### Vascular Biology 2023

#### **Poster Presentations**

#### **MONDAY POSTERS SESSIONS**

### **Blood Flow Regulation**

#### M-01

Upper limb occlusive hyperemia evokes the same response mechanism in the contralateral forearm – data from functional imaging with optoacoustic tomography

Sergio F Andrade MSc, PhD, Tiago Granja PhD, Luis M Rodrigues MSc, PhD

CBIOS – Universidade Lusofona's Research Center for Biosciences & Health Technologies, Lisboa, Lisboa, Portugal

- To better understand the response to reactive hyperemia and the venoarteriolar reflex.
- These are considered to evoke local adaptive responses are used to study vascular physiology.
- Our results demonstrated that any perfusion adaptive response involves a centarlly mediated reflex.

#### M-02

### Maintenance of blood-brain barrier integrity during mammalian hibernation

Maryann Platt PhD<sup>1,2</sup>, Slav Bagriantsev PhD<sup>1</sup>, Elena Gracheva PhD<sup>1,2</sup>

<sup>1</sup>Yale University, New Haven, CT, USA. <sup>2</sup>Yale Kavli Center for Neuroscience, New Haven, CT, USA

- Hibernation provides a naturalistic model of low blood flow in which to study reperfusion.
- Facets of the blood brain barrier are differentially regulated during hibernation.
- Blood flow velocity scales with body temperature during arousal from hibernation.

#### M-03

### Endothelial hemoglobin alpha mediates iron regulation of endothelial nitric oxide

<u>Luke S Dunaway PhD</u>, Shruthi Nyshadham BS, Melissa A Luse MS, Skylar Loeb BS, Adam N Goldfarb MD, Brant E Isakson PhD

University of Virginia, Charlottesville, VA, USA

- Endothelial iron regulates nitric oxide signaling.
- Increased nitric oxide signaling in iron deficiency anemia is not due to reduced blood hemoglobin.
- Endothelial hemoglobin alpha regulates nitric oxide in response to changing iron levels.

#### M-04

### A multiscale mathematical model to examine the role of capillary pericytes in cerebral blood flow control

Niloufar Khakpour PhD Student<sup>1</sup>, Dabasish Kumar Saha PhD Student<sup>1</sup>, Nicholas R. Klug PhD, Postdoctoral Associate<sup>2</sup>, Mark T. Nelson PhD, Distinguished Professor & Chair<sup>2</sup>, <u>Nikolaos M. Tsoukias PhD, Professor</u><sup>1</sup>
<sup>1</sup>Florida International University, Miami, Florida, USA. <sup>2</sup>University of Vermont, Burlington, Vermont, USA

- Present an integrated model to explore pericytes' role in coordinating local blood flow distribution
- Pericytes play a key role in maintaining constant brain perfusion through myogenic autoregulation
- Pericytes promote uniform blood flow distribution preserving supply to vulnerable brain regions

# Flowing through the kidney microvasculature: glomerular endothelial cells and their role in chronic kidney disease

<u>Nathalie Reinhard</u>, Sabine Leonhard, Annick Werner, Barbara Wilmeringwetter, Matthias Mueller, Ivan Formentini, Philipp Hoppe

Novartis Institutes for Biomedical Research (NIBR), Basel, Switzerland

- Modeling kidney hyperfiltration
- Generating novel glomerular endothelial cell model systems
- Microvasculature drug targets in chronic kidney disease

#### M-06

## Sickle trait and alpha thalassemia increase NOS-dependent vasodilation in human arteries through disruption of endothelial hemoglobin-eNOS interactions

Steven Brooks PhD¹, Parker Ruhl MD, MHS¹, Xianke Zeng MD, PhD¹, Phillip Cruz PhD¹, Sergio Hassan PhD¹, Olena Kamenyeva PhD¹, Juraj Kabat PhD¹, Sundar Ganesan PhD¹, Rachel Smith BS¹, Md Hakim PhD¹, Mary Jackson RN¹, Jessica de Rivera BS¹, Jarrett Jackson MD¹, Robert Emeh BS¹, Naomi Tesfuzigta BS¹, Kyeisha Laurence BS¹, Stacy Joyce PA-C², Christina Yek MD¹, Sophana Chea BS¹, Brant Isakson PhD³, Jessica Manning MD¹, Jeremy Davis MD², Hans Ackerman MD, DPhil¹

<sup>1</sup>National Institute of Allergy and Infectious Diseases, Bethesda, MD, USA. <sup>2</sup>National Cancer Institute, Bethesda, MD, USA. <sup>3</sup>University of Virginia, Charlottesville, VA, USA

- Human resistance arteries express hemoglobin that regulates the release of nitric oxide (NO).
- Genetic variation in hemoglobin is associated with NO signaling and blood pressure in humans.
- Disruption of hemoglobin-eNOS interactions increases vascular NO signaling in human arteries.

#### M-07

### Cardiac arrest induces "time sensitive" impairments to cerebrovascular autoregulation

<u>Haishuo Guan</u>, Arvind Pathak, Romergryko G. Geocadin, Nitish V. Thakor, Janaka Senarathna Johns Hopkins University, Baltimore, MD, USA

- Cerebral blood flow regulation changes substantially immediately after resuscitation
- Autoregulation is a key indicator of brain health
- Timely clinical intervention is crucial for mitigating brain injury.

### Diseases (Vascular and Cardiovascular) I

#### M-11

### Evaluation of IMA2a in a rat model of pulmonary arterial hypertension

<u>Boris Tchernychev PhD</u>, Kevin O'Brien PhD, Lisa Flaman MS, Jennifer Howe BS, Daniel Ortiz PhD, Yves Sabbagh PhD

Inozyme Pharma, Boston, MA, USA

- Enpp1 hydrolyzes extracellular ATP to AMP, a precursor of adenosine.
- In pulmonary arterial hypertension (PAH) adenine nucleotide signaling is dysregulated.
- Effect of IMA2a, an Enpp1-Fc protein, on disease progression was evaluated using rats with PAH.

# TERT transcriptional activation is sufficient to restore NO production in blood vessels following Doxorubicin treatment

<u>Makenna Wells</u>, Andreas Beyer PhD Medical College of Wisconsin, Wauwatosa, WI, USA

- Cardio-Oncology
- Endothelial function
- Microcirculation

#### M-13

# Epigenetic perturbations in a mouse model of Loeys-Dietz Syndrome: Stress responses and phenotypic plasticity explored through histone modification analysis in Smooth Muscle Cells

<u>Leda Restrepo PhD</u>, Emily Bramel BS, Wendy Espinoza-Carmejo BS, Elena MacFarlane PhD Johns Hopkins, Baltimore, MD, USA

- LDS showed enrichment of motifs related to phenotypic plasticity, proliferation, and stress response
- Epigenetic changes in LDS SMCs may drive different responses that contribute to aortic disease
- Selectively targeting maladaptive responses could be a promising therapeutic approach in LDS

#### M-14

# Deletion of the acid-sensing ion Channel1A gene leads to hyperaldosteronism-induced hypertension with age

<u>Selina M Garcia PhD</u>, Laura V Gonzalez Bosc PhD, Nikki L Jernigan PhD University of New Mexico School of Medicine, Albuquerque, NM, USA

- The loss of the acid-sensing ion channel 1a contributes to age-induced hypertension
- The loss of the acid-sensing ion channel 1a contributes to hyperaldosteronism
- The loss of the acid-sensing ion channel 1a does not affect angiotensin II levels

#### M-15

### The role of Neuropilin-1 and p130Cas in pulmonary arterial hypertension

James M Berg<sup>1</sup>, Jigisha A Patel PhD<sup>1</sup>, Ameera Milhan<sup>1</sup>, Elena Rahmani<sup>1</sup>, Shahin Moledina MBBS<sup>2,1</sup>, David L Selwood PhD<sup>3</sup>, Lucie H Clapp PhD<sup>1</sup>, Paul Frankel PhD<sup>1</sup>

<sup>1</sup>Institute of Cardiovascular Science, University College London, London, United Kingdom. <sup>2</sup>Pulmonary Hypertension Service for Children, Great Ormond Street Hospital NHS Foundation Trust,, London, United Kingdom. <sup>3</sup>Wolfson Institute for Biomedical Research, University College London, London, United Kingdom

- Pulmonary Arterial Hypertension (PAH) as a Life-Threatening Disease
- Neuropilin-1 (NRP1) and Growth Factor Signalling
- Unravelling Mechanisms and Pathobiology

#### **Metabolism and Metabolic Diseases**

#### M-17

# Identifying how endothelial protease-activated receptors control insulin signaling: implications for diabetes

Rahul Rajala B.A., B.S. 1,2,3, Courtney T Griffin Ph.D. 1,2

<sup>1</sup>Oklahoma Medical Research Foundation, Oklahoma City, OK, USA. <sup>2</sup>University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA. <sup>3</sup>Harold Hamm Diabetes Center, Oklahoma City, OK, USA

- Identifying novel crosstalk between the Insulin Receptor and Protease-Activated Receptors in ECs.
- Identify how insulin receptor splicing affects endothelial insulin transcytosis.
- Identify synergistic roles for PAR1 and PAR4 in endothelial cells.

# Pharmacological inhibition and endothelial cell deletion of tissue-nonspecific alkaline phosphatase disrupt cellular bioenergetics in brain endothelial cells

<u>Shokofeh Rahimpourkaldeh</u>, Sujung Jun, Divine C Nwafor MD/PhD, Candice M Brown PhD West Virginia University, Morgantown, West Virginia, USA

- TNAP, Blood-brain barrier, Brain endothelial cell, Glycolysis, Maximal respiration
- Stroke, TNAP, Oxidative phosphorylation, Glycolysis, Brain endothelial cell
- TNAP, BBB, Stroke, Oxidative phosphorylation, Glycolysis, ATP

### **Pro-Inflammatory Signaling**

#### M-19

### Neuropilin-1 interacts with VE-cadherin and TGFBR2 to stabilize adherens junctions and prevent activation of endothelium under flow

Anissa Chikh PhD¹, Emy Bosseboeuf², Dhilakshani Vignaraja MRes³, Ridhi Rajendrakumar MREs², Tom Mitchell PhD², Thomas D Nightingale PhD², Rayomand S Khambata², Anna M Randi PhD³, Justin C Mason PhD³, Amrita Ahluwalia PhD², <u>Claudio Raimondi PhD</u>²

<sup>1</sup>St. George's University of London, London, London, United Kingdom. <sup>2</sup>Queen Mary University of London, London, London, United Kingdom. <sup>3</sup>Imperial College of London, London, London, United Kingdom

- Under laminar flow, NRP1 stabilizes cell-cell junctions and suppresses endothelial inflammation.
- NRP1 deletion in the endothelium induces vascular inflammation and atherosclerosis
- NRP1 interacts with TGFβ receptor II reducing TGFBR2 membrane localization and TGF-β signaling.

#### M-20

# Hresistin initiates early immune responses through macrophages to activate and proliferate pulmonary smooth muscle cells

<u>Udeshika Kariyawasam PhD</u>, John Skinner B.Sc, Qing Lin MD, Ph.D, Roger Johns MD, Ph.D Department of Anesthesiology and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD, USA

- Hresistin activates macrophages to induce vascular remodeling over time for PH development.
- Hresistin is a critical regulator of early immune responses in PH development.
- Hresistin is a good therapeutic target to prevent inflammation driven vascular remodeling and PH.

#### M-21

### Loss of endothelial *Ripk3* increases vascular permeability following ischemiareperfusion injury by regulating cytokine and adhesion molecule expression

<u>Charmain F. Johnson Ph.D.</u><sup>1</sup>, Kathryn Y. Burge Ph.D.<sup>2</sup>, Hala Chaaban M.D.<sup>2</sup>, Courtney T. Griffin Ph.D.<sup>1,3</sup>

<sup>1</sup>Oklahoma Medical Research Foundation, Oklahoma City, OK, USA. <sup>2</sup>Neonatal-Perinatal Medicine, Department of Pediatrics, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA. <sup>3</sup>Department of Cell Biology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

- Endothelial RIPK3 protects against vascular permeability after ischemia-reperfusion injury (IRI)
- Loss of endothelial Ripk3 increases VCAM-1, ICAM-1 and endothelial IL-6 cytokine expression
- Increased inflammatory markers with loss of Ripk3 contributes to hyperpermeability after IRI

### Macrophage IL-1β signaling activates Rac1-NF-κB-driven transcription of ACE2

Cadence Lee Sc.M.<sup>1,2</sup>, Rachel Carley Pharm.D.<sup>1,2</sup>, Sheila Sharma Sc.M.<sup>1,2</sup>, <u>Julia Pierce A.B.</u><sup>1,2</sup>, Crystal Parry B.S.<sup>1,2</sup>, Elizabeth Amelotte<sup>1,2</sup>, Celia Butler MPH<sup>1,2</sup>, Chris Mantsounga Ph.D.<sup>1,2</sup>, Gaurav Choudhary M.D.<sup>1,2</sup>, Rachel Olson Ph.D.<sup>3</sup>, Alan R Morrison M.D./Ph.D<sup>1,2</sup>

<sup>1</sup>Warren Alpert Medical School at Brown University, Providence, RI, USA. <sup>2</sup>Ocean State Research Institute Inc. at Providence VA Medical Center, Providence, RI, USA. <sup>3</sup>University of Missouri, Columbia, MO, USA

- Macrophage ACE2 expression is dynamic
- Macrophage ACE2 expression is upregulated by inflammatory pathways involving IL-1B-driven NF-kB
- Macrophages may act as a reservoir for ongoing infection through ACE2 upregulation with inflammation

#### M-23

#### Atherosclerotic calcification requires macrophage IL-1B expression

Cadence Lee Sc. $M^{1,2}$ , Joshua Berus Ph $D^{1,2}$ , Rachel Carley Ph $D^{1,2}$ , <u>Elizabeth Amelotte</u><sup>1,2</sup>, Sheila Sharma<sup>1,2</sup>, Julia Pierce  $AB^{1,2}$ , Chris Mantsounga Ph $D^{1,2}$ , Jade Neverson<sup>1,2</sup>, Celia Butler MPH<sup>1,2</sup>, Gaurav Choudhary<sup>1,2</sup>, Alan R. Morrison MD/Ph $D^{1,2}$ 

<sup>1</sup>Warren Alpert School of Medicine at Brown University, Providence, RI, USA. <sup>2</sup>Ocean State Research Institute Inc. at Providence VA Medical Center, Providence, RI, USA

- IL-1β-deleted animals demonstrated significantly decreased atherosclerotic calcification
- Plasma analysis demonstrated modest changes in lipid metabolism
- Calcified human plaques have CD68+ macrophages expressing IL-1β adjacent to areas of calcification.

