The **only conference** dedicated to convergent research in translational immunology and engineering.

About The Symposium

The mission of the Immune Modulation & Engineering Symposium is to bring together researchers in biomedical engineering and basic and translational immunology to advance the rapidly emerging field of immune engineering. The speakers and attendees represent leaders in this field, with expertise in collaborating across disciplines to generate innovative solutions to treat disease and injury by modulating the immune system.

More at https://drexel.edu/biomed/research-and-design/overview/IMES2023/
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Reception Location:

Behrakis Grand Hall

3210 Chestnut Street

Philadelphia, PA USA

Symposium Location:

The Study Hotel

20 S. 33rd Street

Philadelphia, PA USA

Poster Session Location:

Papadakis Integrated Sciences Building (PISB)

3245 Chestnut Street

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Peter Gaskill, PhD

Michele Kutzler, PhD

Christopher Rodell, PhD

Gabriele Romano, PhD

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Symposium Agenda

Day 1: November 29, 2023

5:00-7:30 PM	**Opening Reception: Diverse Perspectives in Immune Engineering (Behrakis Grand Hall)** Sue Van, President and CEO, Wallace H. Coulter Foundation

Day 2: November 30, 2023

8:00 AM	**Breakfast**
9:00 AM	**Opening Remarks	Kara Spiller, PhD**
9:05 AM	**Session 1: Cell & Gene Therapy**
Moderator: **Eric Kmiec, PhD**	**Denise Montell, PhD**	University of California, Santa Barbara *RaceCAR-M: Enhancing Whole Cell Engulfment and Killing with Activated Rac2* **Adam Snook, PhD**	Thomas Jefferson University *Compartmentalized Antigens as Safe and Effective Cell Therapy Targets* **Maria Grazia Roncarolo, MD**	Stanford University *Graft Engineering to Promote Immune Tolerance After Hematopoietic Stem Cell Transplantation*
10:35 AM	**Coffee Break**
10:55 AM	**Session 2: Novel Approaches for Oncoimmunology**
Moderator: **Gabriele Romano, PhD**	**Francesca Taraballi, PhD**	Houston Methodist *Biomaterials for Targeting and Tuning the Immune System* **Ann-Marie Chacko, PhD**	Duke-NUS Medical School, Singapore *Noninvasive Imaging of the Tumor Immune Microenvironment* **Jennifer Hope, PhD**	Drexel University *Harnessing PSGL-1 To Enhance Anti-tumor Immunity*

Symposium Agenda

12:25 PM	**Lunch Break**
2:00 PM	**Session 3: Engineering the Anti-cancer Immune Response**
Moderator: **Xiao Huang, PhD**	**Melody Swartz, PhD** | University of Chicago *Modeling the Tumor-Immune Microenvironment for Immunotherapy Responses* **Li Tang, PhD** | EPFL *A Metabolically Armored CAR-T Cell Eradicates Solid Tumors and Promotes Stem-Like Memory* **Stacey Finley, PhD** | University of Southern California *Computational Modeling Explains Evolution and Heterogeneity of T Cell Exhaustion*
3:30 PM	**Coffee Break**
3:50 PM	**Session 4: Nanomedicine in Immune Engineering**
Moderator: **Yinghui Zhong, PhD**	**Jeffrey Hubbell, PhD** | University of Chicago *Cytokine Engineering To Turn Immunity On or Off* **Daniel Anderson, PhD** | MIT *Nonviral RNA delivery and Genome Editing of the Immune System* **Mohamad-Gabriel Alameh, PhD** | University of Pennsylvania *Adjuvanticity of Lipid Nanoparticles, and Development of Next-Generation mRNA-LNP Vaccines*
5:20-7:30 PM	**Poster Session and Cocktail Reception** **Papadakis Integrated Sciences Building** **3245 Chestnut St, Philadelphia, PA 19104** Poster session abstracts available online Hover your camera over this image

