheet formation from ASC's endogenous extracellular matrix secretion and assembly upon long-term ascorbic acid supplementation. In parallel to cell sheet formation, adipogenic or osteogenic differentiation was induced for subgroups, leading to adipose or bone-like sheets, respectively.

RESULTS: Proliferation was quite similar between ASC-nOb and ASC-Ob populations over these passages under our culture conditions. However, our assays revealed a 2.1-fold decrease in the mean adipogenic potential (Oil Red O staining) for the ASC-Ob group ($p<0.05$). A 6.2-fold reduction in mineralization potential was observed in the ASC-Ob group after Alizarin Red staining of the reconstructed bone-like cell sheets ($p<0.05$). Finally, assessment of cell sheet manipulability without tearing revealed that while success rates of 100% and 90% were achieved, for ASC-nOb derived connective and adipose cell sheets, respectively, these rates were only 92% and 42% for ASC-Ob derived tissues.

CONCLUSION: Overall, while ASC proliferation was not significantly impacted, reduced adipogenic and osteogenic differentiation potentials in a 3D environment were observed for ASC derived from severely obese donors. In addition, extracellular matrix production/assembly was altered for cell sheets produced from obese donors, especially for adipocyte-containing cell sheets. These results highlight the importance of taking into account the metabolic status of adipose tissue donors in order to design strategies that would favor the engineering of autologous tissues in regenerative medicine.

Comparison of Adipocyte Like Spheroids from Human Vascular Fraction and Adipose Stromal/Stem Cells in Various Culture Conditions

Presenter: Miia Juntunen, PhD - Finland
Affiliation: Tampere Univeristy
Authors: Miia Juntunen, Niklas Lostedt, Alma Yrjänäinen, Marika Kuuskeri, Susanna Miettinen

INTRODUCTION: Due obesity epidemic, need for studying adipocytes and adipose tissue biology has increased. Adipocytes are difficult to culture and maintain, therefore different ways to produce adipose tissue like structures have been investigated such as spheroid cultures. With 3D spheroid cultures, larger unilocular lipid droplets (LDs) have been observed. In this study, the aim was to compare human stromal vascular fraction (SVF) cells and adipose stromal/stem cells (ASCs) in formation of adipocyte like spheroids in both adipogenic and endothelial cell supporting conditions.

METHODS: SVF and ASCs were isolated from human adipose tissue samples (n=3). 10 000 cells were plated on low attachment 96-well plate in different culture conditions: basic medium (BM), adipogenic medium (AM), endothelial medium (EM), and AM and EM combinations. The size of the spheroids was monitored with microscopy for 28 days. Formation of LDs within spheroids was studied with confocal microscopy. In addition, adipogenic and angiogenic gene expression, secretion of adiponectin and lactate hydrogenase (LDH) was measured.

RESULTS: SVF cells and ASCs formed spheroids in all studied conditions. Largest spheroids were formed with combination media. LDs were formed with AM conditions with SVF cells and ASCs and spheroids in AM started to float before 21 days of culture with ASCs. Adipogenic gene expression was highest with AM cultured spheroids with both SVF cells and ASCs. EM alone or in combination media did not increase expression of angiogenic genes. Highest secretion of LDH was observed with largest spheroids in combination conditions and highest section of adiponectin in AM and combination conditions with both SVF cells and ASCs.

CONCLUSION: Both SVF and ASCs showed adipocyte like spheroid formation capacity and differentiated towards adipocyte like spheroids in adipogenic culture conditions.

A Novel Barrier-free, Open-top Microfluidic Chip for Generating Merged 3D Vascular Networks

Presenter: Alma Yrjänäinen, MSc - Finland
Affiliation: Tampere Univeristy
Authors: Alma Yrjanainen, Elina Kalke, Ella Lampela1, Jose Kreutzer, Jorma Vihinen, Jorma Vihinen, Kaisa Tornberg, Hanna Vuorenpää, Susanna Miettinen, Pasi Kallio and Antti-Juhana Mäki

INTRODUCTION: Microfluidic chips designed to recapitulate human tissue functions are a significant advancement from the traditional 2D cell cultures. Still, establishing 3D co-cultures requires better resolution of the microfluidic chips enabling distinct cell culture compartments for different co-cultures. Here, we introduce a novel microfluidic chip design allowing the generation of two barrier-free 3D cell culture compartments within the device under fluid flow. We studied the formation of two vascular networks and quantified the vasculature in terms of vascular volume, total vessel length and average vessel diameter under three different flow conditions. Finally, we assessed the interconnectivity between the vasculatures

METHODS: Two distinct vascular networks were generated in a stepwise manner. Fibrin-embedded GFP-tagged Human Umbilical Vein Endothelial Cells (GFP-HUVECs) and human Adipose Stem/Stromal Cells (ASCs), in 5:1 ratio, were pipetted to the lower cell culture compartment and fibrin-embedded RFP-HUVECs and ASCs were similarly mixed and pipetted to the upper cell culture compartment. Three gravity-based flow conditions were re-established in every 24 hours for five days. The forming vasculatures were imaged daily (Leica DMi8). Chips were stained with phalloidin and DAPI and imaged with a laser scanning confocal microscope (Nikon A1R) to observe and quantify the formed vascular network utilizing 3D image segmentation (Imaris).

RESULTS: SVF cells and ASCs formed spheroids in all studied conditions. Largest spheroids were formed with combination media. LDs were formed with AM conditions with SVF cells and ASCs and spheroids in AM started to float before 21 days of culture with ASCs. Adipogenic gene expression was highest with AM cultured spheroids with both SVF cells and ASCs. EM alone or in combination media did not increase expression of angiogenic genes. Highest secretion of LDH was observed with largest spheroids in combination conditions and highest section of adiponectin in AM and combination conditions with both SVF cells and ASCs.

CONCLUSION: All flow conditions allowed the formation of lumenized, ASC-supported vasculatures. We showed that GFP- and RFP-vascular networks were able to join and form a merged vascular network between the cell culture compartments. Moreover, we observed morphological differences of the vascular networks between the studied flow conditions. We also showed notable variation in vascular volume and total vessel length between the flow conditions.

ABSTRACTS - SATURDAY, OCTOBER 7, 2023
BEST PAPER SESSION

3D Adipose Tissue Model with Tunable Triglyceride Content Using Melt Electrowriting (MEW) Scaffolds Seeded with Multicellular Spheroids

Basic Science - Student

Presenter: Franziska Dusi - Germany
Affiliation: University Hospital Wuerzburg
Authors: Tamara Weidemeier, Martin Watzling, Hannes Horder, Torsten Blunk, Petra Bauer-Kreisel

INTRODUCTION: Representative in-vitro models of adipose tissue are of key importance to understand its multifaceted role in metabolism, but also in the development of diseases such as metabolic disorders and cancer progression. However, 3D models that recapitulate human adipogenesis and adipose (patho-)physiology in long-term culture are still rare. In this study, we present an advanced 3D model consisting of spheroids in a tailored melt electrowriting (MEW) scaffold, which developed a coherent adipose tissue-like structure and could be long-term-cultured. Improved differentiation of adipose-derived stromal cells (ASC) and elevated matrix production, which was tunable by fatty acid supplementation, was demonstrated.