#### M-26

#### Novel mechanisms controlling NFAT-mediated vascular inflammation

<u>Ramoji Kosuru PhD</u><sup>1</sup>, Behshid Ghadrdoost Nakhchi PhD<sup>1</sup>, Guru Prasad Sharma PhD<sup>1</sup>, Akiko Mammoto PhD<sup>2</sup>, Tadanori Mammoto PhD<sup>2</sup>, David Zhang PhD<sup>2</sup>, Paul Goldspink PhD<sup>3</sup>, Mohamed Trebak PhD<sup>4</sup>, Magdalena Chrzanowska PhD<sup>1,2</sup>

<sup>1</sup>Versiti Blood Research Institute, Milwaukee, WI, USA. <sup>2</sup>Medical College of Wisconsin, Milwaukee, WI, USA. <sup>3</sup>The University of Illinois Chicago, Chicago, IL, USA. <sup>4</sup>University of Pittsburgh, PA, USA

- Rap1A restricts Orai1-mediated Ca2+ entry and expression in endothelial cells
- Endothelial Rap1 restricts NFAT-mediated transcription and vascular inflammation.
- A novel role for Rap1A in controlling vascular integrity

#### M-27

### Interleukin-1 $\beta$ induced neuroinflammation inhibits blood-brain barrier development

Audrey R Fetsko BS, Dylan J Sebo BS, <u>Michael R Taylor PhD</u> University of Wisconsin-Madison, Madison, WI, USA

- Induction of IL-1β in the CNS of zebrafish embryos promotes neuroinflammation.
- IL-1β inhibits CNS angiogenesis and the acquisition of blood-brain barrier properties.
- IL-1\( \text{blocks Wnt/}\( \beta\)-catenin signaling in brain endothelial cells during neurovascular development.

#### M-28

## Implication of non-histone protein citrullination in smooth muscle cell degeneration and abdominal aortic aneurysm

Zain Islam<sup>1</sup>, Li Yin<sup>1</sup>, Aaron Marcum<sup>1</sup>, Eric Kent<sup>1</sup>, Nicholas Hoyt<sup>1,2</sup>, Quang Le<sup>1</sup>, Nina Islam<sup>1</sup>, Campbell Johnson<sup>1</sup>, Mengxue Zhang<sup>1,3</sup>, Yatao Shi<sup>4</sup>, Lian-wang Guo<sup>1</sup>, Lingjun Li<sup>4</sup>, Bowen Wang<sup>1</sup>

<sup>1</sup>University of Virginia, Charlottesville, VA, USA. <sup>2</sup>George Washington University School of Medicine and Health Sciences, Washington, D.C., USA. <sup>3</sup>University of Chicago Pritzker School of Medicine, Chicago, IL, USA. <sup>4</sup>University of Wisconsin-Madison, Madison, WI, USA

- Non-histone Citrullination links AAA with PADI3 and GCN2
- Novel PTM regulates SMC degeneration
- New Insights into SMC glycolysis

### Biomaterials, Bioengineering and Matrix Biology

#### M-29

# Extracellular matrix hydrogel targeting thrombospondin-2 and hypoxia improves diabetic wound healing via angiogenesis

Yaqing Huang<sup>1,2</sup>, Hao Xing Ph.D.<sup>1,3</sup>, Themis Kyriakides Ph.D.<sup>1,2,3</sup>

<sup>1</sup>Vascular Biology and Therapeutics Program, Yale University, New Haven, CT, USA. <sup>2</sup>Department of Pathology, Yale University, New Haven, CT, USA. <sup>3</sup>Department of Biomedical Engineering, Yale University, New Haven, CT, USA

- Impaired HIF-1a in diabetic wounds prevents hypoxia-induced repression of TSP2.
- Stabilization of HIF-1a using DMOG reduced TSP2 production in diabetic fibroblasts.
- TSP2KO ECM hydrogel with DMOG enhanced angiogenesis and healing in diabetic wounds.

#### M-30

#### Role of Shp2 in angiogenic matrix degradation

<u>Barbara Szynal</u>, Jordan Fauser PhD, Vincent Huyot, Jennifer Klomp PhD, Andrei Karginov PhD University of Illinois Chicago, Chicago, IL, USA

- Shp2 regulates endothelial matrix degradation in a non-phosphatase dependent manner.
- Shp2 substrate interactions drive initiation and localization of matrix degradation.
- NS-ML Shp2 mutants show altered intracellular localization and matrix degradation.

#### M-31

# Embedding biomimetic vascular networks via coaxial sacrificial writing into functional tissues

<u>Paul P Stankey</u><sup>1,2</sup>, Sebastien G.M. Uzel PhD<sup>1,2</sup>, Katharina K Kroll PhD<sup>1,2</sup>, Alexander J Ainscough PhD<sup>1,2</sup>, Daniel S Reynolds PhD<sup>1,2</sup>, Alexander Elamine<sup>1,2</sup>, Jennifer A Lewis ScD<sup>1,2</sup>

<sup>1</sup>Harvard University, Cambridge, MA, USA. <sup>2</sup>Wyss Institute, Boston, MA, USA

- We report a novel technique termed coaxial sacrificial writing into functional tissue (co-SWIFT).
- We have developed a method to 3D print hierarchically branching networks of core-shell vasculature.
- We have embedded biomimetic, multilayer vasculature into thick cardiac tissue via co-SWIFT.

#### M-32

# Exploring endothelial protein c receptor as a therapeutic target: mapping distribution and correlation with nanoparticle targeting

<u>Grace D.M. Eriksen PhD student</u>, Andrew J. Urquhart Associate professor, Martin Bak Senior Officer, David Schultz PhD student, Heidi Arps, Doha Ghannam MSc, Anja Brus PhD, Tsinat Berhane MSc, Thomas L. Andresen Professor Department of Health Technology, Kgs.Lyngby, Denmark

- EPCR targeting in disease dysfunction: Challenges and potential
- Mapping EPCR distribution for enhanced drug delivery
- Nanoparticle strategies for addressing endothelial dysfunction

#### Microcirculation

#### M-33

# A high-fidelity computational study of red blood cell trafficking and capillary hemodynamics in tumor/angiogenic microvascular networks

Abhay Mohan, Prosenjit Bagchi

Rutgers University, Piscataway, NJ, USA

- tumor/angiogenic microvascular networks
- red blood cells and blood flow distribution
- computational model, wall shear stress

#### M-34

# Regulatory role of IncRNA CASC15 in vascular remodeling and its implications for chronic kidney disease

<u>Cristina Espinosa-Diez</u><sup>1,2</sup>, Ibrahim Ahmed<sup>1</sup>, Jianxin Wei<sup>1</sup>, Mingjun Liu<sup>1</sup>, Scott Hahn<sup>1</sup>, Satoshi Okawa<sup>1</sup>, Thiago Bruder-Nascimento<sup>1</sup>, Adam C Straub<sup>1</sup>, Sruti Shiva<sup>1</sup>, Delphine Gomez<sup>1</sup>

<sup>1</sup>University of Pittsburgh, Pittsburgh, PA, USA. <sup>2</sup>Wayne State University, Detroit, MI, USA

- Inhibition of Ang-II dependent IncRNA prevents contribution to vascular remodeling
- Loss of this IncRNA could exarcebate CKD progression
- Rescue of Ang-II dependent IncRNA could enhance kidney revascularization and prevents CKD.

#### M-35

# Oncostatin-M signaling drives capillary leak in critically ill children by inducing phenotypical changes in endothelial cells and a novel pathway of transcellular permeability

<u>Giulio Fulgoni PhD</u>, Weiming Ni PhD, Alam Khan PhD, Francesc Lopez PhD, Guilin Wang PhD, John Giuliano MD, Jordan Pober MD, PhD, Richard Pierce MD

Yale University, New Haven, CT, USA

- Oncostatin-M (OSM) signaling is upregulated in ECs isolated from patients who develop capillary leak
- OSM induce transcellular endothelial permeability, possibly through PLVAP1-dependent PM-structures
- OSM signals through a JAK/STAT3 pathway and broadly reprogram EC transcriptome and function

#### M-36

# Do capillary endothelial cell characteristics differ along the length of a capillary: implications for active hyperaemia

Mackenzie E Charter, Barbara M Hyde-Lay, Coral L Murrant

University of Guelph, Guelph, ON, Canada

- Endothelial cells are heterogeneous across a single capillary in skeletal muscle
- Endothelial cell heterogeneity could have implications for how capillaries coordinate blood flow
- Endothelial cell heterogeneity could be an important organizational component of capillary units

#### M-37

# Redox-sensitive mitochondrial acid-sensing ion channel 1a regulates mitochondrial membrane potential in pulmonary arterial smooth muscle cells

<u>Megan N Tuineau</u>, Lindsay M Herbert, Tracylyn R Yellowhair, Thomas C Resta PhD, Nikki L Jernigan PhD University of New Mexico School of Medicine, Albuquerque, NM, USA

Acid-sensing ion channel 1 is expressed in mitochondria in pulmonary arterial smooth muscle cells

- Mitochondrial acid-sensing ion channel 1 promotes mitochondrial membrane potential depolarization
- Oxidants increase localization of acid-sensing ion channel 1 to mitochondria

# The phosphodiesterase-9A inhibitor PF04447943 via a peroxiredoxin mechanism improves coronary microvascular rarefaction in the ZSF1 rat model of HFpEF

<u>Katie Anne Fopiano</u><sup>1</sup>, William M Pearson<sup>1</sup>, Vadym Buncha<sup>1</sup>, Davis J Hardell<sup>1</sup>, Liwei Lang PhD<sup>1</sup>, Nazha Hamdani MD, PhD<sup>2</sup>, Zsolt Baqi MD, PhD<sup>1</sup>

<sup>1</sup>Medical College of Georgia at Augusta University, Augusta, USA. <sup>2</sup>Ruhr University Bochum, Bochum, Germany

- Coronary microvascular rarefaction contributes to the development of HFpEF.
- Coronary angiogenic endothelial sprouting can be improved via a peroxiredoxin mechanism.
- Treatment with selective PDE9A inhibitors improve coronary microvascular density.

#### M-39

# Stimulating in vivo angiogenesis with sustained local release of an optimized proangiogenic protein cocktail

<u>Stephanie M Roser M.Sc</u>, Alicia J Minor Ph.D., Rajeev J Kant Ph.D., Collin Polucha B.S., Kareen LK Coulombe Ph.D. Brown University, Providence, Rhode Island, USA

- Regeneration
- Biomaterials
- Ischemia

### **Angiogenesis**

#### M-40

## Differential endothelial cell cycle status in post-natal retinal vessels revealed using a novel PIP-FUCCI reporter

 $\underline{ZIQING\ LIU\ PhD}^{1,2}$ , Natalie T Tanke BS $^1$ , Alexandra Neal BS $^1$ , Tianji Yu BS $^1$ , Jean G Cook PhD $^1$ , Victoria L Bautch PhD $^1$ 

<sup>1</sup>UNC-Chapel Hill, Chapel Hill, NC, USA. <sup>2</sup>Medical College of Wisconsin, Milwaukee, WI, USA

- A novel PIP-FUCCI mouse for improved labeling of cell cycle phases with fluorescent reporters
- PIP-FUCCI precisely distinguish the onset of S phase and the S/G2 transition in primary EC and mice
- A novel image analysis pipeline to define EC cell cycle status in distinct vascular zones

#### M-41

### Investigating the role of inflammasome agonism in pathological angiogenesis

<u>Ryan D Makin</u><sup>1,2,3</sup>, Ivana Apicella PhD<sup>1,2</sup>, Roshni Dholkawala MD<sup>1,2</sup>, Shinichi Fukuda MD, PhD<sup>4</sup>, Shuichiro Hirahara MD, PhD<sup>5</sup>, Yoshio Hirano MD, PhD<sup>4</sup>, Younghee Kim PhD<sup>1,2</sup>, Ayami Nagasaka PhD<sup>1,2</sup>, Yosuke Nagasaka MD, PhD<sup>1,2</sup>, Siddharth Narendran MD<sup>6</sup>, Felipe Pereira MD<sup>7</sup>, Akhil Varshney PhD<sup>8</sup>, Shao-bin Wang PhD<sup>1,2</sup>, Jayakrishna Ambati MD<sup>1,2,9,10</sup>, Bradley D Gelfand PhD<sup>1,2,11</sup>

<sup>1</sup>Center for Advanced Vision Science, University of Virginia School of Medicine, Charlottesville, VA, USA.

<sup>2</sup>Department of Ophthalmology, University of Virginia School of Medicine, Charlottesville, VA, USA.

<sup>3</sup>Molecular and Cellular Basis of Disease Graduate Program, University of Virginia School of Medicine, Charlottesville, VA, USA.

<sup>4</sup>Department of Ophthalmology, University of Tsukuba, Tsukuba, Ibaraki, Japan.

<sup>5</sup>Department of Ophthalmology and Visual Science, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan.

<sup>6</sup>Aravind Eye Care System, Madurai, India.

<sup>7</sup>Departamento de Oftalmologia e Ciências Visuais, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil.

<sup>8</sup>Dr. Schroff's Charity Eye Hospital, Daryaganj, Delhi, India.

<sup>9</sup>Department of Pathology, University of Virginia School of Medicine, Charlottesville, VA, USA.

<sup>10</sup>Department of Molecular Biology, Immunology, and Cancer Biology, University of Virginia School of Medicine, Charlottesville, VA, USA. <sup>11</sup>Department of Biomedical Engineering, University of Virginia School of Engineering, Charlottesville, VA, USA

- Inflammasome agonists exacerbate experimental laser-induced choroidal angiogenesis.
- Inflammasome agonist-induced laser CNV exacerbation is inflammasome-dependent.
- Inflammasome-dependent macrophage migration drives CNV exacerbation and is mediated by IL-1β

#### M-42

### The sexual dimorphism of IgG1 anti-angiogenic activity depends on Y chromosome genes

<u>Dionne Argyle  $MS^1$ </u>, Felipe Pereira  $MD^2$ , Yosuke Nagasaka  $PhD^3$ , Shao-bin Wang  $PhD^1$ , Jayakrishna Ambati  $MD^1$ , Bradley Gelfand  $PhD^1$ 

<sup>1</sup>University of Vriginia, Charlottesville, VA, USA. <sup>2</sup>Universidade Federal de Sao Paulo, Sao Paulo, Brazil. <sup>3</sup>University of Virginia, Charlottesville, VA, USA

- The Fc fragment of all human IgG1 antibodies has angiosuppressive properties
- Research suggests that there is a sexual dimorphic response when using IgG1 antibodies in treatment
- A possible tool to explore why there is a sexual dimorphic response with IgG1 is the Y chromosome

#### M-43

#### Dab2 regulates VEGFR2 trafficking during angiogenesis in diabetes

Sudarshan Bhattacharjee PhD, Hong Chen PhD

Boston Children's Hospital, Harvard Medical School, Boston, MA, USA

- Disabled-2 (Dab2) affects VEGFR2 trafficking, impacting angiogenesis in diabetes.
- Dab2 deficiency reduces VEGF signaling, impeding endothelial cell responses.
- Stabilizing Dab2 could enhance angiogenesis for improved wound healing in diabetes.