Symposium Agenda

Day 3: December 1, 2023

8:00 AM	**Breakfast**
9:00 AM	**Opening Remarks**
9:05 AM	**Session 5: Infectious Disease and Vaccines**
Moderator: **Michele Kutzler, PhD**	**Rogier Sanders, PhD** | Amsterdam University *Stabilized HIV-1 Envelope Protein Vaccines* **Michal Tal, PhD** | MIT *Re-examining the Immune-pathogen Battles in Lyme Disease* **Dionna Williams, PhD** | Johns Hopkins University *Molecular Mechanisms of HIV Infections and Neuroinflammation*
10:35 AM	**Coffee Break**
10:55 AM	**Session 6: Neuro-immune Modulation**
Moderator: **Peter Gaskill, PhD**	**Katrin Richter, PhD** | Justus-Liebeg-Universitat *The Role of Noncanonical Nicotinic Receptors (NCNR) of Innate Immune Cells in Inflammation and Inflammatory Pain* **Habibeh Khoshbouei, PhD** | University of Florida *Dopamine Transporter: The Immune System Influencer* **Seena Ajit, PhD** | Drexel University *Immune Regulation by Macrophage-derived Small Extracellular Vesicles in Attenuating Inflammatory Pain*
12:25 PM	**Lunch Break**

Symposium Agenda

2:00 PM — **Session 7: Engineering Immune Tolerance**

Moderator:
Hao Cheng, PhD

Matthias von Herrath, MD | La Jolla Institute & Novonordisk
Immune Modulation To Cure Type I Diabetes

Alice Tomei, PhD | University of Miami
Immunoengineered Platforms for Type I Diabetes

Ali Naji, MD, PhD | University of Pennsylvania
Enhancing Viability of Transplanted Islets for Type I Diabetes

3:30 PM — **Coffee Break**

3:50 PM — **Session 8: Short Talks from Trainee and Junior PI Award Winners**

Moderator:
Chris Rodell, PhD

Leadership in Diversity: Samantha Hall | University of Memphis
Evaluating the Immunomodulatory Effects of Raspberry Ketone In-vitro for Guided Bone Regeneration

Translational Research: Benjamin S. Haslund-Gourley | Drexel University
Antigen-specific IgM Glycans Promote Severe COVID-19 Infection

Collaboration and Community Engagement: Sabrina VandenHeuvel | Texas A&M University
Macrophage Nano-immunotherapy Reduces Ovarian Cancer Metastasis in 3D Model

Innovative Research: Christopher Ashdown | Stony Brook University
Low Intensity Vibration Increases Proliferation in Human Primary T-Cells While Preserving Phenotype: A Non-Invasive Strategy for Improving CAR-T Manufacturing

Outstanding Early Career Researcher:
Matthew T. Wolf, PhD | National Cancer Institute
Extracellular Matrix Scaffold-assisted Tumor Vaccines Induce Tumor Regression and Long-term Immune Memory

5:30 PM — **Concluding Remarks**

Our Speakers

Sue Van
President and CEO, Wallace H. Coulter Foundation

Established in 1999, the Foundation began scientific and medical research programs and gave substantial grants to domestic biomedical societies to teach scientific and technological advances in less-resourced countries. Begun in 2005, the Translational Research Program in Biomedical Engineering generated over $5 billion in follow-on funding. Prior to establishing the Foundation, Sue was Coulter Corporation's Executive VP and CFO. The Foundation also addresses the underrepresentation of Asian Americans, Native Hawaiians and Pacific Islanders, and American Indian and Alaskan Natives, providing risk capital and seed investments for civic engagement. Sue emigrated from her native Shanghai, China to the U.S. at age five.