METHODS: ASC differentiation was performed in self-assembling spheroids, generated in low-adherence agarose micromolds. Spheroids were seeded into MEW scaffolds with spheroid size-adapted, box-structured pores and differentiated for three weeks using a hormonal cocktail. Further stimulation was conducted with either palmitic acid (PA) (100 µM), oleic acid (OA) (250 µM) or linoleic acid (LA) (250 µM). Differentiation and lipid storage were assessed via triglyceride (TG) quantification and gene expression analysis of adipogenic marker genes. Extracellular matrix development was characterized by immunohistochemical staining of matrix components.

RESULTS: Culture in spheroids and MEW scaffolds exhibited improved differentiation of ASCs, as compared to conventional 2D culture, indicated by an increased TG/DNA content and elevated ECM production. Expression analysis of adipogenic marker genes confirmed distinct adipogenesis within the 3D constructs. Histology and staining of ECM deposition indicated a coherent, adipose tissue-like structure, which was maintained in long-term culture over 10 weeks. Stimulation with OA and LA significantly increased lipid droplet size and triglyceride content. Fatty acid treatment led to a further increase in collagen deposition in spheroid culture. Additional physiological characterization of fatty acid stimulated adipocytes such as lipolysis and secretion of inflammatory cytokines is currently conducted.

CONCLUSION: The presented easy-to-handle 3D adipose tissue model exhibits improved differentiation of ASCs and matrix production yielding coherent adipose tissue constructs that can be long-term cultured. Fatty acid supplementation increased lipid droplet size and TG content, as well as ECM deposition, underlining the plasticity of the model and demonstrating its potential as a tool for studies on adipose tissue (patho-)physiology.

Acquisition of Myofibroblast Phenotype by Adipose Stromal Cells in Inflammatory Environments Depends upon Autocrine Activin A Activity

Basic Science - PI

Presenter: Dmitry Traktuev, PhD - USA
Affiliation: University of Florida
Authors: Stephanie Merfeld-Clauss, Keith L. March, Dmitry O. Traktuev

INTRODUCTION: Many pathologies are associated with tissue ischemia and inflammation. Prolonged inflammation leads to functional deterioration of organs, often due to progressive loss of microvasculature and fibrosis. Mesenchymal stromal cells are numerous in the perivascular niche and likely play a key role in both tissue and vascular homeostasis and pathologies, including fibrosis. Many pathologies are accompanied by systemic increases in Activin A (ActA), a factor active in immune-modulation, angiogenesis and fibrosis. Here, the effects of inflammatory cells and factors, particularly IL-1β, in modulation of the phenotype of adipose stromal cells (ASC) were assessed, with a specific focus on the contribution of ActA to this process.

METHODS: Peripheral blood mononuclear cells from healthy donors, activated with LPS (10 ng/mL; aPBMC), were presented to ASC and expression of smooth muscle cell (SMC)/myofibroblast markers were evaluated 5 days later. Expression of factors that induce myofibroblast generation, including ActA, transforming growth factors 1-3 (TGFβ1-3) and connective tissue growth factor (CTGF) were assessed in ASC. Neutralizing antibodies and silencing RNAs to ActA, TGFβ1-3, and CTGF were used to define the signaling cascade of aPBMC. Endothelial cell proliferation in response to factors produced by ASC and ASC+aPBMC co-cultures were compared.

RESULTS: ASC, exposed to aPBMC, upregulated SMC markers, including αSMA, SM22α, and Calponin I. A similar effect was achieved by exposing ASC to IL-1β, whereas blocking IL-1β prevented aPBMC-induced ASC differentiation. aPBMC induced ActA expression, upregulated TGFβ1-3, and tripled expression of CTGF, a key pro-fibrotic factor. Silencing IL-1β activity prevented aPBMC-induced expression of ActA, activity of which was essential for upregulation of CTGF and αSMA expression in ASC. ActA upregulated mRNAs for several extracellular matrix proteins, but to a lesser extent than TGFβ1, suggesting that ActA is a weaker pro-fibrotic agent than TGFβ1. ASC secretome promoted endothelial cell proliferation, whereas secretome of ASC+aPBMC co-cultures was ineffective until ActA was scavenged, which then restored ASC angiogenic activity.

CONCLUSION: aPBMC, through IL-1β, induce expression of ActA in ASC, that, in an autocrine fashion, induces transition of ASC from a progenitor toward a myofibroblast phenotype. ActA is weakly fibrotic, upregulates pro-fibrotic CTGF, and inhibits ASC paracrine angiogenic activity.

Stress-Induced Premature Senescence and Senolytic Intervention in the Adipose Stromal Vascular Niche

Translational - Student

Presenter: Marlene Wahlmueller, MSc - Austria
Affiliation: Ludwig Boltzmann Institute for Traumatology
Authors: M. Wahlmueller, MS Narzt, K. Missfeldt, V. Arminger, A. Krasensky, I. Lämmermann, B. Schaedl, M. Mairhofer, S. Suessner, S. Wolbank, E. Priglinger

INTRODUCTION: Adipose tissue senescence plays a central role in obesity and aging. Here, senescent cells are involved in the generation of a pro-inflammatory environment, in the evolution of chronic diseases and progression of age-related metabolic dysfunction. Targeting and elimination of senescent cells have become important tools to ameliorate pathological states, outlining the therapeutic relevance of senolytic compounds – and in consequence to study their activity in relevant models.

METHODS: We established treatment conditions to generate stress-induced premature senescence (SIPS) 2D and 3D in vitro models representing the human adipose stromal vascular niche. We started from adipose-derived stromal/stem cells (ASC), which we adapted to freshly isolated microtissue-stromal vascular fraction (MT-SVF), where cells are embedded within their native extracellular matrix. We demonstrated induction of senescence on different cellular levels, including morphology, cell cycle arrest, senescence-associated β-galactosidase (SA-βgal) activity, mRNA expression by qPCR and protein expression by histological stainings. We determined the abundance of senescent cells in adipose tissue and MT-SVF, with respect to aged and lipedema patients. To eliminate senescent cells using inhibitors of arachidonic acid converters, we optimized the senolytic treatment in the senescent 2D ASC in vitro model and in the ex vivo MT-SVF samples. Senolytic activity was determined by viability measurements and live fluorescence apoptosis monitoring using caspase staining.

RESULTS: The optimal treatment conditions to generate SIPS in vitro models in 2D and 3D were defined as two subsequent exposures with 200 nM Doxorubicine for six days. We confirmed induction of senescence in the 2D in vitro models through SA-βgal activity, at the mRNA level (LMNB1, CDK1, p21) and additionally by G2/M phase cell cycle arrest in ASC. Significant differences in Lamin B1 and p21 protein expression confirmed senescence in our MT-SVF 3D model. Senolytic treatment of SIPS ASC and endogenous MT-SVF induced apoptosis detected by caspase activity in senescent cells.

CONCLUSION: As multiple cell types cause heterogeneity and complexity in adipose tissue senescence, our established microtissue models representing the perivascular niche are highly relevant for future studies. They give great value to studying adipose tissue pathologies linked to senescence and facilitate analysis of the endogenous senescent state.