#### M-44

#### Cx40 suppresses sprouting angiogenesis in vitro

Edward K Looker BS<sup>1</sup>, Femke J Aan BS<sup>1</sup>, Christopher J Hatch BS<sup>2</sup>, Christopher CW Hughes PhD<sup>2</sup>, Michelle L Matter PhD<sup>1</sup>, Jennifer S Fang PhD<sup>1</sup>

<sup>1</sup>Tulane University, New Orleans, LA, USA. <sup>2</sup>UC-Irvine, Irvine, CA, USA

- Cx40 knockdown increases sprouting angiogenesis in the in vitro Bead Assay model.
- Cx40 knockdown increases endothelial cell proliferation, but not migration.
- Cx40 regulates Cx37 expression, and Cx37 knockdown alone produces hypersprouting in the Bead Assay.

#### M-45

### Hypoxia regulate developmental coronary angiogenesis potentially through VEGFR2and SOX17-mediated signaling

Halie E Vitali MS<sup>1</sup>, Bryce Kuschel MS<sup>1</sup>, <u>Chhiring Sherpa BS</u><sup>1</sup>, Brendan W Jones BS<sup>1</sup>, Nisha S Jacob BS<sup>1</sup>, Syeda A Madiha MS<sup>1</sup>, Samuel Elliott BS<sup>1</sup>, Eddie Dziennik BS<sup>1</sup>, Lily Kreun BS<sup>1</sup>, Cora Conatser BS<sup>1</sup>, Bhupal P Bhetwal Ph.D.<sup>2</sup>, Bikram Sharma Ph.D.<sup>1</sup>

<sup>1</sup>Ball State University, Muncie, IN, USA. <sup>2</sup>Marian University, Indianapolis, IN, USA

- Hypoxia regulate embryonic coronary growth in mice
- Hypoxia stimulate developmental coronary growth through SOX17 mediated pathway
- Hypoxia stimulate developmental coronary growth through VEGF-R2 mediated pathway

### Hemogenic Endothelium/Endothelial Diversity

#### M-46

# The chromodomain helicase DNA binding protein 8, CHD8, regulates embryonic erythropoiesis through modulating DNA methylation in endothelial cells of the dorsal aorta

<u>Masahide Sakabe Ph.D.</u>, Nong Chen, Mark Verba, Qing Richard Lu Ph.D., Mei Xin Ph.D. Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

- Investigate the role of CHD8 during embryonic erythropoiesis
- The genes that regulate hematopoietic stem cell differentiation was downregulated in CHD8 KO embryos
- CHD8 regulates embryonic erythropoiesis through modulating DNA methylation

#### M-47

## ABCA1-dependent cholesterol efflux can regulate membrane cholesterol content in rat mesenteric artery endothelial cells

<u>Jacob R Anderson B.S.</u>, Nancy L Kanagy Ph.D., Laura V Gonzalez Bosc Ph.D., Jay S Naik Ph.D. UNM, ABQ, NM, USA

- Regional variation in endothelial cell membrane cholesterol exists in the mesenteric circulation
- Membrane cholesterol regulates H2S-signaling
- ABCA1-dependent cholesterol efflux participates in the regulation of membrane cholesterol content

#### M-48

# Exploring the impact of sex on endothelial cell functions in vascular diseases – Insights from lineage tracing mice, cultured cells, and RNA sequencing

Olga A Cherepanova PhD

Cleveland Clinic, Cleveland, OH, USA

- endothelial cells in atherosclerosis
- sex differences of the vascular pathologies
- mitochondrial functions in endothelial cells

#### M-49

### Elucidating Adam10a function during the endothelial to hematopoietic transition

Beatriz C Mercado B.S., Taylor S Turner B.S., Dionna M Kasper PhD

Dartmouth Geisel School of Medicine, Hanover, NH, USA

- Hematopoietic stem cells (HSCs) are made via an endothelial to hematopoietic transition (EHT)
- The mechanisms which regulate EHT remain elusive.
- . We identify the metalloprotease Adam10 as a candidate regulator of EHT

### Stem Cells/Organoids/In vitro models

#### M-50

### Modeling the 3D neurovascular unit with human-induced pluripotent stem cells Raphael Lis PhD

Weill Cornell Medicine, NYC, NY, USA

- Current model of the BBB are not relying on bona fide endothelial cells
- Overexpression of ETS transcription factor in neuroectordermal epithelial cells -> EC fate
- Reprogrammed ECs are more sensitive to neuro stimuli and adopt a BBB identity

# In vitro modeling of human vasculature using blood vessel organoids provides a robust platform for studying blood vessels in normal and pathological conditions

<u>Ishpreet Dhillon</u><sup>1</sup>, Sara Pippard<sup>1</sup>, Ravenska Wagey<sup>1</sup>, Reiner Wimmer<sup>2</sup>, Josef Penninger<sup>2,3</sup>, Ryan Conder<sup>1</sup>, Allen C. Eaves<sup>1,4</sup>, Sharon A. Louis<sup>1</sup>, Valentina Marchetti<sup>1</sup>

<sup>1</sup>STEMCELL Technologies Inc., Vancouver, Canada. <sup>2</sup>IMBA, Vienna, Austria. <sup>3</sup>Life Sciences Institute, UBC, Vancouver, Canada. <sup>4</sup>Terry Fox Laboratory, BC Cancer, Vancouver, Canada

- Human pluripotent stem cell derived blood vessel organoid (BVO) to model blood vasculature
- Exposure of BVO's to "diabetic" conditions induces basement membrane (BM) thickening
- Identified compounds that modulate signaling pathways involved in BM thickening in "diabetic" BVO's

#### M-52

### Generation of functional pluripotent cell-derived brain endothelial cells for in vitro modelling of the neurovascular unit and blood-brain barrier

<u>Tyler M Lu MS</u><sup>1,2</sup>, Ugur Akcan PhD<sup>3</sup>, Alexander Rhee BS<sup>1</sup>, Aomeng Cuit BS<sup>3</sup>, Sean Houghton MS<sup>1</sup>, Fuqiang Geng PhD<sup>1</sup>, Victor Martinez BS<sup>4</sup>, Jenny Xiang MD<sup>1</sup>, Irene Pedersen PhD<sup>4</sup>, Dritan Agalliu PhD<sup>3</sup>, Raphael Lis PhD<sup>1</sup> Weill Cornell Medicine, New York, NY, USA. <sup>2</sup>SUNY Downstate School of Graduate Studies, Brooklyn, NY, USA. <sup>3</sup>Columbia University Medical Center, New York, NY, USA. <sup>4</sup>Scintillon Institute, San Diego, CA, USA

- Previous models of in vitro BBB have generated epithelial barrier forming cells rather than ECs.
- Our reprogrammed ECs can adopt a vascular phenotype in 2D and 3D.
- Cellular identity is multifaceted and in vitro models must reflect that.

#### M-53

### Robust differentiation of human pluripotent stem cells into mural progenitor cells via transient activation of NKX3.1

*Umji Lee Ph.D*<sup>1,2</sup>, *Yonglin Zhu Ph.D*<sup>1,2</sup>, *Allen Chilun Luo MS*<sup>1,2</sup>, *Liyan Gong Ph.D*<sup>1,2</sup>, *Yunhye Kim Ph.D*<sup>1,2</sup>, *Ke Yuan Ph.D*<sup>1,2</sup>, *Juan Melero-Martin Ph.D*<sup>1,2</sup>

<sup>1</sup>Boston Children's Hospital, Boston, MA, USA. <sup>2</sup>Harvard Medical School, Boston, MA, USA

- Effective differentiation using transient activation of NKX3.1 to generate mural progenitors
- iMPCs mature into heterogenous mural cell subtypes
- Potential for modeling vascular diseases and therapeutic vascularization in-vivo

#### M-54

### ETV2 induces transdifferentiation of stem cell-derived pancreatic islet-lineage cells toward an endothelial fate

Daniel M Tremmel PhD, Juan Melero-Martin PhD

Boston Children's Hospital / Harvard Medical School, Boston, MA, USA

- Stem cell-derived islets lack vasculature, limiting their use to model islet function in vitro
- ETV2 rapidly and efficiently drives differentiation of stem cells toward an endothelial fate
- ETV2 rapidly and efficiently drives differentiation of stem cells toward an endothelial fate

# The vascularized islet-VMO platform provides a unique ex vivo tool for studying insulin secretion and the role of leukocyte trafficking in type 1 diabetes pathogenesis

<u>Benjamen T. ODonnell PhD</u>, Hugh Bender PhD, Celeste N. Sanchez B.S., Sima Tahmouresie B.S., Christopher C.W. Hughes PhD

University of California Irvine, Irvine, CA, USA

- We have developed an islet micro-organ model that integrates human islets with vasculature.
- Islets demonstrate superior cell viability and glucose stimulation compared to standard models.
- Perfusable vasculature supports perfusion, extravasation, and killing by activated T-Cells.

#### M-56

# Integrated transcriptomics maps a spatially defined adventitial progenitor niche in human blood vessel

<u>Neelima Thottappillil Ph.D</u><sup>1</sup>, Yiyun Wang Ph.D<sup>1</sup>, Mario Gomez-salazar Ph.D<sup>1</sup>, Robert Tower Ph.D<sup>2</sup>, Qizhi Qin Ph.D<sup>1</sup>, Mingxin Xu Ph.D<sup>1</sup>, Ray Cheng Ph.D<sup>1</sup>, Mary Archer B.S.<sup>1</sup>, Sashank Reddy M.D.<sup>1</sup>, Kristen Broderick M.D.<sup>1</sup>, Bruno Peault Ph.D.<sup>3</sup>, Aaron W James M.D. Ph.D.<sup>1</sup>

<sup>1</sup>Johns Hopkins University, Baltimore, MD, USA. <sup>2</sup>University of Texas Southwestern Medical Center, Dallas, USA. <sup>3</sup>University of California Los Angeles, Los Angeles, USA

- Human vascular adventitial stem cell niche participates in vessel homeostasis and is poorly defined.
- There exists a spatially organized mesenchymal progenitor hierarchy within the adventitial niche.
- Cells with high expression of CD201(PROCR) were primitive progenitors regulated by Wnt signaling

#### M-57

# Modeling early events in prosthetic valve endocarditis using the high-throughput organ-on-chip PREDICT96 platform with physiologically relevant fluid shear stress

<u>Logan R Rubio MS</u><sup>1</sup>, Kirsty A McFarland PhD<sup>1</sup>, Maghnus O'Seaghdha PhD<sup>2</sup>, Corin Williams PhD<sup>1</sup>

The Charles Stark Draper Laboratory, Cambridge, MA, USA. <sup>2</sup>Suffolk University, Boston, MA, USA

- Prosthetic valve endocarditis is a rare but serious condition that currently has no good models
- Factors that affect bacterial adhesion involve complex interactions at the valve material surface
- Here we present a microphysiological model that recapitulates early events in PVE

#### M-58

### Macrophages improve the vascularization of iPSC-derived kidney organoids in coculture

<u>Cory P Johnson PhD</u><sup>1</sup>, Yulia Kiian PhD<sup>2</sup>, Ekaterina Chernobrivaia B.S.<sup>2</sup>, Sergey Tkachuk PhD<sup>2</sup>, Hannah M Somers BS<sup>1</sup>, Hermann Haller MD<sup>1,2</sup>

<sup>1</sup>MDIBL, Bar Harbor, Maine, USA. <sup>2</sup>MHH, Hannover, Lower Saxony, Germany

- Kidney organoids do not recapitulate adult morphology and functionality in vitro
- Kidney organoids lack vascularity
- Macrophages improve kidney organoid development and vascularity in vitro

•

#### Vascular Malformations

#### M-59

#### A SOX18-mevalonate pathway axis drives vascular growth in infantile hemangioma

<u>Joyce Bischoff Ph.D.</u><sup>1</sup>, Annegret Holm M.D.<sup>2</sup>, Luke Borgelt B.S.<sup>2</sup>, Wei Heng Tan B.S.<sup>2</sup>, Jill Wylie-Sears M.A.<sup>2</sup>, Matthew S. Graus Ph.D.<sup>3</sup>, Liang Sun Ph.D.<sup>2</sup>, Mathias Francois Ph.D.<sup>3</sup>

<sup>1</sup>Boston Children's Hospital and Harvard Medical School, Boston, MA, USA. <sup>2</sup>Boston Children's Hospital, Boston, MA, USA. <sup>3</sup>Centenary Institute, Sydney, NSW, Australia

- Repurposing statins for infantile hemangioma
- SOX18-mevalonate pathway axis is central to endothelial differentiation in infantile hemangioma
- Non-beta blocker enantiomer of propranolol blocks vasculogenesis in infantile hemangioma

#### M-60

#### Recruited macrophages in GNAQ p.R183Q driven capillary malformations

<u>Sana Nasim PhD</u><sup>1</sup>, Colette Bichsel PhD<sup>1</sup>, Sanda Alexandrescu MD<sup>2</sup>, Stephen Dayneka BS<sup>2</sup>, Robert Mannix PhD<sup>1</sup>, Donald Ingber MD,PhD<sup>1,3</sup>, Anna Pinto MD,PhD<sup>1</sup>, Joyce Bischoff PhD<sup>1</sup>

<sup>1</sup>Boston Childrens Hospital, Boston, MA, USA. <sup>2</sup>Boston Childrens Hospital, boston, MA, USA. <sup>3</sup>Wyss Institute, Boston, MA, USA

- We found activated macrophages expressing MRC1, CD163, LYVE1, and CD68 in SWS brain vascular beds.
- Increased ICAM1 in SWS brain endothelium suggesting a mechanism for macrophage recruitment.
- In vitro showed increased leukocyte transmigration and flow-induced rolling/adhesion in EC-R183Q.