Denise J. Montell, PhD
University of California, Santa Barbara

Professor Montell earned her BA degree in Biochemistry and Cell Biology from UCSD and a PhD in Neuroscience from Stanford. After postdoctoral studies in Developmental Genetics at the Carnegie Institution, she rose through the ranks at The Johns Hopkins School of Medicine where she was the Founding Director of the Center for Cell Dynamics. Montell returned to California in 2013. She has served on the Councils of the American Cancer Society and NIGMS, on the National Cancer Institute Board of Scientific Counselors and as the 2020 President of the Genetics Society of America. She is a fellow of AAAS and ASCB and a member of the US National Academy of Sciences.

Adam Snook, PhD
Thomas Jefferson University

Adam Snook, PhD, is an Associate Professor at Thomas Jefferson University and is an Assistant Program Leader of the Immune Cell Regulation and Targeting (IRT) Program of the Sidney Kimmel Cancer Center. He is also Associate Director of the Clinical & Translational Research track of the JeffMD Scholarly Inquiry Program of the Sidney Kimmel Medical College. His research focuses on developing novel immunotherapeutic approaches, particularly for gastrointestinal malignancies, including cancer vaccines and CAR-T cell therapies, targeting compartmentalized antigens. His work has led to 7 investigator-initiated clinical trials examining colorectal cancer chemoprevention, cancer vaccines, and CAR-T cell therapies.

Our Speakers

Maria Grazia Roncarolo, MD
Stanford University

Dr. Maria Grazia Roncarolo is one of the world's foremost experts in translational medicine and a pioneer in cell and gene therapy. She is recognized globally for her leadership in translating scientific discoveries in genetic diseases and regenerative medicine into novel patient therapies. The George D. Smith Professor in Stem Cell and Regenerative Medicine, Professor of Pediatrics and of Medicine at Stanford University, Dr. Roncarolo established the Stanford Center for Definitive and Curative Medicine to cure patients with currently incurable diseases through the development of innovative stem cell and gene-based therapies.

Francesca Taraballi, PhD
Houston Methodist

Dr. Taraballi is an assistant professor in Orthopedic Surgery at Houston Methodist Hospital and serves as Director for the Center for musculoskeletal Regeneration affiliated to the Orthopedics and Sports Medicine Department. She is also a faculty member of the Center for RNA therapeutics and have adjunct position at the Department of Nanomedicine and Neal Cancer Center of the Houston Methodist Hospital. Dr. Taraballi own a master in biochemistry and a Ph.D. in Nanotechnology from the University of Milan-Bicocca. Dr. Francesca Taraballi works in the field of immune engineering. Her expertise lies in the intersection of nanotechnology, biomaterials, and immunology.

Ann-Marie Chacko, PhD
Duke-NUS Medical School, Singapore

Dr. Ann-Marie Chacko obtained her PhD in Pharmacology at the University of Pennsylvania with a speciality in Radiopharmaceutical Sciences. In 2015, she joined Duke-NUS Medical School in Singapore, where she established the Laboratory for Translational and Molecular Imaging (LTMI). Her research centres on the design, synthesis and preclinical validation of molecularly-targeted systems for PET, SPECT, and optical imaging of immune response and inflammation, and its resolution in cancer and viral infection. Dr Chacko currently leads Singapore's national platform, the Cancer ImmunoTherapy Imaging (CITI) Programme, to address the urgent call for biomarker-driven approaches to monitor tumour immune responses.

Our Speakers

Jennifer Hope, PhD
Drexel University

Dr. Jennifer Hope is an Assistant Professor in the Department of Microbiology and Immunology at Drexel University College of Medicine and Associate Member of the Sidney Kimmel Cancer Center (Jefferson Health) in the Immune Cell Regulation and Targeting (IRT) Program of Excellence. Dr. Hope's research is aimed at understanding intrinsic and microenvironment-derived signals that drive T cell differentiation and T cell exhaustion. Her lab leverages mouse models of melanoma and pancreatic cancer to model immunoresponsive and non-responsive tumors and assess the efficacy of new therapeutic interventions.