Molecular Evaluation of Microfragmented Adipose Tissue Correlated to Clinical Outcomes in Patients Undergoing Treatment for Knee Osteoarthritis

Clinical Science - Student

Presenter: Joshua Harrison, MD - USA
Affiliation: University of New Mexico, School of Medicine
Authors: Joshua Harrison, Melody Sun, Erin Milligan, Anil Shetty, Dustin Richter

INTRODUCTION: Microfragmented adipose tissue (MFAT) is an emerging therapy for treatment of inflammatory conditions including osteoarthritis (OA). In our previous study, we conducted a randomized placebo controlled trial comparing MFAT with a saline placebo (P) and corticosteroids (CS) for treatment of knee OA. During our trial, the processed MFAT was cryopreserved from the 25 patients in our treatment group. This study evaluates how the chemokine and cytokine profile of the MFAT correlates the profile to pain relief and functional improvement after knee OA treatment with MFAT.

METHODS: Patients with radiographic knee OA, a minimum pain score of 3 on the visual analog scale (VAS), and absent history of knee injections were eligible for inclusion. The VAS pain scale, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Knee Injury and Osteoarthritis Outcome Score scale (KOOS) were recorded pre-procedure and at specified time points post-procedure up to one year. The adipose tissue from the 25 patients in our MFAT group underwent analysis with Enzyme-linked immunosorbent assay (ELISA) and Polymerase chain reaction (PCR) for evaluation of the milieu's chemokine and cytokine profile. The results were correlated with the functional outcome scores of the patients in our prior study.

RESULTS: During the evaluation of the MFAT, we identified a propensity for an anti-inflammatory profile within the MFAT milieu. Additionally, patients who were found to have an increased clinical response to treatment had chemokine and cytokine profiles of their MFAT that were skewed to markers consistent with an anti-inflammatory profile. On the contrary, patients that were found to have subdued clinical responses to treatment were found to have increased markers consistent with inflammation.

CONCLUSION: MFAT is an effective treatment for knee OA. This data indicates MFAT injection consistently provides the largest improvement in outcome scores at 6-12-month follow-up compared with the P and CS groups, however, patients respond to the MFAT treatment with varying degrees. The patients that were found to be high responders to MFAT treatment were shown to have increased production of anti-inflammatory chemokine and cytokines when compared to patients that did not respond as well to the treatment.

Assessment and Outlook for the Treatment of Scleroderma 2009-2023

Clinical Science - PI

Presenter: Guy Magalon, PhD - France
Affiliation: Aix Marseille Universite France
Authors: Guy Magalon, Jeremy Magalon, Florence Sabatier, Aurélie Daumas, Brigitte Granel

INTRODUCTION: The Treatment of Scleroderma has benefited from Regenerative Surgery with the use of Microfat, PRP, Stromal Vascular Fraction and now, Mechanical Preparations. Between 2009 and 2023, we participated in 5 clinical trials. The results were very favorable for the treatment of the face and the technique is now used routinely. For hand treatment, despite two randomized trials, it is still impossible, due to obtain an authorization to use Stromal Vascular Fraction.

METHODS: Aiming at volumetric and trophic effects. We used 16 to 22 cc of fat, which was harvested with 14 gauge or 2mm cannulas, and reinjected with 21 gauge or 0.8mm cannula. In addition, we treated hands with the Stromal Vascular Fraction, aimed at an angiogenic and anti-fibrotic effects. We harvested 135-270 g of fat which allowed us to get 5 cc of stromal vascular fraction with the Celution system. We got on average 50x106 cells which were divided into 10 doses of 1 cc. A subcutaneous injection was performed in the patient's every finger with 25 gauge or 0.5mm cannula.

Both facial and finger procedures were performed under local anesthesia.

RESULTS: On the face, we observed a continuous improvement process. The pain was reduced in the temporomandibular joints, the tissues softened, the buccal aperture was improved with special consideration to the aesthetic enhancement. The improvement was immediately assessed. Some patients underwent a second injection procedure, 2 years after the first one. On the hands, we observed interesting results, with a very rapid improvement of the vascularization of the fingers and later of trophic disorders that allowed a functional enhancement and a better quality of life.

CONCLUSION: New randomized clinical trials must be set up according to the requests of health authorities with even more data and our hopes are to develop a strategy in Asia, facilitated by the large number of patients.

Modeling Hormone-Sensitive Breast Cancer Using a Novel Three-Dimensional Microphysiological System

Transitional - PI

Presenter: Megan Campbell Benz - USA
Affiliation: Tulane University
Authors: Megan C. Benz, Katherine L. Hebert, Elizabeth D. Martin, Frank H. Lau, Matthew E. Burrow

INTRODUCTION: Breast cancer is a heterogeneous disease that is exacerbated by an accumulation of signaling cues from cell-intrinsic and cell-extrinsic factors. Many of these cues are derived from the tumor microenvironment (TME). The TME is a bio-mechanical and biochemical reservoir for extracellular matrix (ECM) and signaling factors (cytokines, growth factors, lipids, and hormones). Additionally, the TME houses a diverse array of cell populations including adipocytes, vasculature, stem cells, immune cells, and cancer cells. This has relevance to breast cancer pathology, as it is well established that the TME can modulate cellular proliferation, survival, and ultimately result in resistance to therapy in breast cancer. Despite our understanding of the complex interaction of cancer cells within the TME, there is currently a gap in the ability of in vitro models to accurately mimic the TME in vivo, thus limiting the development of novel therapeutics.

METHODS: The goal of this study is to develop a complex and dynamic micro-physiological 3D tumor model for pre-clinical studies for use in hormone receptor positive cancers. Here, we have developed a technique to maintain healthy human breast tissue (HBT) alive ex vivo for up to 2 weeks in the presence of breast cancer (BC) cells, creating a breast cancer micro-physiological system (BC-MPS). RNA sequencing was performed to detect breast cancer cell line signatures retained in the BC-MPS system.

RESULTS: Results demonstrate the retention of the breast cancer cell line transcriptome for up to 14 days in vitro. In addition, we identify alterations to genes in the HBT associated with the TME in the presence of BC cells, specifically the ECM and metabolism. Finally, we demonstrate that cancer cells in our system respond to hormone treatment as observed by the increase in progesterone receptor gene expression in our system following treatment with 17-beta estradiol.

CONCLUSION: Given the impact of the TME in breast cancer pathology, it is critical for the contributions of the TME to be included in pre-clinical models of breast cancer. Our novel model will allow for the modulation of estrogen receptor signaling in a complex 3D system, providing a new avenue to test endocrine therapies.

ABSTRACTS – SATURDAY, OCTOBER 7, 2023
FREE PAPER SESSION# 6: Adipose Tissue Processing

Millifat, Microfat, Stromal Vascular Tissue: Mechanical Preparation, Lipoconcentrate Gel, Topical Washing Buffer...Which Product for Which Application

Presenter: Sophie Menkes, MD - Switzerland
Affiliation: Clinique Nescens
Authors: Sophie Menkes

INTRODUCTION: We aimed to show that our millifat, microfat, stromal vascular tissue, lipoconcentrate, topical washing buffer... procedures improve volumes, skin quality, while yielding a regenerative effect.
These new techniques can also achieve good results in neck, decolletage, hands, and genital area with improvement of vaginal dryness, mucosa trophicity, genito-urinary symptoms of menopause (GSM), loss of elasticity and volume of external genitalia, but also in hair loss.

METHODS: This presentation aims to present different techniques, different products: restoration of volumes of fat compartments, regenerative therapies for skin, tear trough, hair, or vaginal mucosa.