#### M-61

### Cure HHT research network: building the roadmap to cure HHT

<u>Cassi M Friday PhD</u>, Nolie Krock MPH, Nicole Schaefer, Marianne S Clancy MPA Cure HHT, Monkton, MD, USA

- Hereditary Hemorrhagic Telangiectasia
- Vascular Malformations
- Drug Discovery

#### M-62

# The dual effects of ginsenoside Re in tumor formation and melanogenesis through microphthalmia-associated transcription factor downregulation

<u>Su Jung Hwang Ph.D</u>, Hye Jung Bang Bachelor, Hyo-Jong Lee Ph.D Sungkyunkwan university, Suwon, Gyeonggi-do, Korea, Republic of

- The ginsenoside Re reduces melanin contents in zebrafish embryos and B16F10 melanomas.
- Re decreases the expression of MITF and its target genes.
- Re showed inhibitory effects on skin melanoma growth and induced tumor vascular normalization.

#### M-63

## Development of a translational rat model of Glenn circulation and pulmonary arteriovenous malformations

Tina Wan PhD, Carol Mattern RDCS, Monica Merbach MS, <u>Andrew D Spearman MD</u> Medical College of Wisconsin, Milwaukee, Wisconsin, USA

- A surgical rat model of Glenn circulation phenocopies clinical Glenn circulation.
- Pathologic intrapulmonary shunting starts within 4 weeks in Glenn circulation.
- Non-invasive echocardiography can accurately and safely monitor post-surgical blood flow in rats.

### Generation and characterization of iPSC derived TIE2L914F endothelial cells for study of vascular anomalies

Bojana Lazovic<sup>1,2,3</sup>, Tuan Nguyen<sup>4</sup>, Franziska Kohl<sup>3</sup>, Mohammadhassan Ansarizadeh<sup>2</sup>, Miguel Carracedo Ortiz<sup>5</sup>, John Wiseman<sup>3</sup>, Prateek Singh<sup>4</sup>, Bilada Bilican<sup>3</sup>, Pratik Saxena<sup>1</sup>, Xuechong Hong<sup>1</sup>, Lauri Eklund<sup>2</sup>, Ryan Hicks<sup>1,6</sup>
<sup>1</sup>BioPharmaceuticals R&D Cell Therapy, Research and Early Development, Cardiovascular, Renal and Metabolism (CVRM), BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden. <sup>2</sup>Oulu Center for Cell-Matrix Research, Biocenter Oulu and Faculty of Biochemistry and Molecular Medicine, University of Oulu, Oulu, Finland. <sup>3</sup>Translational Genomics, Discovery Sciences, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden. <sup>4</sup>Finnadvance Ltd, Oulu, Finland. <sup>5</sup>Research and Early Development Cardiovascular, Renal and Metabolism, BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden. <sup>6</sup>School of Cardiovascular and Metabolic Medicine and Sciences, King's College London, London, United Kingdom

- iPSC-derived locus targeted lines allows for studying mutations at an endogenous expression level.
- iPS-derived Tie2 LF ECs showed migratory and incomplete tube formation phenotypes.
- iPSC-derived models can be used for studies of EC related diseases and/or drug screening.

#### M-65

#### Modeling and pathogenesis of KRAS and RIT1 lymphovenous disease in zebrafish

<u>Scott `Paulissen PhD</u>, Dhyanam Shukla BS, Christopher Marshall BS, Benjamin Sempowski BS, Kristina Woodis BS, Sarah Sheppard MD/PhD

NIH, Bethesda, MD, USA

- Modeling human lymphatic anomalies in zebrafish
- Screening for drug effectiveness in patient genetic variants in model organisms
- High-resolution characterizations of disease onset and progression using imaging and NGS techniques

#### M-66

# Therapeutically targeting proteostasis defects downstream of PI3K hyperactivation in venous and lymphatic malformations

Noa Franklin-Shapiro  $BS^1$ , Ema Iaconetti  $MD^1$ , Joseph McCarron  $BS^1$ , Samantha Kaplan  $BS^1$ , Meghan Perez  $BS^1$ , Daniella Rogerson  $MD^1$ , Averil I Clapp  $BS^1$ , Hai Li Ph $D^2$ , Santiago Barbar  $BS^1$ , Charles Karan Ph $D^3$ , June K Wu  $MD^1$ , Carrie J Shawber Ph $D^1$ 

<sup>1</sup>Columbia University, New York, NY, USA. <sup>2</sup>Columbia University, New York, NY, USA. <sup>3</sup>Columbia University University, New York, NY, USA

- PI3K hyperactivation promotes overexpression and mislocalization of CD31 and VE-CADHERIN.
- VMs and LMs have proteostasis defects that can be therapeutically targeted.
- Proteasome inhibitors preferentially induce cell death of ECs with PI3K hyperactivation.

#### M-67

### Recapitulation of the vascular phenotypes of diabetic retinopathy by endotheliumspecific activation of H-Ras independent of diabetes

Qingfen Li Ph.D., Kevin Pumiglia Ph.D.

Albany Medical College, Albany, NY, USA

- Explore the role of endothelial-activated HRas in the pathologic development of retinal vasculature.
- HRAS activation leads to retinal vascular pathological development similar to diabetic retinopathy.
- Rapamycin and the ROS scavenger N-acetyl-cysteine treatment markedly reduced retinal pathology.

#### **TUESDAY POSTERS SESSIONS**

### Cardiovascular Cell Biology I

#### T-01

### Dissecting pericyte-endothelial relationships during brain angiogenesis

Cynthia U Adjekukor<sup>1,2</sup>, Sarah J Childs<sup>1,2</sup>

<sup>1</sup>Department of Biochemistry and Molecular Biology, University of Calgary, Calgary, Alberta, Canada. <sup>2</sup>Alberta Children's Hospital Research Institute, Calgary, Alberta, Canada

- Endothelial cell signals (VEGFR, Wnt) are necessary for recruiting the correct number of pericytes.
- Recruited pericytes develop secondary processes to support the matured blood vessel.
- Brain angiogenesis and pericyte recruitment are necessary to support cognitive development.

#### T-02

#### Role of the retinoic acid in placental vascularization

<u>Aleksandra Cwiek MS</u>, Karen Hirschi PhD University of Virginia, Charlottesville, VA, USA

- Placental Vascularization
- Arterial-venous specification
- Placental insufficiency

#### T-03

#### Eph-ephrin signaling couples endothelial cell sorting and arterial specification

Jonas Stewen<sup>1</sup>, Kai Kruse<sup>1</sup>, Anca T. Godoi-Filip<sup>1</sup>, Hyun-Woo Jeong<sup>1</sup>, Susanne Adams<sup>1</sup>, Frank Berkenfeld<sup>1</sup>, Martin Stehling<sup>1</sup>, Kristy Red-Horse<sup>2</sup>, Ralf H. Adams<sup>1</sup>, <u>Mara E. Pitulescu</u><sup>1</sup>

<sup>1</sup>Max Planck Institute for Molecular Biomedicine, Muenster, Germany. <sup>2</sup>Stanford University, Stanford, CA, USA

- EphB4-ephrin-B2 balance is critical for arterial specification and arteriovenous patterning
- EphB4 and ephrin-B2 regulate arterial specification directly through VEGF and Notch signaling
- EphB4-dependent EC dynamics regulation under arterial flow requires Dach1

#### T-04

### The protective role of endothelial Ripk3 during ischemic retinopathy

Xiang Ma Ph.D., Christopher M Schafer, Courtney T Griffin Ph.D.

Oklahoma Medical Research Foundation, Oklahoma City, OK, USA

- We identified a potent anti-angiogenic protein by studying key cell death pathway components.
- RIPK3 is a multifunctional protein that is tightly regulated in pathophysiological conditions.
- We leveraged a scRNAseq dataset and validated it with endothelial-specific gene modification.

#### T-05

### Macrophage-smooth muscle cell communication in neointima initiation

 $\underline{\mathit{Mark}\ \mathit{C}\ \mathit{Renton\ PhD}^{1}}$ ,  $\mathit{Meghan\ W}\ \mathit{Sedovy\ BS}^{1,2}$ ,  $\mathit{Xinyan\ Leng\ PhD}^{1}$ ,  $\mathit{Kailynn\ Robert}^{1,3}$ ,  $\mathit{Melissa\ Leaf\ DVM}^{1,4}$ ,  $\mathit{Farwah\ Iqbal\ PhD}^{1,4}$ ,  $\mathit{Scott\ R}\ \mathit{Johnstone\ PhD}^{1,3,4}}$ 

<sup>1</sup>1. The Fralin Biomedical Research Institute at Virginia Tech Carilion, Center for Vascular and Heart Research, Roanoke, VA, USA. <sup>2</sup>2. Translational Biology, Medicine, and Health Graduate Program, Virginia Tech, Blacksburg, VA, USA. <sup>3</sup>3. Department of Biological Sciences, Virginia Tech, Blacksburg, VA, USA. <sup>4</sup>4. Virginia Tech Carilion School of Medicine, Roanoke, VA, USA

Macrophage accumulation occurs early in vascular injury and is associated with neointimal formation.

- Macrophages and smooth muscle cells communicate directly through connexin 43 gap junctions.
- Macrophage signaling may initiate Cx43-mediated smooth muscle cell proliferation.

#### T-06

# Hyperhomocysteinemia augments smooth muscle cell phenotypic modulation and atherosclerosis through heat shock factor 1 (HSF1) activation and increased cholesterol biosynthesis

<u>Abhijnan Chattopadhyay PhD</u>, Suravi Majumder PhD, Callie S Kwartler PhD, Dianna M Milewicz MD, PhD The University of Texas Health Science Center at Houston, Houston, TX, USA

- Homocysteine activates HSF1→HMGCR→PERK signaling and phenotypic modulation in smooth muscle cells.
- Blocking HSF1, HMGCR, or PERK reverses homocysteine-induced phenotypic modulation of SMCs.
- SMC-specific Perk deletion and pravastatin treatment reduce plaques in hyperhomocysteinemic mice.

#### T-07

#### SH2 domain protein E (SHE) and ABL signaling regulate blood vessel size

<u>SURENDRA K. ANAND Ph.D.</u><sup>1</sup>, Jennifer A. Schumacher Ph.D.<sup>2,3,4</sup>, Zoë A. Wright<sup>2</sup>, Diandra R. Florat MS<sup>1</sup>, Manish Dasyani Ph.D.<sup>2,1</sup>, Laurita Klimkaite<sup>2</sup>, Suman Gurung Ph.D.<sup>1</sup>, Gretchen M. Koller<sup>5</sup>, Kalia N. Aguera<sup>5</sup>, George E. Davis Ph.D.<sup>5</sup>, Saulius Sumanas Ph.D.<sup>2,3,1</sup>

<sup>1</sup>University of South Florida, Department of Pathology and Cell Biology, USF Health Heart Institute, Tampa, FL, USA. <sup>2</sup>Cincinnati Children's Hospital Medical Center, Division of Developmental Biology, Cincinnati, OH, USA. <sup>3</sup>University of Cincinnati College of Medicine, Department of Pediatrics, Cincinnati, OH, USA. <sup>4</sup>Department of Biological Sciences, Miami University, Hamilton, OH, USA. <sup>5</sup>University of South Florida, Department of Molecular Pharmacology and Physiology, Tampa, FL, USA

- Loss of She function results in enlarged vascular lumen size and defects in blood flow.
- She acts as a negative regulator of Abl signaling.
- She regulates vascular lumen size by promoting claudin 5a (cldn5a) expression.

#### T-08

### Androgen and mineralocorticoid receptor signaling contribute to pubertal vascular rupture in Vascular Ehlers-Danlos Syndrome (VEDS) mice

<u>Emily Juzwiak BS</u><sup>1,2</sup>, Caitlin Bowen MD, Ph.D<sup>1,2</sup>, Nicole Anderson Ph.D<sup>1,2</sup>, Anthony Zeng BS, MS<sup>1,2</sup>, Harry C Dietz  $MD^{3,2}$ 

<sup>1</sup>Department of Genetic Medicine, Johns Hopkins University, Baltimore, Maryland, USA. <sup>2</sup>Howard Hughes Medical Institute, Chevy Chase, Maryland, USA. <sup>3</sup>Department of Genetic Medicine, Johns Hopkins University, Baltimore, Maryland, USA

- In VEDS, males experience more pubertal arterial rupture than females.
- Blocking the androgen and mineralocorticoid receptors greatly improve survival in VEDS mice.
- Single nucleus RNAseq on VEDS aortas reveal cellular heterogeneity & crosstalk.

### **Lymphatic Biology and Development**

#### T-09

### Engineering biomaterials with stem cells for therapeutic lymphangiogenesis

Donny Hanjaya-Putra Ph.D.

University of Notre Dame, Notre Dame, IN, USA

• Robust differentiation of human pluripotent stem cells into lymphatic endothelial cells.

- Hyaluronic acid hydrogels to control lymphatic vascular morphogenesis.
- Engineered lymphatic vessels can integrate and function in vivo.

#### T-10

# Interleukin-19 promotes lymphatic permeability and lymphangiogenesis though diverse mechanisms

Amanda M Peluzzo BS, Michael V Autieri PhD, Sheri Kelemen

Temple University LKSOM, Philadelphia, PA, USA

- Cytokine Regulation of Lymphatic Permeability
- Cytokine Regulation of Lymphangiogenesis
- Transcriptional Regulation and Lymphatic Function

#### T-11

#### Chemokine signaling regulates early lymphatic development

Meriem Bkhache, Long Do, <u>Xiaolei Liu</u>

Temple University, Philadelphia, USA

- Lymphatic chemokine signaling Cxcr4/cxcl12 regulates early lymphatic development
- Cxcl12/Cxcr4 is required for vegfc mediated lymphangiogenesis
- Cxcr4 activity is required for sustain lymphatic endothelial cell surface VEGFR3 abundance

#### T-12

# Impact of Goreisan on Human Dermal Lymphatic Endothelial protein/mRNA expression

<u>Celene Totry</u>, Laurelis Santiago M.S., Jerome W Breslin PhD USF, Tampa, FL, USA

- Goreisan treatment alters the HDLEC proteome.
- Mitochondrial function appears to be a target of Goreisan in HDLEC.
- Goreisan stimulates MMP3 mRNA expression in HDLEC.