Melody Swartz, PhD
University of Chicago

Melody Swartz is the William B. Ogden Professor of Molecular Engineering at the University of Chicago and co-director of the Chicago Immunoengineering Innovation Center. Her research is focused on the lymphatic system and aims to understand its roles in immunity and pathophysiology, especially in cancer and chronic inflammation, and translate that to novel immunotherapies. Towards both basic and translational goals, her lab has developed numerous model systems, including an in vitro tumor-immune circuit for immunotherapy screening. She is a MacArthur Fellow and member of the NAM, NAE, and the American Academy of Arts & Sciences.

Li Tang, PhD
EPFL

Li Tang received his B.S. in Chemistry from Peking University, China, in 2007, and Ph.D. in Materials Science and Engineering from University of Illinois at Urbana-Champaign, USA, in 2012, under the supervision of Prof. Jianjun Cheng. He was an CRI Irvington Postdoctoral Fellow in the laboratory of Prof. Darrell Irvine at Massachusetts Institute of Technology during 2013-2016. He joined the faculty of Institute of Bioengineering, and Institute of Materials Science & Engineering, at École polytechnique fédérale de Lausanne (EPFL), Switzerland, as a Tenure-Track Assistant Professor in 2016, and promoted to Associate Professor with tenure in 2022. His research focuses on developing multidimensional immunoengineering approaches for enhanced cancer immunotherapies.

Our Speakers

Stacey Finley, PhD
University of Southern California

Dr. Stacey Finley received her B.S. in Chemical Engineering from Florida A & M University and obtained her Ph.D. in Chemical Engineering from Northwestern University. She completed postdoctoral training in Biomedical Engineering at Johns Hopkins University. Dr. Finley joined the faculty at USC in 2013, where she leads the Computational Systems Biology Laboratory. Dr. Finley has joint appointments in Quantitative and Computational Biology, and in Chemical Engineering and Materials Science. Dr. Finley is a member of the USC Norris Comprehensive Cancer Center, and is also a standing member of the NIH Modeling and Analysis of Biological Systems (MABS) Study Section.

Jeffrey Hubbell, PhD
University of Chicago

Jeffrey Hubbell is Eugene Bell Professor in Tissue Engineering at the Pritzker School of Molecular Engineering of the University of Chicago. Before moving to Chicago, he was on the faculty of the Swiss Federal Institute of Technology Lausanne (EPFL, where he served as Director of the Institute of Bioengineering and Dean of the School of Life Sciences), the Swiss Federal Institute of Technology Zurich and University of Zurich, the California Institute of Technology, and the University of Texas in Austin. He holds a BS from Kansas State University and a PhD from Rice University, both degrees being in chemical engineering.

Daniel Anderson, PhD
Massachusetts Institute of Technology

Daniel G. Anderson is a Professor in the Department of Chemical Engineering and the Institute for Medical Engineering and Science at MIT. The research done in Prof. Anderson's laboratory is focused on developing medical technology and has led to advances in a range of areas, including medical devices, cell therapy, drug delivery, gene therapy and material science, as well the publication of over 500 papers, patents, and patent applications. These advances have led products that have been commercialized or are in clinical development, as well as to the foundation of companies in the pharmaceutical, biotechnology, and consumer products space.

Our Speakers

Mohamad-Gabriel Alameh, PhD
University of Pennsylvania

Dr. Alameh works on the development of mRNA-based vaccines against viral and bacterial pathogens, and aims to understand the interaction between lipid nanoparticles with the immune system to improve their reactogenicity and fine-tune vaccine responses. He also develops novel proprietary ionizable lipids, and LNP formulations for therapeutic and vaccine applications, and work on the scale-up of mRNA and LNP production processes.