RESULTS: Millifat is the gold standard to refill the deep fat compartment of the face, microfat to refill the superficial fat compartments of the face or labia majora, stromal vascular tissue and modified stromal vascular tissue to regenerate skin, tear trough, hair, or genital mucosa.

CONCLUSION: Fat grafting has revolutionized regenerative medicine, aesthetic and reconstructive surgery. Fat grafting provides a safe and minimally invasive technique to improve signs of aging, sun damage, smoking ... Many unanswered questions remain in terms of the biology, survival mechanisms, and regenerative properties. The future of fat grafting includes cell-based therapy, extracellular matrix–based scaffolds, Exosomes...

Impact of Preparation Methods on the Extracellular Matrix Components of Different Fat Grafts

Presenter: Eddy Hsi Chun Wang - USA
Affiliation: L'Oreal Research & Innovation
Authors: Eddy Hsi Chun Wang, Chloe Trotzier, Clement Bellanger, Wan-Yi Yen Sweelin Chew, I-Chien Liao, Ying Chen, Qian Zheng, Charbel Bouez, Kun Qian

INTRODUCTION: Autologous fat grafts like Coleman-Fat (CF), Nanofat (NF), and SVF-Gel (SG) have shown regenerative properties beyond simply adding volume to the skin, offering anti-aging effects. However, there hasn't been a direct comparison of how the different preparation methods for these grafts affect the extracellular matrix (ECM), despite ECM being a major component of fat grafts. This study aimed to compare the preparation methods and their impact on the morphology and ECM profile of the grafts to understand their potential anti-aging properties.

METHODS: Lipoaspirate (LPA) was obtained from 14 donors and processed into three types of fat grafts (CF, NF, SG) through emulsification and filtration. Morphological analysis of the grafts was conducted using immunohistochemistry, and ECM protein quantification was performed using Western blot. High-resolution topology analysis was performed using cryo-SEM.

RESULTS: The analysis revealed noticeable macro and micro-level differences in the morphology of each graft type. CF exhibited a compact and firm structure compared to LPA. NF and SG, on the other hand, were highly disrupted due to emulsification and filtering, resulting in poorer shape retention. An enrichment of ECM was observed in NF and SG, with only a few remaining adipocytes. The enriched ECM appeared to trap cells, and the presence of CD34+ cells was observed. Micro-level analysis with cryo-SEM showed that NF and SG experienced micronization of adipocytes, while SG also displayed ECM enrichment between the remaining adipocytes. Histology and Western blot confirmed an enrichment of collagen (Collagen1, 5, 6), laminin, and fibronectin in NF and SG. SG exhibited a relative enrichment of Col6:Col1 and Laminin:Fibronectin while NF also demonstrated enrichment of Col5:Col1.

CONCLUSION: By utilizing the same LPA source to prepare different fat grafts, this study provided an unbiased assessment of how preparation techniques can significantly influence the relative enrichment of key ECM components. Emulsification and filtering increased the amount of ECM, particularly in SG. Notably, NF showed higher ratios of Col5:Col1, Col6:Col1, and Laminin:Fibronectin, which are known to be involved in the adipogenesis process. Additionally, the enriched ECM was found to sequester CD34+ cells, offering new insights into the regenerative mechanisms of fat grafts.

Fat Graft Processing Using the REVOLVE™ System Versus LipoGrafter and Decantation: In Vitro Properties and Tissue Quality

Presenter: Nimesh Kabaria, MS - USA
Affiliation: Allergan Aesthetics, an AbbVie Company
Authors: Sachin Shridharani, Nimesh Kabaria, Carrie Fang, Jared Lombardi, Eric Stec, Li-Ting Huang, Hui Li

INTRODUCTION: This study compared quality and properties of fat grafts processed using the REVOLVE™ system (Allergan Aesthetics, an AbbVie company), a filtration-based device; the LipoGrafter™ System (MTF Biologics), a decantation-based device with controlled vacuum liposuction; or standard decantation.

METHODS: Lipoaspirate (N=6 patients) was processed using REVOLVE, LipoGrafter, or decantation. Analyses of each graft included volume composition (free oil, fat, aqueous fluid, and cellular debris), hematocrit content, fat particle size, viable adipocyte count, and adipocyte activity, and stromal vascular fraction (SVF) was analyzed for viable progenitor cell count (CD45/CD31-/CD34+ cells) and colony-forming units (CFU).

RESULTS: Mean (±SEM) fat content of grafts was higher with REVOLVE than LipoGrafter or decantation: 77.7%±3.6% vs 71.2%±4.1% vs 60.8%±3.8%, respectively ($p<0.01$, REVOLVE vs decantation). Free oil was significantly lower with REVOLVE than LipoGrafter or decantation (0%±0.4% vs 6.2%±2.0% vs 15.6%±4.0%, respectively; $p<0.05$). Aqueous fluid content was similar, and cellular debris content was minimal. Hematocrit levels were lower with REVOLVE than LipoGrafter or decantation (0.5±0.1 vs 4.5±6.3 vs 5.5±6.7 optical density, respectively). Mean fat particle size was higher with REVOLVE than LipoGrafter and decantation (1418.9±30.5 µm vs 989.3±51.1 µm vs 1180.0±76.2 µm, respectively; $p<0.05$ for all comparisons). Percentage of tissue particles >1000 µm was highest with REVOLVE at 67.6%±1.5% (LipoGrafter: 47.6%±2.6%; decantation: 55.1%±2.8%; $p<0.01$ vs REVOLVE), and percentage of particles <200 µm was lowest with REVOLVE at 7.2%±1.0% (LipoGrafter: 28.0%±3.0%; decantation: 19.3%±4.4%; $p<0.05$ vs REVOLVE). More viable adipocytes and greater adipocyte activity resulted with REVOLVE than LipoGrafter or decantation (respectively, 4.2×105±1.0×105 cells/cc vs 2.6×105±0.6×105 cells/cc vs 2.7×105±0.5×105 cells/cc and 4.3±0.3 µg glycerol/cc processed fat vs 3.8±0.3 µg glycerol/cc processed fat vs 3.7±0.2 µg glycerol/cc processed fat; log-transformed values). REVOLVE SVF contained more progenitors than LipoGrafter or decantation (22,686±10,623 cells vs 13,743±4549 cells vs 10,184±4794 cells); CFU in SVF was comparable (7.3±1.0 CFU/cc vs 7.3±0.6 CFU/cc vs 6.0±1.0 CFU/cc, respectively; log-transformed values).

CONCLUSION: Lipoaspirate processed using REVOLVE resulted in the highest quality fat grafts, the largest fraction of concentrated graftable fat, which was high in large-particle fat globules, and the lowest free oil and hematocrit content, which may contribute to greater fat retention and lower complication rates clinically.

Whole Proteomic Analysis of Skin Regenerative Factors in Coleman-Fat, Nanofat, and SVF-Gel

Presenter: Sweelin Chew, PhD - China
Affiliation: L'Oreal (China) Research & Innovation
Authors: Sweelin Chew, Wan-yi Yen, Eddy Hsi Chun Wang, I-Chien Liao, Ying Chen, Qian Zheng, Nan Huang, Charbel Bouez, Kun Qian

INTRODUCTION: Autologous fat grafts such as Coleman-Fat, nanofat, and SVF-Gel, have been widely used for volume correction as well as facial rejuvenation. While the regenerative efficacy is mostly contributed to the stem cells in these fat grafts, other components of the fat grafts may also play a key role. To gain an insight into the skin rejuvenation efficacy of fat grafts and the impact of adipose tissue on skin aging, we aim to elucidate the differences between these fat grafts.