#### T-13

### $\beta$ -arrestin1/2 is essential for embryonic lymphatic vessel development

<u>Yanna Tian</u>, Danica D Dy, Bryan Michael Kistner, Elizabeth S Douglas, Kathleen M Caron University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

- Characterization of the effect of  $\beta$ -arrestin1/2 deficiency in lymphatic development.
- In vivo study to investigate the role of β-arrestin1/2 in the mouse lymphangiogenesis
- Assessment of the consequences of lymphatic specific deletion of β-arrestin1/2

#### T-14

# Elucidation of the role of ACKR3 in the lymphangiogenic response after ischemic heart injury

<u>Laszlo Balint PhD</u><sup>1</sup>, Hua Zhang MD<sup>1</sup>, Amir Aghajanian MD, PhD<sup>1,2</sup>, Shubhangi H. Patel<sup>1</sup>, Kathleen M. Caron PhD<sup>1</sup>

<sup>1</sup>Department of Cell Biology and Physiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.

<sup>2</sup>Department of Medicine, Division of Cardiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

- Characterization of the mechanisms promoting lymphangiogenic response after ischemic cardiac injury.
- Spatial characterization of ACKR3 activation after ischemic heart injury.

Assessment of the consequences of lymphatic deletion of ACKR3 in under basal and injury conditions.

#### T-15

#### Investigating the role of the microRNA miR-223 in lymphatic development

Carolyn L Winston B.A., Elizabeth Jones B.S., Dionna M Kasper Ph.D.

The Geisel School of Medicine at Dartmouth, Hanover, NH, USA

- The function of miR-223 in early vascular progenitors and lymphatic endothelial cells is unknown.
- Zebrafish mutants lacking mature miR-223 show defects in forming early lymphatic structures.
- Etv2 and Prox1a, essential endothelial factors, are predicted to contain miR-223 binding sites.

#### T-16

### Exploring lymphatic system dynamics in edema formation and resolution: Lessons from zebrafish

<u>Olamide Olayinka</u>, HyunMin Jung University of Illinois, Chicago, IL, USA

- Developed a new zebrafish edema model by inducing osmotic stress
- Osmotic edema-induced lymphangiogenesis
- Lymphatic clearance of edema fluid

#### Mechanical Forces and the Vasculature

#### T-18

#### Novel roles for centriolar protein WDR90 in endothelial cells and cardiac tissue

Sarah Colijn PhD, Sheng-Chih Jin PhD, Amber Stratman PhD

Washington University, St. Louis, MO, USA

- De novo mutations in centriolar protein WDR90 have been identified as drivers of CHD
- Adult zebrafish wdr90 mutants display partial lethality, stenosis, and small hearts
- Endothelial WDR90 co-localizes with VE-cadherin and the tips of microtubules

#### T-19

### Pathophysiological hemodynamic changes in choroidal microvasculature

Joseph J Olivieri B.S., Bradley Gelfand Ph.D.

University of Virginia, Charlottesville, VA, USA

- Assess the biomechanical environment of the choroid for its potential to influence AMD pathology
- Shear-responsive TM expression in the choroidal microvasculature may yield mechanistic insights
- Linking microvascular dysfunction and hallmark AMD features inspires hemodynamic-based therapeutics

#### T-20

### Hormone-free medium impairs pulmonary artery endothelial cell response to shear stress

<u>Cassandra K. Conway-O'Donnell Ph.D.</u>, Christopher J. Hatch B.S., Robel K. Bekele B.S., Christopher C.W. Hughes Ph.D., Naomi C. Chesler Ph.D.

University of California, Irvine, Irvine, CA, USA

- The absence of steroid hormones disrupts pulmonary artery endothelial cell mechanotransduction.
- 1nM 17β-estradiol does not improve pulmonary artery endothelial cell adaptation to flow.
- The absence of steroid hormones induced stress and upregulated pro-inflammatory cytokines.

### **Emerging Topics in Microcirculation**

#### T-22

# A novel approach to restore endothelial glycocalyx in sepsis using liposomal nanocarriers of preassembled glycocalyx, followed by quantitative analysis of endothelial glycocalyx with sidestream dark field image

<u>Shinya Ishiko M.D., Ph.D</u>, Ghada Ben Rahoma M.D., Ph.D, Sharath Kandhi M.D., Ph.D, An Huang M.D., Ph.D, Dong Sun M.D., Ph.D

New York Medical College, Valhalla, NY, USA

- Novel therapy using liposome to deliver preassembled glycocalyx to endothelial cells was introduced.
- Significantly impaired flow-induced dilation in septic mice was fully restored in response to LNPG.
- Chronic changes of EG and effect of LNPG can be monitored by cranial window approach.

#### T-23

# Oxidation of low-density lipoprotein (oxLDL) by hemoglobin causes lung microvascular endothelial barrier dysfunction via lectin-like oxLDL receptor-1 (LOX-1)

<u>Jamie E Meegan PhD</u>, Lorraine B Ware MD, Julie A Bastarache MD

Vanderbilt University Medical Center, Nashville, TN, USA

- Cell-free hemoglobin (Hb) is a mechanistic driver of microvascular endothelial injury.
- Oxidation of LDL by hemoglobin (Hb-oxLDL) worsens lung microvascular barrier dysfunction.
- Hb-oxLDL disrupts lung microvascular endothelium through lectin-like oxLDL receptor-1 (LOX-1).

#### T-24

# Al-enabled vascularized biological systems: Evaluation of oxygen transport from microscopic images

Jonathan Tronolone<sup>1</sup>, <u>Abhishek Jain PhD</u><sup>2,3</sup>

<sup>1</sup>Texas A&M Universityy, College Station, TX, USA. <sup>2</sup>Texas A&M University, College Station, TX, USA. <sup>3</sup>Houston Methodist Research Institute, Houston, TX, USA

- Machine learning enabled vascularized microphysiological systems
- Oxygen or species transport can be predicted
- Standardized analysis of microphysiological systems of the vasculature

#### T-25

### Perivascular adipose tissue as a mediator for anticontractile activity in the coronary microcirculation

Sharanee P Sytha<sup>1</sup>, Trevor S Self<sup>1</sup>, Jeff F Bray<sup>1</sup>, Cristine L Heaps<sup>1,2</sup>

<sup>1</sup>Texas A&M University, College Station, TX, USA. <sup>2</sup>Michael E. DeBakey Institute for Comparative Cardiovascular Science & Biomedical Devices, College Station, TX, USA

- Coronary arterioles with perivascular adipose tissue demonstrate enhanced anticontractile activity
- K+ channel activation contributes to perivascular adipose tissue-mediated anticontractile activity
- Perivascular adipose tissue mediates anticontractile activity in the swine coronary microcirculation

# Predicting 3D blood flow and hematocrit distributions in microvascular networks using machine learning techniques

Saman Ebrahimi PhD, <u>Prosenjit Baqchi PhD</u> Rutgers University, Piscataway, NJ, USA

- Machine learning and artificial intelligence (AI) application in microcirculation
- Coupling high-fidelity data and Machine learning for microvascular hemodynamics
- Blood flow, hematocrit and wall-shear stress prediction in microvascular networks using AI

#### T-27

# Heparan sulfate modulation affects breast cancer cell adhesion and transmigration across in vitro blood-brain barrier (BBB)

Yunfei Li MS, Bingmei Fu Ph.D

The City College of New York, New York, NY, USA

- Heparan sulfate (HS) of endothelial cells is disrupted by VEGF which enhances HS of tumor cells
- Disrupted/enhanced HS of endothelial/tumor cells increases tumor cell adhesion/transmigration
- Endothelial HS enhancing agents disrupt HS of tumor cells and reduce their adhesion/transmigration

#### T-28

### Neuropilin 1 (NRP1) acts as a mediator of SEMA3A chemorepulsive cues to guide vessel sprouting

Marco Spreafico<sup>1</sup>, Elena Guzzolino<sup>1</sup>, Francesca Fanuele<sup>1</sup>, Carlotta Tacconi<sup>1</sup>, Valeria Catroppa<sup>1</sup>, Gaia Gestri<sup>2</sup>, Laura Denti<sup>3</sup>, Caroline Pellet-Many<sup>4</sup>, Christiana Ruhrberg<sup>3</sup>, <u>Alessandro Fantin</u><sup>1</sup>

<sup>1</sup>University of Milan, Department of Biosciences, Milan, Italy. <sup>2</sup>UCL Department of Cell and Developmental Biology, University College London, London, United Kingdom. <sup>3</sup>UCL Institute of Ophthalmology, University College London, London, United Kingdom. <sup>4</sup>Department of Comparative Biomedical Sciences, Royal Veterinary College, London, United Kingdom

- Human endothelial cells are repelled by SEMA3A in a NRP1-dependent manner
- Zebrafish Nrp1a and Nrp1b cooperate to prevent ectopic ISV sprouting and vascular overgrowth
- Nrp1 and Sema3a cooperate to regulate ISV sprouting without affecting endothelial proliferation

#### T-30

# Endothelial ADAM10 utilization defines a molecular pathway of vascular injury in bacterial sepsis

<u>Danielle N Alfano MD</u>, Mark J Miller PhD, Juliane Bubeck Wardenburg MD, PhD Washington University School of Medicine, St Louis, MO, USA

- Lack of ADAM10 on the endothelium alone is sufficient to improve S. aureus mortality in mice.
- Endothelial injury induced by Hla-ADAM10 complex incites formation of microvascular thrombi.
- ADAM10 differentiates molecular pathways of disease among common human sepsis pathogens.

#### Atherosclerosis I

#### T-31

A new role of ATP-binding cassette B8 in preventing endothelial dysfunction and atherosclerosis

Ahmed bey CHAKER Ph.D, Nicki Dyson Ph.D, Rayomand Khambata PhD, Amrita Ahluwaila Professor, <u>Claudio</u> Raimondi Ph.D

William Harvey Research Institute, Barts and the London School of Medicine and Dentistry Queen Mary University of London, London, UK, London, United Kingdom

- ABCB8 is a key regulator of vascular health
- ABCB8 disruption in endothelial cells induces inflammation and plaques formation
- ABCB8 suppresses TGF-beta pathway activation

#### T-32

# Identifying the novel role of IncRNA-SPANXA2-OT1 in macrophage chemotaxis through a systems-based target discovery approach

<u>Prabhash K Jha Ph.D.</u><sup>1</sup>, Lucas Yuji Umesaki Itto<sup>1</sup>, Aatira Vijay Ph.D.<sup>2</sup>, Adrien Lupieri Ph.D.<sup>1</sup>, Sarvesh Chelvanambi<sup>1</sup>, Yuto Nakamura<sup>1</sup>, Miguel C Barbeiro<sup>1</sup>, Thanh-Dat Le<sup>1</sup>, Taku Kasai<sup>1</sup>, Dakota Becker-Greene<sup>1</sup>, Abhijeet R Sonawane<sup>1</sup>, Sasha A Singh<sup>1</sup>, Elena Aikawa<sup>1</sup>, Shizuka Uchida<sup>3</sup>, Masanori Aikawa<sup>1</sup>

<sup>1</sup>Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA. <sup>2</sup>Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA. <sup>3</sup>Center for RNA Medicine, Department of Clinical Medicine, Aalborg University, Copenhagen, Denmark

- IncRNA SPANXA2-OT1 plays a key role in macrophage chemotaxis in CAD
- Co-expression network analysis for functional characterization of long noncoding RNAs
- IncRNAs can interact with DNA, RNA, miRNA, and proteins, making them potential therapeutic targets.

#### T-33

### Endothelial deletion of Nck1 reduces atherosclerosis in ApoE-/- mice

<u>Cyrine Ben Dhaou PhD</u>, Gerardo Ali Cruz Marquez, Mabruka Alfaidi PhD, Elizabeth Cockerham, Matthew Scott PhD, Brenna Pearson, Arif Yurdagul Jr PhD, Wayne Orr PhD LSU Health Shreveport, Shreveport, LA, USA

- Endothelial-specific Nck1 deletion significantly reduced atherosclerotic plaque formation.
- Activating Transcription Factor 3 ATF3 was selected as a Nck1-selective binding partner
- Nck1 inhibition did not affect angiogenesis or limb perfusion.

#### T-34

# Effects of activity levels on aortic calcification in hyperlipidemic mice as measured by MicroPET/MicroCT

<u>Andy Hon</u>, Jeffery J. Hsu MD, PhD, Angelica Zambrano, Yuxuan Xia, Mimi Lu BS, David Echeverri BS, Sophia Kalanski, Linda L. Demer MD, PhD, Yin Tintut PhD, Soban Umar Md,PhD UCLA, Los Angeles, CA, USA

- Aortic calcium content increased significantly in both control and treadmill groups.
- Low-speed regimen reduced aortic mineral surface area and vertebral bone density in female mice.
- Low-speed regimen blunted the Western diet-induced LV hypertrophy observed in controls in male mice.

#### T-35

# The role of EphA2 in vascular smooth muscle cell proliferation, migration, and mitogenic signaling

<u>Matthew Scott Ph.D.</u>, Alexandra Finney Ph.D., Shantel Vital, Brenna Pearson-Gallion, Alika Shum, Wayne Orr LSU Health Shreveport, Shreveport, LA, USA

- The EphA2 receptor is simultaneously necessary for and antagonistic to VSMC mitogenic signaling.
- EphA2 expression correlates significantly with SMC phenotypic modulation.

EphA2 expression is sufficient to downregulate expression of SMC contractile genes.