Rogier Sanders, PhD
Amsterdam University

Rogier Sanders (1975) obtained his PhD (cum laude) from the University from Amsterdam in 2004. He is Professor of Virology in Amsterdam and holds an affiliate position at Weill Medical College of Cornell University in New York. His research focuses on viral glycoprotein vaccines, in particular those based on native-like trimers, several of which are now in clinical trials. Rogier's proline-based glycoprotein stabilization was applied in many COVID-19 vaccines. Rogier has (co-)authored more than >250 articles in scientific journals. In 2023 he received an honorary doctorate from the University of Southampton, UK.

Michal Tal, PhD
Massachusetts Institute of Technology

Michal Caspi Tal, PhD, is an immunoengineer, and a principal scientist at the Massachusetts Institute of Technology (MIT). Dr. Tal leads the Tal Research Group within the department of Biological Engineering and also serves as the associate scientific director of the Center for Gynepathology Research. Michal is working to identify the connections between infections and chronic diseases. Her research is focused on creating predictive diagnostics, and generating actionable information providers can use to connect with and care for patients to improve diagnosis and treatments for invisible chronic diseases.

Our Speakers

Dionna Williams, PhD
Johns Hopkins University

Originally from Bridgeport, Connecticut, Dr. Williams's early love for science and desire to understand human disease focused their aspirations towards biomedical research. A first-generation college student, Dr. Williams graduated Cum Laude from Hofstra University before attending the Albert Einstein College of Medicine for their graduate studies, followed by Johns Hopkins University for her postdoctoral fellowship. Dr. Williams' research is dedicated to increasing understanding of the intersection between substance abuse and HIV neuroscience. Specifically, her research focuses on interactions between substances of abuse and antiretroviral therapy efficacy in limiting HIV infection in the brain and the mechanisms by which neuroinflammation promotes neurologic dysfunction during HIV.

Katrin Richter, PhD
Justus-Liebig University of Giessen

Katrin Richter studied biology and earned a degree as a Dr. rer. nat. at the Justus-Liebig University of Giessen. Since 2023, she is a junior research group leader at the Laboratory of Experimental Surgery in Giessen. She has an expertise in physiology and immunology and is experienced in electrophysiological two-electrode voltage-clamp and patch-clamp recordings. Her research interest focuses on mechanisms that regulate the release of the pro-inflammatory cytokine interleukin (IL)-1β by cells of innate immunity. Further, she discovered a cholinergic mechanism that controls the ATP-mediated inflammasome assembly and release of IL-1β via noncanonical nicotinic receptors.

Habibeh Khoshbouei, PhD
University of Florida

Over the past two decades, our research has focused on determining the biology of dopamine transporter (DAT) and the cellular mechanism of dopamine transmission in health and disease conditions. Recent reports suggest DAT modulates innate and adaptive immunity in peripheral immune cells via immunosuppressive actions that modify immune responses during acute inflammation, such as bacterial infections, or chronic inflammation. Whereas immune suppressive cytokines such as TGF-b and IL10 reshaped monocytes' phenotype to high DAT expressing state. Our data support the hypothesis that the DAT activity on peripheral monocyte and monocyte derived macrophages represents an endogenous compensatory mechanism for attenuating monocytic responses to inflammation.

Our Speakers

Seena Ajit, PhD
Drexel University

Dr. Seena Ajit is a Professor in the Department of Pharmacology & Physiology at Drexel University College of Medicine. Her research focuses on the epigenetic mechanisms mediating pain, with an emphasis on noncoding RNAs. Her laboratory aims to be at the interface between basic and clinical research to identify molecular determinants contributing to pain. She is investigating circulating microRNA as biomarkers in patients with complex regional pain syndrome and rodent models of pain. She is also studying the role of small extracellular vesicles in intercellular communication, and their potential utility as a pain therapeutic and biomarker.