METHODS: Total protein was purified from freshly isolated Coleman, micro-, nano-fat and SVF-gel from 8 female donors aged 33 to 55. After which, whole proteomic analysis was carried out via nano-flow liquid chromatography-mass spectrometry. Annotated biomarkers were further analyzed for differential expression between lipoaspirate, Coleman-Fat, nanofat and SVF-Gel. Downstream pathway analysis was done to identify prevalent protein networks in each fat graft. Correlation analysis was performed to identify biomarker signatures specific to age group, body mass index and ethnicity.

RESULTS: For the first time, we compared whole proteome of Lipoaspirate, Coleman-Fat, nanofat, and SVF-Gel from single donors. Initial results revealed significant differences in abundance of lipids, extracellular matrix proteins, cytokines, and growth factors. Abundant adipokines such as leptin did not differ significantly between donor groups. However, we observed a difference in collagen and growth factor abundance over body mass index.

CONCLUSION: In conclusion, our pilot study revealed that nano-fat and SVF contain the highest concentration of secretory factors with relevance to skin regeneration and anti-aging. Whole proteomic analysis for a panel of regenerative biomarkers prior to fat grafting may support personalization of fat graft processing to maximize patient satisfaction.

Activated Fat Grafting: A Novel Approach for Enhanced Fat Graft Retention and Natural Long-Term Results

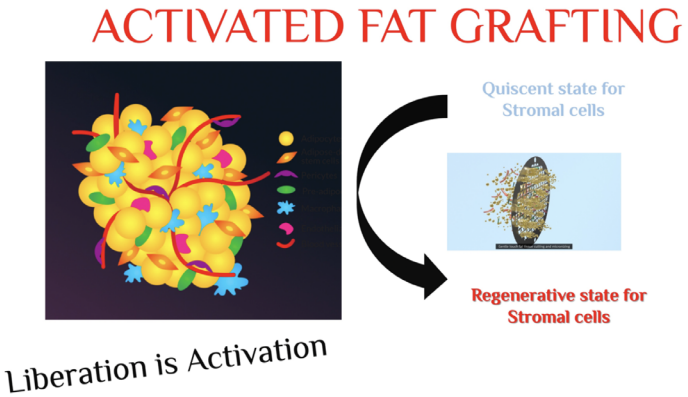
Presenter: Eray H. Copcu, MD - Turkey
Affiliation: Mest Health Services Inc
Authors: Sule Oztan, Eray Copcu

INTRODUCTION: Fat grafting is a commonly performed procedure in plastic surgery with a long history of application. Despite numerous studies on the pathophysiology of fat grafting, many aspects remain unclear. The survival of fat grafts is influenced significantly by the presence of fat-derived stromal cells. To enhance fat graft retention and achieve better outcomes, "cell-enriched" fat grafting has been proposed. This study introduces a novel technique called "activated fat grafting," which involves releasing stromal cells using ultra-sharp blades without damaging the fat tissue parenchyma, followed by the application of fat grafting.

METHODS: Different sizes of fat grafts (2400, 1200, 600, 400, 200, and 100 microns) were prepared using ultra-sharp blades specific to each anatomical area and depth. The process involved releasing stromal cells within the adipose tissue. A total of 128 patients underwent fat grafting on various body areas, including the face, breast, extremities, genital areas, and others. Patients were followed up for a minimum of 6 months and a maximum of 6 years. Flow cytometric and dual fluoroscopy analyses were performed to confirm the liberation, number, and viability of stromal cells. Histopathological examination evaluated the integrity of adipocyte cells using a sharp blade system. Long-term results were assessed by both clinicians and patients, with additional radiological assessment through MRI examinations.

RESULTS: Laboratory studies demonstrated that the use of sharp blades allowed the desired diameter of adipose tissue to be achieved without completely disrupting the parenchyma, while also releasing stromal cells and determining their presence and quantity. Clinicians and patients reported satisfactory long-term results in all cases. The regenerative effect was observed through both volume improvement in the tissue and increased fat graft retention.

CONCLUSION: Adipose tissue contains parenchymal cells, predominantly adipocytes, interconnected with stromal cells through bonds and bridges. By separating these bonds using sharp blades, the stromal cells can be released without compromising the viability of adipocytes. This approach, termed "activated fat grafting," enables improved graft retention and the preparation of different-sized fat grafts tailored to each anatomical area and depth. Consequently, this technique facilitates the attainment of natural, long-term results while minimizing complications such as graft visibility.



Examining Long-Term Responses of Diverse Human Body Systems and Disorders to Mechanically Obtained Fat-Derived Stromal Cells

Presenter: Eray H. Copcu, MD - Turkey
Affiliation: Mest Health Services Inc.
Authors: Eray Copcu, Sule Oztan

INTRODUCTION: Regenerative medicine holds immense promise as a rapidly growing field that utilizes the body's inherent healing capacity for targeted treatments. Adipose tissue is an excellent source of stromal cells, which play a crucial role in regenerative therapies. Mechanical methods, particularly those involving ultra-sharp blade systems, have shown exceptional success in efficiently obtaining stromal cells from adipose tissue. However, the response of different body systems and organs to regenerative applications can vary significantly. This study aims to evaluate these responses using ultra-sharp blade systems.

METHODS: Regenerative treatments were administered in 442 cases across various indications, and their long-term outcomes were assessed over a minimum of 2 years and a maximum of 7 years. The procedure involved manually extracting fat under local or general anesthesia using a specialized cannula. After centrifugation and removal of blood and tumescent fluid, the resulting condensed fat was sectioned using Adinizer ultra-sharp blades with diameters of 2400, 1200, 600, and 400 microns to separate stromal cells. The isolated stromal cells were then applied according to specific protocols for each indication. Patients were monitored extensively during the follow-up period.

RESULTS: Regenerative treatments utilizing stromal cells were successfully employed for both aesthetic and therapeutic purposes in various anatomical regions, including skin and subcutaneous tissues (aging, burns, cancer, radiation injury, diabetic foot), urogenital region (erectile dysfunction, Peyronie's disease, ovarian insufficiency, endometrial and testicular rejuvenation, bladder reconstruction, urinary incontinence), scalp, vocal cord, bone tissue (aseptic necrosis), joints (osteoarthritis), adipose tissue (lipodystrophy, necrosis), plantar fascia, and lung (regenerative rehabilitation).

CONCLUSION: The acquisition of stromal cells from adipose tissue can be categorized into two approaches: direct methods targeting the connections between parenchymal and stromal cells, such as enzyme and ultra-sharp blade systems, and indirect methods that may compromise parenchymal cell viability. Among these approaches, ultra-sharp blade systems have demonstrated the most successful outcomes. Stromal cells obtained using this method have shown remarkable efficacy in treating various challenging clinical conditions. Notably, the urogenital and skeletal systems exhibit the most favorable responses to regenerative interventions.