#### T-36

# Knockdown of AdipoR2 compromises adiponectin's anti-inflammatory actions by mainly promoting a pro-inflammatory chemokine and cytokine secretory profile in THP-1 macrophages

<u>Ioanna Gianopoulos MSc</u>, Stella S. Daskalopoulou MD, MSc, DIC, PhD
Research Institute of the McGill University Health Centre (RI-MUHC), McGill University, Montreal, Quebec, Canada

- Adiponectin increases cell surface levels of AdipoR1/R2 despite AdipoR intracellular knockdown
- Loss of AdipoR2 versus AdipoR1 leads to a pro-inflammatory profile in response to adiponectin
- Selectively targeting AdipoR2 may promote plaque stabilization by reducing inflammatory mediators

### **Vascular Function in Health Disparities**

#### T-37

# Looking further into the significance of perfusion asymmetries in the lower limb of healthy individuals

Margarida Florindo MSc<sup>1,2</sup>, Joao Gregorio MSc, PhD<sup>1</sup>, <u>Luis M Rodrigues MSc, PhD</u><sup>1</sup>

<sup>1</sup>CBIOS – Universidade Lusofona's Research Center for Biosciences & Health Technologies, Lisboa, Lisboa, Portugal. <sup>2</sup>ESSCVP—Department of Physiotherapy, The Portuguese Red Cross Health School, Lisboa, Portugal

- perfusion variations between limbs have been commonly found in healthy individuals
- to study potential relations between these limb perfusion variations and hemodynamics
- perfusion asymmetries might accelerate peripheral vascular disease if other determinants are present

#### T-38

# Isolated human mesenteric arteries from organ donors as a model to determine arterial reactivity

<u>Laura Hurtado Osorio Biomedical Engineering</u>, Patricia Zamora Diaz Biomedical Engineering, Charissa Bloom BS, Jenna McQueen, Isabela Zimmermann Rollin, Vishnu Iyer, Chris Katnik, Jerome W Breslin PhD University of South Florida, Tampa, Florida, USA

- Arteries from donated human organs remain viable and are suitable for studies of function
- Age, sex, Body Mass Index, hypertension, and diabetes did not impact arterial responses to ET-1
- Sex, Body Mass Index, hypertension, and diabetes altered responses to phenylephrine and U46619

#### T-39

### Altered impact of sigma receptor agonists on adrenergic-induced contraction of human mesenteric arteries from donors with a history of heavy alcohol use

<u>Patricia Zamora Diaz</u>, Laura Hurtado Osorio, Jenna F. McQueen, Charissa Bloom, Isabela Zimmermann Rollin, Vishnu V. Iyer, Jerome W. Breslin

University of South Florida, Tampa, FL, USA

- The sigma receptor agonist PRE-084 attenuates phenylephrine-induced contraction of human arteries.
- Sigma receptor antagonists shift the phenylephrine concentration-response upward in human arteries
- Heavy alcohol use reduces the impact of sigma receptor agonists or antagonists on human arteries.

#### **Vascular Anomalies**

#### T-40

# Ips-derived endothelial cells facilitate modeling of vascular malformations and enable drug testing

<u>Franziska Kohl</u><sup>1,2</sup>, Mikel Roscales<sup>1,2</sup>, Bojana Lazovic<sup>3,2</sup>, Luc Krimpenfort<sup>1</sup>, Xuechong Hong PhD<sup>2</sup>, Ryan Hicks PhD<sup>2</sup>, Lars Jakobsson PhD<sup>1</sup>, John W Wiseman PhD<sup>2</sup>

<sup>1</sup>Karolinska Institutet, Stockholm, Sweden. <sup>2</sup>AstraZeneca, Gothenburg, Sweden. <sup>3</sup>University of Oulu, Oulu, Finland

- Create cell models by knocking out ENG or ACVLR1 in iPS cells to mimic HHT
- Differentiate iPS cells to endothelial cells and characterize these cell models
- Screen a selection of drugs to identify compounds that affect KO phenotype

#### T-41

# Expression of mutant KRAS in endothelial cells leads to hypertranscription and altered ribosome biogenesis

Negar Khosraviani<sup>1,2</sup>, Ruilin Wu<sup>1,2</sup>, Emilie Boudreau<sup>2</sup>, Joshua D. Wythe<sup>3</sup>, Jason E. Fish<sup>1,2</sup>

<sup>1</sup>Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada. <sup>2</sup>Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada. <sup>3</sup>Cardiovascular Research Institute, Baylor College of Medicine, Houston, TX, USA

- Upregulation of ribosomal RNA synthesis in KRAS-G12V ECs.
- ECs with KRAS-G12V mutation undergo hypertranscription.
- Increased protein synthesis in KRAS-G12V ECs.

#### T-42

### FLVCR2 transports choline at the Blood brain barrier

<u>Dibyanti Mukherjee PhD</u><sup>1</sup>, Rosemary Cater PhD<sup>2</sup>, Ji Hyun Katie Koo B.S<sup>1</sup>, Filippo Mancia PhD<sup>2</sup>, Thomas Arnold MD<sup>1</sup> <sup>1</sup>University of California, San Francisco, San Francisco, California, USA. <sup>2</sup>Columbia University Irving Medical Center, New York, New York, USA

- Identifying Flvcr2 as a novel choline transporter at Blood Brain Barrier
- Loss of Flvcr2 causes vascular defects and hydrocephalus
- Choline transport across the blood brain barrier is required for neuro vascular development

#### T-43

### Collagen Col22a1 functions together with Col5a1 to maintain vascular stability in zebrafish trunk

<u>Vishal Y Mardhekar M. Pharm</u>, Suman Gurung PhD, Kaitlin Ferrari MS, Saulius Sumanas PhD USF Morsani College of Medicine, Tampa, Florida, USA

- Role of Col22a1 in Zebrafish vascular stability.
- Collagen subtypes associated with vascular aneurysms
- Studying vascular abnormalities

#### T-44

# Ras isoform specificity in endothelial cell function and their role in dysfunctional morphogenesis

<u>Samantha King</u>, Kevin Pumiglia PhD Albany Medical College, Albany, NY, USA

- Ras isoforms (HRas and KRas) have distinct endothelial signaling and functional outputs.
- KRas protein expression levels are diminished relative to HRas through codon bias.
- Optimizing codons of KRas does not account for differences in AKT signaling or proliferation.

### **Endothelium in Health and Disease I**

#### T-46

# Endothelial PHD2 deficency promotes angiotensin-II-induced arterial stiffness and coronary microvascular dysfunction

Heng Zeng<sup>1</sup>, Jian-Xiong chen<sup>2</sup>

<sup>1</sup>University of Mississippi Medical Center, Jackson, MS, USA. <sup>2</sup>university of Mississippi Medical Center, Jackson, MS, USA

- Prolyl hydroxylase protein-2
- endothelial specific knockout mouse
- coronary microvascular dysfunction

#### T-47

#### Orchestration of endothelial growth and osteogenesis

<u>yang yang</u>, yan zhao, Xiuju Wu, Li Zhang, Xinjiang Cai, Kristina Bostrom, Yucheng Yao UCLA, Los Angeles, california, USA

- Endothelial cells and osteogenic cells alternately showed the potential mutual regulation in femur.
- In skull, endothelial and osteogenic cells followed similar patterns without alternation
- The orchestration of endothelial and bone cells is different between long and flat bones formation.

#### T-48

### Regulating the cell shift of endothelial cell-like myofibroblasts in pulmonary fibrosis

Xiuju Wu M.D., Ph.D.<sup>1</sup>, Daoqin Zhang Ph.D.<sup>2</sup>, Li Zhang Ph.D.<sup>1</sup>, Xinjiang Cai M.D., Ph.D.<sup>1</sup>, Yan Zhao Ph.D.<sup>1</sup>, John A. Belperio M.D.<sup>3</sup>, Kristina I. Boström M.D., Ph.D.<sup>1</sup>, Yucheng Yao M.D., Ph.D.<sup>1</sup>

<sup>1</sup>Division of Cardiology, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA. <sup>2</sup>Department of Pediatrics, Stanford University, Stanford, CA, USA. <sup>3</sup>Division of Pulmonary and Critical Care Medicine, Clinical Immunology, and Allergy, David Geffen School of Medicine, UCLA, Los Angeles, CA, USA

- Identify a previously unknown cell population that contributes myofibroblasts to pulmonary fibrosis.
- A small molecule is discovered to redirect myofibroblasts and reduces pulmonary fibrosis.
- COVID-19 infection drives endothelial-lineage cells towards myofibroblasts in pulmonary fibrosis.

#### T-49

# Endothelial reprogramming and enhanced TGF- $\beta$ signaling persist after completion of chemotherapy

<u>Kass Sjostrom BS</u>, Shixin Tao PhD, Nataliya Kibiryeva MD, Melissa Cobb MS, Eugene Konorev MD, PhD Kansas City University, Kansas City, MO, USA

- Doxorubicin treatment causes long-term changes in endothelial cell expression
- Long-term endothelial cell changes are likely mediated by the canonical TGF-β pathway.
- Suppressing the canonical TGF-β pathway may alleviate cardiovascular damage caused by doxorubicin.

### GSK3β inhibition reduced vascular calcification of Ins2<sup>Akita/+</sup> and Apoe<sup>-/-</sup> mice

<u>Yan Zhao PhD</u>, Xinjiang Cai MD, PhD, Xiuju Wu MD, PhD, Yang Yang MD, PhD, Li Zhang PhD, Kristina Bostrom MD, PhD, Yucheng Yao MD, PhD

David Geffen School of Medicine at UCLA, Los Angeles, California, USA

- GSK3b inhibition reduces vascular calcification in the models of diabetes and atherosclerosis.
- GSK3b inhibition redirects endothelial cell (EC)-derived osteoblast-like cells back to EC lineage.
- GSK3b inhibition induced b-catenin and reduced SMAD1 in diabetic arteries and atherosclerosis.

#### T-51

# The RNA m6A demethylase, FTO, regulates vascular remodeling in the pathogenesis of pulmonary arterial hypertension

Jingbo Dai, Northwestern University, Chicago, IL, USA

- FTO expression level is markedly elevated in the endothelial cells of idiopathic PAH patients.
- The Tie2-Cre-Fto mice exhibited inhibited PH under hypoxia treatment.
- MCT-rat PAH model showed attenuated PAH phenotype with pharmacological inhibition of FTO.

#### T-52

### Infection and pulmonary pathology in a novel model of COVID-19

Cadence Lee M.S.<sup>1,2,3</sup>, Rachel Carley PharmD<sup>1,2,3</sup>, Sheila Sharma M.S.<sup>1,2,3</sup>, Julia Pierce B.S.<sup>1,2,3</sup>, <u>Crystal Parry B.S.</u><sup>1,2,3</sup>, Elizabeth Amelotte<sup>1,2,3</sup>, Celia Butler MPH<sup>2,3</sup>, Chris Mantsounga PhD<sup>1,2,3</sup>, Gaurav Choudhary MD<sup>1,2,3</sup>, Alan R. Morrison MD/PhD<sup>1,2,3</sup>

<sup>1</sup>Brown University, Providence, RI, USA. <sup>2</sup>Ocean State Research Institue, Providence, RI, USA. <sup>3</sup>VA Providence, Providence, RI, USA

- novel model of COVID-19
- Histopathologic analysis of COVID-19
- ACE2 expression in regards to SARS-CoV-2 infection

### Signaling

#### T-54

### Matrix Gla protein directs cell transitions in brown adipose development

<u>LI Zhang</u>, Xinjiang Cai, Yan Zhao, xiuju wu, yucheng yao, Kristina I. Boström UCLA, Los Angeles, California, USA

- MGP is expressed in endothelial and adipose progenitor cells.
- EC-derived MGP prevented the triggering of white adipogenesis in the perivascular region of BAT.
- MGP plays a complex role in the transitioning of cell populations during brown adipogenesis

#### T-55

The in vitro and in vivo analysis of the mechanism underlying the accumulation of NOTCH3 CADASIL mutant protein

<u>Shodai Suzuki</u><sup>1</sup>, Yohei Tsukamoto<sup>2</sup>, Taiki Mashiko<sup>1</sup>, Hideyuki Takeuchi PhD<sup>3</sup>, Tetsuya Okajima PhD<sup>2,4</sup>, Eiryo Kawakami MD, PhD<sup>5,6</sup>, Motoyuki Itoh PhD<sup>1</sup>

<sup>1</sup>Biochemistry, Graduate School of Pharmaceutical Sciences, Chiba University, Chiba, Chiba, Japan. <sup>2</sup>Molecular and Cellular Chemistry, Graduate School of Medicine, Nagoya University, Nagoya, Aichi, Japan. <sup>3</sup>Biochemistry, Graduate School of Pharmaceutical Sciences, University of Shizuoka, Shizuoka, Shizuoka, Japan. <sup>4</sup>Institute for Glyco-core Research (iGCORE), Graduate School of Medicine, Nagoya University, Nagoya, Aichi, Japan. <sup>5</sup>Department of Artificial Intelligence Medicine, Graduate School of Medicine, Chiba University, Chiba, Chiba, Japan. <sup>6</sup>Advanced Data Science Project (ADSP), RIKEN Information R&D and Strategy Headquarters, RIKEN, Yokohama, Kanagawa, Japan

- The glycosylation mediated by Radical fringe is involved in an aggregation of NOTCH3 CADASIL mutant.
- The aggregation of NOTCH3 mutant is promoted by RFNG in the cell- not purified protein-based assay.
- Deconvolution analysis with RNA-seq revealed that CADASIL-like zebrafish shows reduction of OPC.

#### T-56

### Role of neural EGR1 in blood flow recovery after hindlimb ischemia

<u>Gaganpreet Kaur PhD</u><sup>1,2</sup>, Amada Caliz  $MS^{1,2}$ , Heather Learnard  $MS^3$ , Hyung-Jin Yoo  $MS^{1,2}$ , Soonsang Yoon PhD<sup>1,2</sup>, Shashi Kant PhD<sup>1,2</sup>, John F. Keaney  $MD^{1,2}$ 

<sup>1</sup>Brigham and Women's Hospital, Boston, MA, USA. <sup>2</sup>Harvard Medical School, Boston, MA, USA. <sup>3</sup>University of Massachusetts, Worcester, MA, USA

- Neuronal EGR1regulates the expression of different growth factors like VEGFα, PGF, and HBEGF.
- Regulation of growth factors secretion by EGR1 can effect endothelial cell function.
- The overexpression of EGR1 increases blood flow recovery after mouse hindlimb ischemia

#### T-57

## Dissecting the regulatory elements of microRNA-223 in zebrafish vascular and blood development

<u>Elizabeth A Jones BS</u>, Dionna M Kasper PhD Dartmouth College, Hanover, NH, USA

- microRNA (miR)-223 is a key regulator of endothelial cell fate and hematopoiesis.
- miR-223 is expressed in different tissues at different times in hematovascular development.
- The promoter has binding sites for vascular and hematopoietic regulatory factors.

#### T-58

### Roles of Wnt5a signaling in inflammation and cancer are dependent on tissue context

<u>Ramiro Malgor MD</u><sup>1</sup>, Karen Coschigano Ph.D.<sup>1</sup>, Alyx Hazen BS<sup>1</sup>, Brakstin Hockley<sup>1</sup>, Ian Ackers D.O. Ph.D.<sup>2</sup>
<sup>1</sup>Biomedical Sciences, Ohio University, Athens, OH, USA. <sup>2</sup>Department of Physical Medicine and Rehabilitation, Sparrow Hospital, Michigan State University, Lansing, Michigan, USA

- Wnt5a signaling, a complex pathway activated in inflammation and cancer
- Could Wnt5a be one of the links responsible for the relationship inflammation/cancer?
- Wnt5a modulates innate immunity in tissue microenvironment

#### T-60

### Thoracic aortic aneurysms in Marfan Syndrome: from elastic fibers to integrin $\alpha\nu\beta8$

<u>Soheila Ali Akbari Ghavimi PhD</u>, Ryan Martinez, Mariam Kerolos, Amarri Harrison, Kim de la Cruz, Marie Billaud Brigham and Women's Hospital, Boston, MA, USA

• Marfan syndrome caused by mutation of FBN1 and shows overactivity of TGFβ.