Matthias von Herrath, MD
La Jolla Institute & Novonordisk

Matthias von Herrath is a highly respected physician-scientist in the field of immunology and drug development for T1D. His research focuses on understanding the molecular mechanisms that underlie T1D, with particular interest in studying the role of the immune system in the development and progression of T1D. He is the Scientific Director of the Diabetes Research Institute and Stacey Joy Goodman Chair at the University of Miami, and Vice President and Senior Medical Officer at Novo Nordisk. His efforts have been recognized by numerous awards and honors.

Alice Tomei, PhD
University of Miami

Dr. Tomei is the Miami Engineering Career Development Associate Professor in Biomedical Engineering. At the University of Miami Miller School of Medicine Diabetes Research Institute, she is applying her unique background in bioengineering and immunology to develop novel immunoengineering platforms to prevent rejection after islet transplantation and to promote antigen-specific tolerance for a cure of type-1 diabetes. Dr. Tomei has received grants from the NIH, JDRF, Semma Therapeutics and Sernova Corp., for $6.75 million as PI, and $7.64 million as co-investigator so far. She is also a standing member of the NIH BMBI and the CIRM grant working groups.

Our Speakers

Ali Naji, PhD
University of Pennsylvania

Dr. Naji is the Jonathan E. Rhoads Professor of Surgery at the University of Pennsylvania Medical School. He is a transplant surgeon and immunologists and his basic and translational research focus on immunobiology of islet transplantation and immune pathogenesis of type 1 diabetes.

Abstract Award Winners

Leadership in Diversity:
Samantha Hall, University of Memphis

Title:
Evaluating the Immunomodulatory Effects of Raspberry Ketone In-vitro for Guided Bone Regeneration

Abstract

Guided bone regeneration (GBR) is an alveolar bone loss procedure that utilizes barrier membranes to occlude soft tissue infiltration. Electrospun chitosan membranes (ESCMs) have shown promise for enhanced GBR due to drug loading capabilities, biocompatibility, and pro-healing properties. Raspberry Ketone (RK) is a phenolic compound of red raspberry that has shown significant potential in the promotion of macrophage polarization toward the M2, pro-healing, phenotype. The aim of this study was to use an in vitro macrophage polarization model and microarray analysis to evaluate the immunomodulatory effects of RK when released from ESCMs. RAW cells were seeded in 24 well plates at 100,00 cell/ml in DMEM + 10% FBS-1% PSN media. After 24 hours, M1, pro-inflammatory, activation was induced using lipopolysaccharide (LPS). After 24 hours of LPS incubation, medium was replaced with complete DMEM, DMEM containing 300 ng/ml PGE2, or 10mm diameter ESCMs loaded with 0, 50, 100, 250, or 500 µg RK/membrane. Positive controls only received 1 µg/mL LPS, and negative controls did not receive any treatment. Groups (n=3) were assayed on days 1, 3, and 5 for 20 pro and anti-inflammatory cytokines present in the culture medium using microarray analyses (RayBiotech Mouse Cytokine Array Q1, GA). Results showed that RK treated groups had a decreased production of the immune cell recruitment chemokine, RANTES. RK groups also saw an increase in M2 associated, pro-inflammatory inhibiting factors IL-10, IL-9, and IL-4 in comparison to non-treated groups. Additionally, RK groups saw an increased production in the angiogenic factor VEGF-A at day 3. RK groups also saw an increased production of the osteogenic cytokine IFNY at days 1 and 3 in comparison to RK treated groups. This indicates that RK has potential for uses in GBR and other biomaterials-based applications for the facilitation of wound healing.