ABSTRACTS – SATURDAY, OCTOBER 7, 2023
FREE PAPER SESSION# 7: Fat Grafting Retention and Mechanisms

Improving Fat Graft Volume Retention with Vitamin D3

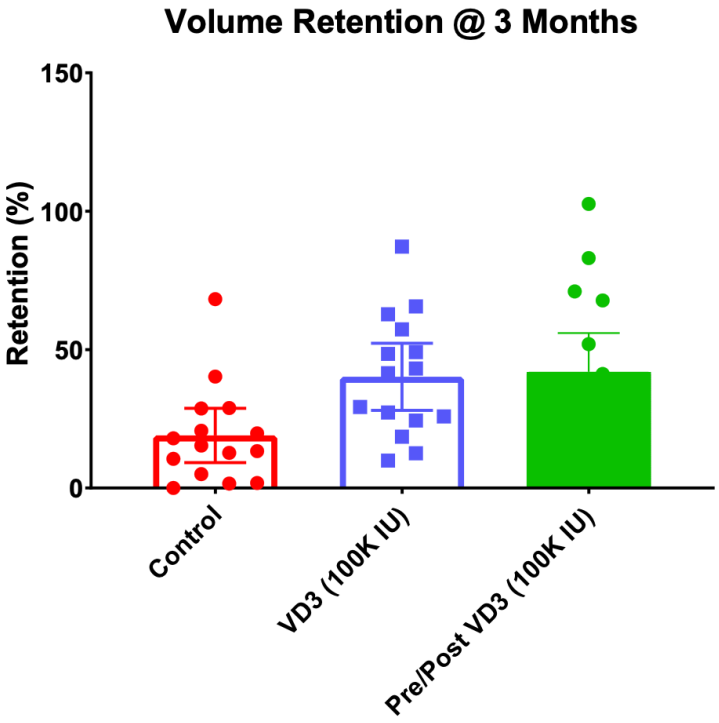
Presenter: Amr Elmeanawy, MD - Egypt
Affiliation: University of Pittsburgh
Authors: A. Elmeanawy, S. Loder, A. Vagonis, B. Bengur, V. Nerone, R. Ricketts, Y. Villalvazo, Y. Surucu, P. Humar, J. Arellano, H. Malekzadeh, B. Shaaban, D. Ramkumar, A. Gavrilescu, PLL Lee, J. Rubin, L. Kokai

INTRODUCTION: Our long-term research goal is to improve the mean volume of autologous fat graft retention for all patients and reduce the number of low retention outliers. Toward this, we have investigated vitamin D3 in both inactive (cholecalciferol) and active (calcitriol) forms as a therapeutic approach to augmenting retention. VD3 has established functions in immunomodulation and cell maturation, which we hypothesize improves macrophage and adipogenic precursor maturation for enhanced graft healing. We have previously shown VD3 as beneficial in murine and allogeneic pig models. In this final preclinical study, we investigate oral, high dose VD3 in a clinically relevant, autologous fat grafting pig model.

METHODS: Autologous inguinal adipose was harvested from each of 3 female Yucatan pigs, placed into sterile receptacles and manually minced with surgical scissors. Warm saline was used to prevent lipid coagulation. The fat product was Coleman processed with removal of free oil/fluid. 5cc adipose aliquots were weighed and injected bilaterally in 16 well-defined areas on the dorsum. Pigs received one of the following treatments: Naïve control, post-grafting VD3, and pre and post-grafting VD3. Oral inactive VD3 (cholecalciferal) was administered thrice weekly as 2, 50K IU capsules with food. Following euthanasia, the fat grafts were meticulously extracted from the dorsum, quantified in relation to both volume and weight, and flash frozen or histologically processed.

RESULTS: All pigs tolerated the procedures well and had no serious adverse events. Ultrasound images showed that fat graft placement was consistent and within the mid- to deep dermal white adipose tissue, with no leakage into muscle. All fat grafts were identifiable at three months, with clear differences noted in the quality of grafts at a macropscopic level based on treatment group. While control grafts were pale and fibrotic, VD3 pre-treated grafts were soft, pliable and appeared very healthy. Finally, both post- and pre/post- VD3 treatment significantly improved graft retention by over 200%. Naïve grafts had a mean retention of 19 +/- 17% compared to 40 +/- 22% for post- VD3 and 42 +/- 26% for pre/post VD3.

CONCLUSION: Cholecalciferol, also known as inactive Vitamin D3, has shown potential as a drug for improving long-term fat grafting outcomes. Our data suggests that it is a safe and effective approach for increasing fat graft retention through multiple mechanisms of action including increased revascularization.



Long Time Results After Breast Augmentation by Fat Graft

Presenter: Klaus Ueberreiter, MD - Germany
Affiliation: Park-Klinik Birkenwerder
Authors: Klaus Ueberreiter, Charlotte Ueberreitern

INTRODUCTION: Transplantation of autologous fat is a powerful tool and increasingly common in aesthetic and reconstructive surgery.
Here we present our results of a long-term study after fat transplantation for aesthetic breast augmentation.

METHODS: 14 patients underwent MRI investigations of the breast:

1. before the first graft,
2. 6 months after the first graft
3. 6 months after the second graft
4. 5–9 years later

All graft were carried out according to the BEAULI-protocol of fat graft (Ueberreiter 2010). The difference in fat volume was calculated with the open-source software OsiriX®.

RESULTS: There was a direct constellation between breast volume and increased weight over the time.
We compared therefore patients in two groups:

1. stable weight (less than 1 BMI gain)
2. patients who had increased their BMI up to 4 kg/m2

Results: An average of 176 ml fat was transplanted per breast and each surgical procedure.
In the first group a mean volume survival of 74 % (IQR 58 % – 92 %) was observed.
In the second group an increase of 135 % (IQR 105 % – 318 %) compared to the short-term result of the volume of transplanted fat was observed.
To prove the results were related to the fat graft, the volume of the pectoralis muscle as part of the original transplantation was calculated. The same amount of increase could be found there.

CONCLUSION: Transplantation of autologous fat with a reliable protocol renders stable long-term results. The correlation between change of weight and fat transplant volume over the years is significant.
In our clinic we treated until now more than 2000 patients.
Indications:

- Aesthetic
- Reconstructive
- Removal of silicone implant.
- Tuberous breasts

No negative side effects except for rare oily cysts were observed. Patient satisfaction rate is high.
Autologous fat transplantation can be considered as a safe and efficient alternative for breast augmentation.

Optimizing Adipose Stem Cell Therapy through Cell Supplemented Engineered Grafts

Presenter: Summer Hanson, MD, PhD - USA
Affiliation: University of Chicago Medicine and Biological Sciences
Authors: Summer Hanson, Miguel Gonzalez, Luke Zhang

INTRODUCTION: Little is known about the regenerative mechanism of fat when transferred from one part of the body to another as in autologous fat grafting. This is particularly pressing, given the rich proteins and progenitor cells, including adipose derived stem cells (ASCs), within the stromal vascular fraction (SVF) of fat. The purpose of this work was to develop a model of engineered adipose tissue grafts supplemented with stromal or stem cells for soft tissue regeneration.

METHODS: Discarded lipoaspirate was used. A 2 x 2 grid was devised on the flanks of 8-week-old nude mice with 0.5mL of graft (or saline ASC control). Engineered grafts were supplemented with either pure ASCs or cells from the SVF (SVCs). Standard grafts and cell solution were used as controls. At 1, 2, 4 and 8 weeks, animals were sacrificed, and tissue specimens were processed for volume, histology, and protein expression..