- Aortic tissue from Marfan Syndrome patients had higher expression of MMP14 and integrin αν and β8.
- Targeting integrin ανβ8 offer potential to develop therapeutics to prevent aneurysms in MFS.

### Aging, Metabolism and the Vasculature I

#### T-61

# Endothelial Cpt1a reduction causes hyperoxia-induced pulmonary vascular remodeling by upregulating EndoMT in neonates

Katy Hegarty BS<sup>1</sup>, Jason L Chang BS<sup>1</sup>, Julie Braza BS<sup>2</sup>, Gaurav Chaudhary MD<sup>2</sup>, Phyllis A Dennery MD<sup>1</sup>, <u>Hongwei</u> Yao PhD<sup>1</sup>

<sup>1</sup>Brown University, Providence, RI, USA. <sup>2</sup>Providence VA Medical Center, Providence, RI, USA

- Endothelial Cpt1a reduction promotes pulmonary vascular remodeling by upregulating EndoMT.
- Enhancing fatty acid oxidation inhibits neonatal hyperoxia-induced pulmonary vascular remodeling.
- Blocking EndoMT prevents neonatal hyperoxia-induced pulmonary vascular remodeling.

#### T-62

### Sex hormones may be implicated in sex-specific differences in carotid atherosclerotic plaque instability

<u>Karina Gasbarrino PhD</u><sup>1</sup>, Edward Daly MSc<sup>2</sup>, Huaien Zheng MD, PhD<sup>1</sup>, Ana Carolina Alves dos Santos PhD<sup>3</sup>, Dajana Vuckovic PhD<sup>3</sup>, Stella S. Daskalopoulou MD PhD<sup>1</sup>

<sup>1</sup>Vascular Health Unit, Research Institute of McGill University Health Centre, Montreal, Quebec, Canada. <sup>2</sup>Clinical Proteomics and Mass Spectrometry, Research Institute of McGill University Health Centre, Montreal, Quebec, Canada. <sup>3</sup>Department of Chemistry and Biochemistry, Concordia University, Montreal, Quebec, Canada

- Sex differences exist in plaque composition, where men have more unstable plaques than women.
- High testosterone and low estradiol levels are associated with greater plaque instability in men.
- Sex hormones have been detected for the first time in stable and unstable plaques.

#### T-63

### Function of BRI3 in CD16 monocytes in Parkinson's disease

<u>Kathleen C Paul</u>, Owen M Wilkins Ph.D., Taylor S Turner, Karl E Biggs, Faith Anderson Ph.D., Stephen L Lee M.D., Ph.D., Fred W Killing Ph.D., Dionna M Kasper Ph.D., Matthew C Havrda Ph.D.

Geisel School of Medicine at Dartmouth, Hanover, NH, USA

- Single cell RNA sequencing of PBMCs from Parkinson's patients reveals PD-specific transcriptome.
- Brain Protein I3 is differentially expressed in PD CD16 monocytes, but function in PD is unknown.
- Monocyte-like cell line models and zebrafish inflammation models will elucidate BRI3 function.

#### T-64

### The effects of ageing to the cardiac microvasculature

Guillermo Luxán<sup>1,2,3</sup>, Anita Tamiato<sup>1,2,3</sup>, Colin Bodemer<sup>1,2,3</sup>, Timm Winkelmeier<sup>1</sup>, Mariana Shumliakivska<sup>1,2,3</sup>, Lukas S Tombor<sup>1,2,3</sup>, Ariane Fischer<sup>1</sup>, Marion Muhly-Reinholz<sup>1</sup>, Büşra N Toğru<sup>1</sup>, Mariano Ruz Jurado<sup>1,2,3</sup>, Maximilian Merten<sup>1,2,3</sup>, Jessica Neitz<sup>1</sup>, Stefan Günther<sup>2,3,4</sup>, David John<sup>1,2,3</sup>, Nina Wettschureck<sup>2,3,5</sup>, Stefanie Dimmeler<sup>1,2,3</sup>

11. Institute of Cardiovascular Regeneration, Center of Molecular Medicine, Goethe University Frankfurt, Frankfurt am Main, Germany. <sup>2</sup>2. German Center for Cardiovascular Research DZHK, Frankfurt am Main, Germany. Main, Germany. <sup>3</sup>3. Cardiopulmonary Institute, Goethe University Frankfurt, Frankfurt am Main, Germany. <sup>4</sup>4. Max Planck Institute for Heart and Lung Research, Bioinformatics and Deep Sequencing Platform, Bad Nauheim, Germany. <sup>5</sup>5. Max Planck Institute for Heart and Lung Research, Department of Pharmacology, Bad Nauheim, Germany

- Cardiovascular ageing compromises the microvasculature in the heart
- Age related deregulation of pericyte genes cause cardiac dysfunction and fibrosis in the heart
- Endothelial extracellular matrix is affected in ageing and leads to a pro-inflammatory phenotype

#### T-66

# High levels of O-GlcNAc induce endothelial senescence and vascular dysfunction in a premature vascular aging model

<u>Paula Rodrigues de Barros PhD candidate</u><sup>1,2</sup>, Tiago Januario da Costa PhD², Daniel Rodrigues PhD student¹, Carina Amarante Pedersoli Masters student¹, Jose Teles de Oliveira Neto PhD student¹, Jeimison Duarte dos Santos PhD¹, Laena Pernomian PhD², Camilla Ferreira Wenceslau PhD², Rita de Cassia Aleixo Tostes Passaglia PhD¹ ¹Universidade de Sao Paulo, Ribeirao Preto, SP, Brazil. ²University of South Carolina, Columbia, SC, USA

- High levels of O-GlcNAcylation in endothelial cells induce senescence and vascular dysfunction
- High levels of O-GlcNAcylation modulate ECs oxidative-stress induced senescence and cell function
- Cycling depend kinase inhibitors activation mediates O-GlcNAcylation induced senescence

#### T-67

#### Mechanisms of age-dependent decline in angiogenesis

<u>Yesenia G. Gomez</u>, Tendai Hunyenyiwa, Priscilla Kyi, Tadanori Mammoto, Akiko Mammoto Medical College of Wisconsin, Wauwatosa, Wisconsin, USA

- Angiogenesis is inhibited in aged human adipose endothelial cells.
- The levels of Y-RNA and RNA binding proteins are altered in aged human endothelial cells.
- Y-RNA in EVs may contribute to the age-dependent inhibition of angiogenesis.

#### WEDNESDAY POSTERS SESSIONS

#### Atherosclerosis II

#### W-01

### A Rac1-NF-kB transcriptional axis regulates IL-1β during atherosclerotic calcification

<u>Rachel Carley PharmD</u><sup>1,2</sup>, Cadence Lee ScM<sup>1,2</sup>, Chris Mantsounga PhD<sup>1,2</sup>, Joshua Berus PhD<sup>1,2</sup>, Olivya Caballero  $BS^{1,2}$ , Crystal Parry  $BS^{1,2}$ , Julia Pierce  $AB^{1,2}$ , Elizabeth Amelotte<sup>1,2</sup>, Celia Butler  $MS^{1,2}$ , Gaurav Choudhary  $MD^{1,2}$ , Alan R Morrison  $MD/PhD^{1,2}$ 

<sup>1</sup>Brown University, Providence, RI, USA. <sup>2</sup>Ocean State Research Institute Inc at Providence VA Medical Center, Providence, RI, USA

- Rac1 and NF-kB play a role in regulating IL-1B
- Rac1 and NF-kB play a role in regulating atherosclerotic calcification
- Rac1 and NF-kB regulate IL-1B and vascular calcification

#### W-03

#### Inflammation targeting contrast agent for MR imaging of atherosclerosis

<u>Joshua Rousseau</u>, Ting Yun Wang, Hui-Chun Huang, Kuei-Chun Wang

Arizona State University, Tempe, Arizona, USA

- Targeted MRI contrast agents enhances precise diagnosis of atherosclerosis
- Cloaking nanoparticles with monocyte membrane enables inflammation targeting
- Biomimetic nanoparticles encapsulating MRI contrast agent allows detection of plaque deposition

#### W-04

# Nanoparticles targeting YAP/TAZ dysregulation in atherosclerosis: impact on vascular cells and macrophages

<u>Ting-Yun Wang</u>, Hui-Chun Huang, Joshua Rousseau, Kuei-Chun Wang ASU, Tempe, Arizona, USA

- Developing a lesion-targeted, pathway-specific nanodrug for atherosclerosis treatment
- Unraveling pharmacological effects of the targeted nanodrug at single-cell level
- Investigating pharmacological mechanisms in vascular and immune cells

#### W-05

#### Novel role of endothelial CD47 in the regulation of pathogenesis of atherosclerosis

<u>Bandana Singh PhD</u>, Kui Cui, Qianman Peng, Kathryn Li, Bo Zhu, Sudarshan Bhattacharjee, Daniel Osorio, Beibei Wang, Yunzhou Dong, Donghai Wang, Yao Wei Lu, Hao Wu, Scott Wong, Douglas B. Cowan Cowan, Hong Chen Harvard Medical School, Boston, MA, USA

- Deletion of endothelial cell-specific CD47 protects from atherosclerosis progression.
- Deletion of endothelial cell-specific CD47 promotes efferocytosis of dying cells.
- In the athero-CD47iECKO group, the subpopulation of VSMCs decreased, while EC increased.

#### W-06

#### The role of endothelial microRNA-33 in atherosclerosis

<u>Kathryn Citrin</u>, Yan Huang, Alberto Canfran-Duque, Xinbo Zhang, Carlos Fernandez-Hernando, Yajaira Suarez Yale University, New Haven, CT, USA

- Endothelial lipid metabolism regulates pro-atherogenic EC functions
- The EC-specific role of miR-33, a regulator of lipid metabolism, has not been extensively explored
- EC-specific miR-33 knockout does not significantly regulate atherosclerosis progression

### **Development**

#### W-07

# Characterizing the function of klhl4 during vascular development in zebrafish (Danio rerio)

<u>Kaitlin A Ferrari M.S.</u>, Suman Gurung PhD, Saulius Sumanas PhD University of South Florida Morsani College of Medicine, Tampa, FL, USA

- KLHL4 regulates vascular development
- Genetic pathways governing vasculogenesis and angiogenesis
- Vascular defects result from KLHL4 mutation

#### W-08

# ETV2/ER71 regulates hematovascular lineage generation and vascularization through an H3K9 demethylase, KDM4A

Dong Hun Lee<sup>1</sup>, Min Seong Kim<sup>2,1</sup>, Raham Lee<sup>3</sup>, Heesang Song<sup>4</sup>, Joo Kyung Kim<sup>1</sup>, Bum-Yong Kang<sup>1</sup>, Karl Agger<sup>5</sup>, Kristian Helin<sup>6</sup>, Changwon Park<sup>3,1</sup>

<sup>1</sup>Emory University School of Medicine, Atlanta, USA. <sup>2</sup>LSU Health Science Center, Shreveport, LA, USA. <sup>3</sup>LSU Health Science Center, Shreveport, USA. <sup>4</sup>Chosun University School of Medicine, Gwangju, Korea, Republic of. <sup>5</sup>University of Copenhagen, Copenhagen, Denmark. <sup>6</sup>Memorial Sloan Kettering Cancer Center, New York, USA

- Interaction between ETV2 and KDM4A in differentiating mouse embryonic stem cells
- KDM4A plays an important role in the ETV2-regulated gene expression.
- The novel function of the interaction between ETV2 and KDM4A in neovascularization.

#### W-09

#### ETS transcription factor fli1b is required for hematopoietic development in zebrafish

<u>Valentina Laverde M.S.</u>, Saulius Sumanas PhD

University of South Florida, Tampa, FL, USA

- Specification of vascular endothelial and hematopoietic cells incompletely understood in zebrafish.
- Zebrafish paralog fli1b functions partially redundantly with ETS transcription factor Etv2/Etsrp.
- Role of FLI1 parlog fli1b in zebrafish embryonic hematopoiesis.

#### W-10

### A system-scale approach to uncovering isoforms contributing to endothelial cell differentiation

<u>Madison M. Mehlferber</u><sup>1</sup>, Vasilii Pavelko<sup>1</sup>, Jerryd Meade<sup>1</sup>, Erin D. Jeffery<sup>1</sup>, David Wissel<sup>2</sup>, Elizabeth A. Nelson<sup>1</sup>, Karen K. Hirschi<sup>1</sup>, Gloria M. Sheynkman<sup>1</sup>

<sup>1</sup>University of Virginia, Charlottesville, VA, USA. <sup>2</sup>University of Zurich, Zurich, CH, Switzerland

- A temporal representation of isoforms associated with endothelial cell development
- System-scale approach integrating long-read sequencing and mass-spectrometry
- Stem cell models used to recapitulate development of endothelial cells and analyze splicing patterns

### **Plasticity of the Vasculature**

#### W-13

# PRDM16 suppresses synthetic smooth muscle cell phenotypic modulation in atherosclerosis

<u>Josephine M E Tan PhD</u>, Patrick Seale PhD

University of Pennsylvania, Philadelphia, PA, USA

- PRDM16 is a CAD disease risk gene that regulates vascular plasticity in atherosclerosis
- Enhanced synthetic SMC modulation caused by PRDM16-KO changes lesion composition and structure
- PRDM16 suppresses fibrotic genes associated with synthetic SMC phenotypic switching

#### Endothelial senescence mediates hypoxia-induced vascular remodeling in the lung

<u>Priscilla Kyi</u>, Tendai Hunyenyiwa, Tadanori Mammoto, Akiko Mammoto Medical College of Wisconsin, Milwaukee, WI, USA

- Yap1 activity and EC senescence are stimulated in the pulmonary hypertension (PH) patient lungs.
- Upregulation of PDGFB in PH patient lungs is inhibited by knockdown of p16INK4A or YAP1.
- EC senescence mediates hypoxia-induced vascular remodeling in the lungs via YAP1-PDGFB signaling.