Abstract Award Winners

Translational Research:
Benjamin Haslund-Gourley, Drexel University

Title:
Antigen-specific IgM Glycans Promote Severe COVID-19 Infection

Abstract:

A major factor contributing to severe COVID-19 infection is the extensive deposition of complement in the pulmonary and renal systems. IgM is a potent initiator of complement deposition, containing glycans that can participate in C1q binding. These glycans are sugar structures post-translationally attached to IgM in the Golgi by transferases. However, the glycans on IgM have not been studied during any infectious disease. For the first time, we report alterations in IgM glycosylation significantly correlate with COVID-19 severity and promote higher levels of complement deposition. These findings were confirmed within total IgM and SARS-CoV-2-specific IgM glycan profiles. In contrast to the IgG glycans from severe patients, IgM glycans present more negatively charged sialic acids and unprocessed branching mannose structures. We link the changes of IgM glycosylation with the mRNA expression of Golgi transferases quantified from circulating immune cells. These IgM glycan changes significantly correlate with other markers of disease severity including D-dimer, creatinine, potassium, and blood urea nitrogen. To further explore the role of IgM glycans during severe COVID-19, we developed an antigen-specific complement deposition assay. Using this assay, we observe that IgM-dependent complement deposition is elevated in severe COVID-19 patients. Moreover, we modulated the amount of IgM-dependent complement deposition by enzymatically removing sialic acid glycans from IgM. Taken together, this work identifies the glycans on IgM as biomarkers of COVID-19 severity and highlights a mechanism promoting COVID-19 pathogenesis through complement deposition.

Abstract Award Winners

Collaboration & Community Engagement:
Sabrina VandenHeuvel, Texas A&M University

Title:
Macrophage Nano-immunotherapy Reduces Ovarian Cancer Metastasis in 3D Model

Abstract

The 5-year survival rate of metastasized ovarian cancer (OvCa) is <30%. Clinical biospecimen link poor prognosis to increased macrophage immune checkpoint signaling. OvCa cells express CD47 which binds macrophage checkpoint SIRPa (signal regulatory protein-a) to suppress anti-tumor immunity and enhance OvCa chemoresistance and metastasis. We developed a short interfering RNA (siRNA) nano-immunotherapy (siSIRPa) to disrupt macrophage checkpoint signaling by reducing SIRPa expression. Microfluidic techniques were used to prepare stable and reproducible lipid nanoparticles encapsulating SIRPa siRNA. OvCa/macrophage co-culture heterospheroids were generated on a hanging drop array and maintained for up to 6 days with 25 nM siSIRPa administration on day 2. Resulting SIRPa gene (RT-qPCR) and protein (flow cytometry) expressions as well as spheroid proliferation and carboplatin chemotherapy response (MTS viability assay) were evaluated. Invasive potential was quantified by seeding compact spheroids onto culture dishes and monitoring spheroid area expansion over 5 days. Owing to the terminal differentiation state of macrophages, heterospheroids were smaller and less proliferative than monospheroids (OvCa cells alone). Despite smaller spheroid size, macrophages contributed to carboplatin chemoresistance making heterospheroids 4.7-fold more resistant. OvCa cells in heterospheroids also showed significantly increased invasive potential (compare 11.1-fold to 4.4-fold area increase in monospheroids, ***$p<0.001$). siSIRPa therapy reduced SIRPa gene and protein expression in heterospheroids by 42 and 59%, respectively (****<0.0001) and improved chemosensitivity by 60%. Notably, when siSIRPa was administered to monospheroids, neither chemoresistance nor invasive potential were significantly altered, supporting that our therapy directly affects macrophages in the system, as desired. Our work underscores that CD47-SIRPa signaling inhibitors are a novel therapeutic agent against OvCa progression and chemotherapy resistance. Optimizing nano-therapies is advantageous to control transport, timing and specificity of RNA therapies. An additional benefit is the ability to design these nanoparticles for uptake by intrinsically phagocytic macrophages to treat and curb metastatic OvCa and positively impact survival.