RESULTS: The ASC/saline control had dissipated over the 8-week study period while the standard graft had 59.2% retention. Adipose scaffolds supplemented with pure ASCs and SVCs demonstrate higher volume retention at 8 weeks (76.6% versus 77.3% respectively, $p>0.05$). All grafts expressed comparable concentrations of markers of functional adipose tissue (adiponectin, leptin) with minimal expression in the ASC controls. The adipose scaffold supplemented with SVF cells has higher expression of inflammatory markers such as C reactive protein (CRP) and the ST2 signaling protein. Grafts engineered with pure ASCs demonstrate higher concentration of remodeling proteins including HGF, and MMP-9 as well as VEGF.

CONCLUSION: The authors identified differences in cytokine expression in the engineered grafts particularly in inflammation and wound healing. These secretomes may impact graft retention and fat necrosis in the clinical setting but more importantly allow for promoting regeneration and repair of fibrosis as in radiation injury.

Multiple Administrations of Adipose-derived Stromal Cells Concurrent with Fat Grafting

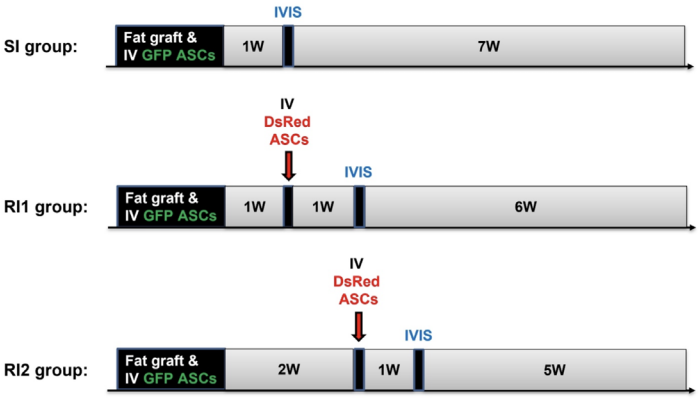
Presenter: Ki Yong Hong, MD, PhD - Korea
Affiliation: Seoul National University Hospital - Korea
Authors: Ki Yong Hong, Hak Chang

INTRODUCTION: Cell-assisted lipotransfer, a fat graft mixed with adipose-derived stromal cells, is known to enhance fat graft retention. Previously, we showed that intravenous injection of adipose-derived stromal cells can improve the survival of grafted fat. In the present study, we investigated the effects of a secondary intravenous injection of adipose-derived stromal cells on fat grafting.

METHODS: Wild-type C57BL/6J (B6) mice were used as donors for grafted fat and as recipients. Adipose-derived stromal cells were harvested from green fluorescent protein and DsRed B6 mice. The recipient mice were divided into three groups: SI (n = 10), RI1 (n = 10), and RI2 (n = 11). All groups received intravenous injections of green fluorescent protein adipose-derived stromal cells immediately after fat grafting. The RI1 and RI2 groups received repeated intravenous injections of DsRed adipose-derived stromal cells at 1 and 2 weeks, respectively, after fat grafting. The grafted fat volume was measured using micro-computed tomography.

RESULTS: Secondarily injected DsRed adipose-derived stromal cells were recruited to the grafted fat and resulted in a higher retention of graft volume and vascular density ($p < 0.05$). The stromal-derived factor-1 and C-X-C chemokine receptor type 4 genes related to stem cell homing were highly expressed in the grafted fat and adipose-derived stromal cells ($p < 0.05$). The RI2 group showed a higher graft volume and vascular density than the SI and RI1 groups ($p < 0.05$).

CONCLUSION: A secondary intravenous injection of adipose-derived stromal cells at a 2-week interval enhances the effect of adipose-derived stromal cell enrichment in fat grafting. These findings refine clinical protocols and enhance the therapeutic value of cell-assisted lipotransfer.



Oil Droplets in Apoptotic Uniocular Adipocytes: A Double-edged Sword in Determining Macrophage Phenotype and Its Implications on Fat Grafting

Presenter: Chen Lei, MD - China
Affiliation: The First Affiliated Hospital of Fujian Medical University
Authors: Songyu WanG, Jong Ye, Meishui Wang, Feng Lu, Biao Wang

INTRODUCTION: Fat grafting procedure is increasingly popular, but is limited by its unstable retention rate. The current research focuses on the revascularization of grafted fat. In this study, we explored the unique properties of apoptotic uniocular adipocytes and their relationship with macrophages.

METHODS: Membrane mature adipocyte aggregate cultures (MAAC) method was used to culture uniocular adipocytes in vitro. STS was used to induce apoptosis in uniocular adipocytes, multiocular adipocytes, and ASCs. The apoptotic uniocular adipocytes were examined under SEM. The fusion of apoptotic adipocytes was stimulated with methanol. Immunofluorescence staining and western blotting were used to distinguish macrophage phenotypes after co-culture with apoptotic uniocular adipocytes and fused oil droplets.

RESULTS: Cultured uniocular adipocytes maintained their morphology even after the induction of apoptosis. In contrast, multi-ocular adipocytes and ASCs cracked and released their cellular components, as confirmed by SEM. Methanol triggered the fusion of apoptotic uniocular adipocytes, and the fused large oil droplets attracted multiple cell debris, as indicated by DAPI/PI staining. Co-culture with apoptotic uniocular adipocytes induced the M2 phenotype, while M1 phenotype was induced when co-cultured with fused oil droplets.

CONCLUSION: In our study, we demonstrated that the surface tension of uniocular adipocytes sustained basic cellular morphology and subsequently induced M2 activation. In an unstable culture environment (such as the addition of methanol), surface tension tore the apoptotic adipocytes by fusion, subsequently inducing M1 activation. These results provide new insights into the effects of cellular morphology, which may influence the outcome of fat grafting.

ABSTRACTS – SATURDAY, OCTOBER 7, 2023
FREE PAPER SESSION# 8: Adipose Tissue Engineering

Porous Poly(glycerol sebacate)-based Scaffolds For Enhancing Adipose Tissue Regeneration

Presenter: Rachel Louise Furmidge - United Kingdom
Affiliation: The University of Sheffield
Authors: Rachel L Furmidge, Victoria Workman, Victoria Giblin, Frederik Claeyssens, Vanessa Hearnden

INTRODUCTION: Autologous fat grafting is still limited by high rates of adipose tissue resorption following transplant, and often additional procedures are required to achieve the desired tissue volume, increasing costs. As such, there is a need for an improved fat graft that can maintain volume following transplantation. A regenerative approach, combining both grafted adipose tissue and a regenerative biomaterial that promotes angiogenesis and cell survival may be an effective strategy for enhancing volume retention of transplanted adipose tissue. Poly(glycerol sebacate) (PGS) is a synthetic biomaterial which is highly suited to adipose tissue engineering, as it is much softer than commonly used biomaterials and is also highly elastomeric, mimicking the mechanical properties of adipose tissue. We herein report the development and optimisation of porous PGS-methacrylate (PGS-M) scaffolds for adipose tissue regeneration applications.

METHODS: Polymerised high internal phase emulsion (polyHIPE) templating of photocurable PGS-M pre-polymer was used to create porous three-dimensional scaffolds. The parameters of material fabrication were altered to investigate the effect on the porous structure, and scaffolds were characterised using scanning electron microscopy (SEM) and the mechanical properties of PGS-M scaffolds were measured. PGS-M scaffolds were seeded with adipose-derived stromal cells (ADSCs) isolated from primary human adipose tissue to assess cell migration through the scaffolds. In addition, a chick chorioallantoic membrane (CAM) assay was performed to assess the angiogenic potential of the scaffolds.