Abstract Award Winners

Innovative Research:
Christopher Ashdown, Stony Brook University

Title:
Low Intensity Vibration Increases Proliferation in Human Primary T-Cells While Preserving Phenotype: A Non-Invasive Strategy for Improving CAR-T Manufacturing

Abstract:

Chimeric antigen receptor T cell (CAR-T) therapy is an incredibly effective cancer therapeutic. Nevertheless, autologous CAR-T therapy is a relatively inefficient process that remains confounded by a time-intensive ex vivo expansion process. Current strategies to reduce this manufacturing time involve adding various cocktails of cytokines or expansion beads. However, these chemical additives can often have deleterious effects on CAR-T therapy outcomes, as the increased expansion they offer comes at the expense of higher levels of T cell exhaustion, which are associated with less functional CAR-T cells. Mechanical signals represent a previously underutilized strategy for improving expansion of suspension cells and may be able to influence cell growth without the side effects generated by traditional chemical manipulation. We tested the hypothesis that mechanical simulation, delivered non-invasively using low intensity vibration (LIV, at: 30 Hz, 0.7g, 2 bouts of 1h/d, 2-hour refractory period) could be used to improve T cell expansion without disrupting phenotype. We found that LIV was able to drive a significant increase in T cell proliferation (30% in 5 days). This increase in proliferation was driven by roughly 20% increase in the number of activated T cells (CD62L-/CD69+), showing that we can mechanically and noninvasively activate T cells with vibration. We also show that LIV may have beneficial effects on T cell exhaustion. Our LIV stimulation caused a 25% decrease in the expression of the inhibitory receptors PD-1 and LAG-3, suggesting that LIV may be used in the future to improve functionality of T cells in addition to proliferation. This proof-of-concept work provides evidence that mechanical stimulation in the form of LIV, can not only be used to significantly improve the speed of CAR-T manufacturing, but that it can do so while generating beneficial phenotypes related to T cell exhaustion, that are often sacrificed during traditional pharmacologic expansion processes.

Abstract Award Winners

Outstanding Early Career Researcher:
Matthew T. Wolf, PhD, National Cancer Institute

Title:
Extracellular Matrix Scaffold-assisted Tumor Vaccines Induce Tumor Regression and Long-term Immune Memory

Abstract:

Injectable scaffold delivery is an immune engineering strategy to enhance the efficacy of cancer vaccine immunotherapy. The type of biomaterial scaffold affects both vaccine release kinetics and immune stimulation via the scaffold host response. Extracellular matrix (ECM) scaffolds prepared from decellularized tissues initiate an alternative inflammatory response following implantation, which facilitates wound healing following tumor resection and promotes local cancer immune surveillance. Here, we engineered an ECM scaffold-assisted therapeutic cancer vaccine that maintained an immune microenvironment consistent with tissue reconstruction. We screened immune adjuvants MPLA, GM-CSF, and CDA to formulate a decellularized small intestinal submucosa (SIS) ECM scaffold cancer vaccine. We found that the STING pathway adjuvant CDA was the most potent cytotoxic inducer with SIS-ECM scaffold delivery. Further, CDA did not diminish hallmark ECM immune responses needed in wound healing such including IL4 signaling. SIS scaffold delivery enhanced therapeutic vaccine efficacy, curing 50-75% of established EG.7 tumors, compared to soluble components alone (0% cured). SIS-ECM scaffold assisted vaccination extended antigen exposure, was mediated by CD8+ cytotoxic T cells, and generated long term anti-tumor memory at least 7 months post-vaccination in both young and mature-aged mice. We then translated this approach to a novel Surgical Genetic Mouse Model Allograft (Surgi-GEMMA) of tumor resection and ECM-vaccine implantation. CDK4(R24C)-Hgf-Tg melanoma allograft tumors had >90% recurrence with surgical resection or neoadjuvant immunotherapy; however we found recurrence rates dropped to 45% when immediately implanted with an FDA approved ECM mesh infused cancer vaccine. Histologic analysis showed CD86 antigen presenting cell recruitment and expected ECM remodeling. This study shows that an ECM scaffold is a promising delivery vehicle to enhance cancer vaccine efficacy while being orthogonal to characteristics of pro-healing immune hallmarks.

Thank You

If you have any questions, please get in touch with us.

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Contact Us

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