RESULTS: Fabricated scaffolds had a range of pore sizes (average pore size 27 μm and 94 μm) and interconnectivity depending on fabrication parameters. PGS-M scaffolds showed elastomeric properties, with mechanical properties within an acceptable range for soft tissue. Migration of ADSCs into the scaffold could be observed following 14 days of in vitro culture. Ingrowth of blood vessels could be observed on the CAM assay in response to the placement of PGSM scaffolds onto the CAM.

CONCLUSION: These results indicate that PGS-M polyHIPE scaffolds can support the growth of ADSCs, and by altering the parameters of fabrication, the pore size can be tuned, enhancing cell migration through the scaffold. PGS-M scaffolds promote an angiogenic response when implanted onto the CAM assay, and we envisage that with further development, these scaffolds could be used to enhance volume retention of grafted adipose tissue.

A Biopolymer Scaffold for Improved Fat Graft Viability and Volume Retention

Presenter: Emily Budziszewski - USA
Affiliation: InSoma Bio
Authors: Emily Budziszewski, Stefan Roberts

INTRODUCTION: To replace the structural stability lost to fat during liposuction harvest and improve the predictability of fat grafting we have developed an injectable tissue support scaffold—Fractomer— using a recombinant elastin biomaterial. This scaffold can be mixed and co-injected with lipoaspirate as liquid; upon interaction with body heat, it undergoes a phase transition to a porous, shapable solid capable of encapsulating injected adipocytes and allowing rapid environmental remodeling. This approach marries tissue engineering with fat grafting to maximize the utility of fat by addressing underlying issues of shape and survivability of transplanted fat in a method intended to reduce the number of required surgical procedures for fat grafting.

METHODS: Human lipoaspirate was obtained under IRB and mixed in different volumetric ratios (1:1 to 9:1) with our scaffold. Molding capacity was tested using 3D printed molds where mixtures were allowed to set for 10 min at 37 °C before removal and testing mechanical integrity. Mixtures were injected subcutaneously in the flanks of nu/nu mice and the cellular response and volume retention was tracked for 3 months. H&E staining was performed to observe graft properties and for scoring of incidence of necrosis. CD31 staining was used to analyze differences in vascular ingrowth.

RESULTS: Upon removal from molds, Fat+ Fractomer mixtures were able to retain the shape of the mold, unlike fat alone. Monotonic compression of mixtures demonstrated a mechanical stiffness (Young's modulus) comparable to native fat. In vivo, fat grafts containing Fractomer developed significantly lower levels of both vacuoles and high-density infiltrate, indicating lower levels of necrosis. Further, Fractomer augmented grafts demonstrated 2x volume retention compared to fat alone at 3 months. CD31 analysis revealed regrowth of vascular networks in areas of high Fractomer density indicating that the network may act as a conduit for vascular penetration into grafts subsequently leading to reduced necrosis.

CONCLUSION: We have developed a thermally responsive biopolymer scaffold that can be combined with lipoaspirate at the point-of-care prior to re-injection tissue repair sites to improve stability, shapeability, and survival of injected fat.

Xenograft-Decellularized Adipose Tissue Derived from Humans and Rabbits Supports Adipose Remodeling in Rabbit Model

Presenter: Hong-Wei Liu, PhD - China
Affiliation: The First Affiliated Hospital
Authors: Wei Liu, Hong-Yin Huang

INTRODUCTION: Decellularized adipose tissue (DAT) provides a suitable microenvironment for adipose stem cells (ADSCs) and promotes their adipogenic differentiation. Recent studies have focused on allogeneic DAT; however, insufficient adipose sources limit its wider application of allogeneic DAT. In this study, we compared the ability of allogeneic and xenogeneic DATs to induce adipose regeneration to explore the feasibility of xenogeneic DAT as an adjunctive material for tissue repair.

METHODS: Decellularized adipose tissue from humans and rabbits was prepared using the Flynn's method. The proliferation, migration, and adipogenic functions of the allogeneic and the xenogeneic groups were compared. Rabbits were used to construct transplantation models: allogeneic (transplanted r-DAT) and xenogeneic groups (transplanted h-DAT). Comparison of DAT transplantation outcomes between the two groups.

RESULTS: Xenogeneic DAT supports adipose regeneration. In vitro, adipose-derived stem cells cultured on DAT developed adipogenesis without media cues and were not statistically different from the effects of allogeneic DAT on cell migration, proliferation, and adipogenic capacity. In vivo, the animal model showed angiogenesis and adipogenesis, and the adipogenic ability of xenogeneic DAT was not statistically different from that of allogeneic DAT.

CONCLUSION: Xenogeneic DATs can induce adipose regeneration, and its adipogenic ability has no statistical difference, compared with allogeneic DATs. Xenografts are expected to be useful for soft tissue repair.

Fat Graft Enriched with Adipose-Derived Stem Cells for Breast Augmentation and Reconstruction: Clinical, Histological, and Instrumental Evaluation

Presenter: Pietro Gentile, MD, PhD - Italy
Affiliation: Associate Professor of Plastic and Reconstructive Surgery, University of Rome
Authors: Pietro Gentile

INTRODUCTION: Fat graft enriched with adipose-derived stem cells (FG-e-ASCs) has been utilized in outcomes of radiotherapy after mastectomy, and breast soft tissue defects. The scientific results using FG-e-ASCs in breast augmentation and breast reconstruction have been reported.

METHODS: A total of 46 patients affected by breast hypoplasia (SG-1) were treated with FG-e-ASCs, comparing results with those of a CG-1 (n = 30) treated with fat graft not enriched with adipose-derived stem cells (FG-ne-ASCs). 121 patients affected by the outcomes of breast oncoplastic surgery (SG-2) were treated with FG-e-ASCs, comparing the results with the CG-2 (n = 50) treated with FG-ne-ASCs. The preoperative evaluation included a complete clinical evaluation, photographic assessment, magnetic resonance imaging (MRI) of the soft tissue, ultrasound (US), and mammography (MG). Biopsy was performed only in SG-2. Postoperative follow-up took place at 1, 3, 7, 12, 24, 36, and 48 weeks, and then annually.

RESULTS: SG-1 patients, treated with FG-e-ASCs showed 58% maintenance of the contour restoring and of 3-dimensional (3D) volume after 3 years compared with the patients of the CG-1 treated with FG-ne-ASCs, who showed only 29% maintenance. In 67.4% (n = 31) of breast augmentation treated with FG-e-ASCs, we observed a restoration of the breast contour and an increase of 10.3 mm in the 3D volume after 36 months, which was observed in only 20.0% (n = 6) of patients in the CG treated with FG-ne-ASCs. Volumetric persistence in the SG-1 was higher than that in the CG-1 ($P < .0001$ SG vs. CG). In 72.8% (SG-2 n = 88) of breast reconstruction treated with FG-e-ASCs, we observed a restoration of the breast contour and an increase of 12.8 mm in the three-dimensional volume after 12 weeks, which was only observed in 27,3% (n = 33) of CG-2. Volumetric persistence in the SG-2 was higher (70.8%) than that in the CG-2 (41.4%) ($p < 0.0001$ vs. control group).

CONCLUSION: The use of FG-e-ASCs was safe and effective in patients of SG-1 and SG-2.