#### W-15

### Mitochondrial complex i promotes vascular smooth muscle cell proliferation and migration

Alishba Maira PhDCandidate, Dario F Riascos Bernal MD PhD, Nicholas E S Sibinga MD Albert Einstein College of Medicine, Bronx, NY, USA

- Mitochondrial respiration in smooth muscle cell biology.
- Mitochondrial dynamic in vascular smooth muscle cell plasticity and vascular remodeling
- The roles of mitochondrial Complex I in vascular smooth muscle cell proliferation and migration.

#### W-16

## Coronary microvascular adaptation to left ventricular inflow obstruction in the late gestation fetal lamb

<u>Matthew W Hagen PhD</u><sup>1</sup>, Samantha Louey PhD<sup>1</sup>, Sarah M Alaniz RVT<sup>1</sup>, Jonathan R Lindner MD<sup>1,2</sup>, George Giraud MD PhD<sup>1,3</sup>, Sonnet S Jonker PhD<sup>1</sup>

<sup>1</sup>Oregon Health & Science University, Portland, Oregon, USA. <sup>2</sup>University of Virginia, Charlottesville, Virginia, USA. <sup>3</sup>Portland VA Medical Center, Portland, Oregon, USA

- We developed a novel large-animal model of late gestation left ventricular inflow obstruction.
- Left ventricular inflow obstruction increases coronary microvascular perfusion of both ventricles.
- RV microvascular perfusion increases to a greater degree than LV following LV inflow obstruction.

### **Adv. Engineering Models & Imaging Techniques**

#### W-17

# Blood science and angiogenesis-enabled Ovarian TME-Chips determine mechanisms and therapeutics against antiangiogenic escape

Lopamudra D. Ghosh PhD<sup>1</sup>, Abhishek Jain PhD<sup>1,2</sup>

<sup>1</sup>Texas A&M University, College Station, TX, USA. <sup>2</sup>Houston Methodist Research Institute, Houston, TX, USA

- Blood and angiogenesis-enabled human tumor microenvironment chip
- The spatiotemporal dynamics of angiogenesis in TME is regulated by blood platelets
- Platelets contribute to antiangiogenic escape

#### W-19

Differential-geometric model of red blood cell equilibrium shapes to investigate skeletal muscle microcirculatory regulation

University of Western Ontario, London, Ontario, Canada

- Red blood cell shape is intimately connected to muscle oxygen regulation.
- Condensed matter theoretical models explain red blood cell convexity/concavity.
- Condensed matter theory/geometry models can explain how red blood cells regulate blood flow.

#### Inflammation

#### W-20

#### Vascular inflammation in neuropsychiatric PASC

<u>Lindsay S McAlpine M.D.</u><sup>1</sup>, Hailey Reisert<sup>2</sup>, Allison Nelson<sup>1</sup>, Jennifer Chiarella<sup>1</sup>, Shelli Farhadian M.D.<sup>1</sup>, Serena Spudich M.D.<sup>1</sup>

<sup>1</sup>Yale University, New Haven, CT, USA. <sup>2</sup>Mt. Sinai Hospital, New York, NY, USA

- Individuals with neuro-PASC demonstrate persistent systemic inflammation.
- Individuals with neuro-PASC demonstrate persistent vascular inflammation.
- Individuals with neuro-PASC may be at risk of accelerated atherosclerosis.

#### W-21

#### Edn1 is a disease-specific marker in endothelial cells during atherosclerosis

<u>Danica M Dy BS</u>, Thiel Lehman PhD, Jessica Lin, Rob Wirka MD UNC-Chapel Hill, Chapel Hill, NC, USA

- A specific population of ECs may undergo EndMT, contributing to the progression of atherosclerosis
- A disease-specific population of ECs are characterized by expression of Edn1
- Pathway analysis predicts that EC transition is driven by EndMT-associated transcription regulators

#### W-22

### VEGF-D improves vascular integrity and resolves inflammation in the lungs

<u>Yifan Yuan</u><sup>1,2</sup>, Lokesh K Sharma PhD<sup>2</sup>, Wenwen Tang PhD<sup>2</sup>, Micha Sam B Raredon MD, PhD<sup>2</sup>, Dianqing (Dan) Wu PhD<sup>2</sup>, Laura E Niklason MD, PhD<sup>3,2</sup>, Naftali Kaminski MD<sup>2</sup>

<sup>1</sup>University of Maryland, Baltimore, MD, USA. <sup>2</sup>Yale University, New Haven, CT, USA. <sup>3</sup>Humacyte Global, Inc, Durham, NC, USA

- scRNAseq data reveals a strong VEGFD-VEGFR2 interaction within the human lung microvascular niche.
- VEGF-D improves vascular integrity and reduces pro-inflammatory response.
- VEGF-D regulates vascular integrity through VEGFR-2- and ROCK-dependent signalling.

### Aging, Metabolism and the Vasculature II

#### W-24

### Aging is associated with organ-specific alterations in level and expression pattern of von Willebrand factor

<u>Parnian Alavi</u><sup>1</sup>, Douglas Brown<sup>2</sup>, John Lewis<sup>2</sup>, Stephane Bourque<sup>3</sup>, Nadia Jahroudi<sup>1</sup>

Department of Medicine, University of Alberta, Edmonton, Alberta, Canada. <sup>2</sup>Department of Oncology,

\*Department of Medicine, University of Alberta, Edmonton, Alberta, Canada. \*Department of Uncology, University of Alberta, Edmonton, Alberta, Canada. \*Department of Anesthesiology & Pain Medicine, University of Alberta, Edmonton, Alberta, Canada

- VWF mRNA and protein are upregulated in aged mice in an organ-specific manner.
- The increasing proportion of microvessels exhibit VWF expression in organs of aged mice.
- P53 knockdown abolished the aged- induced VWF upregulation in endothelial cells.

#### W-25

# Age-related increases in DNA methylation impair HuR-mediated VEGF-A mRNA stability and consequent inflammatory arteriogenesis

Christopher Mantsounga PhD<sup>1</sup>, <u>Olivya Caballero BS</u><sup>1</sup>, Sheila Sharma MSc<sup>2</sup>, Cadence Lee MSc<sup>1</sup>, Rachel Carley PharmD<sup>2</sup>, Crystal Parry BS<sup>2</sup>, Julia Pierce BS<sup>2</sup>, Celia Butler MPH<sup>2</sup>, Elizabeth Amellotte<sup>2</sup>, Gaurav Choudhary MD<sup>2</sup>, Alan Morrison MD, PhD<sup>2</sup>

<sup>1</sup>Brown University, Providence, Rhode Island, USA. <sup>2</sup>Brown University, Providence, RI, USA

- Aging is associated with impaired inflammatory arteriogenesis in response to vascular injury.
- Reduced arteriogenesis was related to decreased muscle tissue VEGF-A and VEGF 165A levels.
- BMDMs from aged mice revealed decreased VEGF-A165a mRNA half-life, and VEGF-A associated with Hur.

#### W-26

# Targeting the microvasculature to treat diabetes-induced heart failure with preserved ejection fraction

<u>Cori Lau</u><sup>1,2</sup>, Kai Ellis<sup>1,3</sup>, Rathnakumar Kumaragurubaran<sup>2</sup>, Garry Yu<sup>2</sup>, Lijun Chi<sup>3</sup>, Paul Delgado-Olguin<sup>3</sup>, Michael D Wilson<sup>3</sup>, Jason E Fish<sup>2</sup>

<sup>1</sup>University of Toronto, Toronto, ON, Canada. <sup>2</sup>Toronto General Hospital Research Institute, Toronto, ON, Canada. <sup>3</sup>SickKids Research Institute, Toronto, ON, Canada

- Transcriptome and chromatin landscape of cardiac endothelial cells in T2D mice
- Transcriptome and chromatin landscape of cardiac endothelial cells in SGLT2 inhibitor-treated mice
- Microvascular analysis in the hearts of T2D mice and SGLT2 inhibitor-treated mice

#### W-27

# Direct heterocellular communication between capillary adipose endothelium and adipocytes can regulate lipid handling

<u>Melissa A Luse MS</u><sup>1</sup>, Luke S Dunaway PhD<sup>1</sup>, Meghan Sedovy<sup>2</sup>, Scott R Johnstone PhD<sup>2</sup>, Brant E Isakson PhD<sup>1</sup> <sup>1</sup>Unviersity of Virginia, Charlottesville, VA, USA. <sup>2</sup>Virginia Tech, Roanoke, VA, USA

- Adipose is enriched with capillary endothelial cells which make contact with adipocytes.
- Contact between capillary adipose endothelial cells dictates gene expression in both cell types.
- Connexin 43 facilities contact between adipocytes and capillary adipose endothelial cells.

#### W-28

### Cav1 inhibition of eNOS regulates Cd36 mediated lipid uptake in endothelium

<u>Melissa A Luse MS</u><sup>1</sup>, Wyatt Schug BS<sup>1</sup>, Luke S Dunaway PhD<sup>1</sup>, Skylar Loeb BS<sup>1</sup>, Rachel Tessema BS<sup>1</sup>, Miriam Cortese-Krott PhD<sup>2</sup>, Brant E Isakson PhD<sup>1</sup>

<sup>1</sup>University of Virginia, Charlottesville, VA, USA. <sup>2</sup>Heinriche Heine University, Dusseldorf, Germany

- Endothelial Caveolin-1 plays a critical role in lipid uptake.
- Cd36 is located within endothelial caveolae and facilitate lipid uptake in vitro and in vivo.
- Nitrosylation of Cd36 by nitric oxide inhibits the transport of fatty acids into the endothelium.

# Therapeutic reactivation of aging-impaired endothelial regeneration and vascular repair for treatment of acute respiratory distress syndrome in elderly patients via repurposing decitabine or endothelium-targeted nanoparticle delivery of FoxM1

Xianming Zhang PhD<sup>1</sup>, <u>Narsa Machireddy PhD</u><sup>1</sup>, Colin E Evans PhD<sup>1</sup>, David Wu MD<sup>2</sup>, Youyang Zhao PhD<sup>1</sup>
<sup>1</sup>Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, IL, USA.
<sup>2</sup>University of Chicago, Chicago, IL, USA

- resident endothelial cell proliferation is the intrinsic mechanism of endothelial regeneration
- Aging impairs the intrinsic endothelial regenerative program via hypermethylation of Foxm1 promoter
- Decitabine treatment or nanoparticle delivery of FoxM1 reactivates endothelial regeneration in aging

#### W-30

## Differences in body composition and lipid profile between vegetarians and omnivorous: Relationship with 10-year cardiovascular risk

Cintia Ferreira-Pego MSc, PhD, Tatiana Fontes MSc, Sofia Lopes MSc, Regina Menezes MSc, PhD, <u>Luis Monteiro</u> Rodrigues MSc, PhD

CBIOS – Universidade Lusófona's Research Center for Biosciences & Health Technologies, Lisboa, Lisboa, Portugal

- To provide evidence on the impact of vegetarian versus omnivore dietary regimens on health
- To identify potential related differences regarding body composition cardiometabolic markers
- To compare cardiovascular risk of participants from both dietary regimens

### **Neurovascular Unit and Disease**

#### W-31

# Studying Erythromelalgia through the laser Doppler flowmetry perfusion components and skin temperature

Joana Caetano MD,  $MSc^{1,2,3}$ , Hugo T.D. Ferreira MD,  $PhD^4$ , Clemente Rocha Msc,  $PhD^1$ , Sergio F. Andrade MSc,  $PhD^1$ , Jose D. Alves MD,  $PhD^{2,3}$ , <u>Luis M Rodrigues MSc</u>,  $PhD^1$ 

<sup>1</sup>CBIOS - Research Center for Biosciences and Health Technologies, Universidade Lusófona, Lisboa, Lisboa, Portugal. <sup>2</sup>Immuno-mediated Systemic Diseases, Medicina IV Hospital Fernando Fonseca, Amadora, Lisboa, Portugal. <sup>3</sup>Nova Medical School, Lisboa, Lisboa, Portugal. <sup>4</sup>Institute of Biophysics and Biomedical Engineering, Faculty of Sciences - University of Lisbon, Lisboa, Lisboa, Portugal

- To better characterize Erythromelalgia a still poorly understood disease
- To apply the Wavelet transform to the LDF signals obtained under challenge
- To prove the concept after testing outcomes following a new therapeutical approach

#### W-32

# Development of stem cell-derived microfluidic models of the blood-brain barrier in Alzheimer's disease

Lily E Takeuchi MSc<sup>1,2</sup>, Craig A Simmons PhD<sup>1,2,3</sup>

<sup>1</sup>Institute of Biomedical Engineering, University of Toronto, Toronto, Ontario, Canada. <sup>2</sup>Translational Biology and Engineering Program, Ted Rogers Centre for Heart Research, Toronto, Ontario, Canada. <sup>3</sup>Department of Mechanical and Industrial Engineering, University of Toronto, Toronto, Ontario, Canada

- There is an unmet need for physiological models of the blood-brain barrier in Alzheimer's disease.
- We demonstrate functional impairment to iPSC-derived brain endothelial cells from a patient with AD.
- Shear stress impairs immune activation of the cerebral vasculature in Alzheimer's disease.

#### W-33

# Circulating extracellular vesicles from mice with chronic cerebral hypoperfusion perturb brain endothelial cell function

<u>Brandon Kirby</u>, Audrey Plumtree, Duaa Dakhlallah PhD, Ekaterina Weil PhD, Candice M Brown PhD West Virginia University School of Medicine, Morgantown, WV, USA

- Vascular contributions to cognitive impairment and dementia results from extensive vascular disease.
- Mechanisms underlying the pathophysiology of VCID are not well-understood.
- Plasma-derived extracellular vesicles may be a key modulator in the pathophysiology of VCID.

#### W-34

### Activation of Wnt/ $\beta$ -catenin signaling in radial glial cells disrupts BBB development

<u>Dylan J Sebo B.S.</u>, Audrey R Fetsko B.S., Michael R Taylor PhD

University of Wisconsin - Madison, Madison, WI, USA

- Wnt signaling works cell non-autonomously within the NVU to inhibit BBB development.
- Wnt and Vegf ligands released from radial glial cells, are sensitive to Wnt signaling.
- Wnt signaling within radial glial cells must be finely controlled for proper CNS and BBB development

#### W-35

### Reduced endothelial levels of splice factor TDP-43 associated with ALS/FTD- mutations TARDBPG348C causes hallmarks of FTD in an animal model

<u>Ashok Cheemala PhD</u><sup>1</sup>, Amy Kimble B.A.B<sup>1</sup>, Jordan Tyburski B.S.<sup>1</sup>, Melissa Murphy B.S.<sup>1</sup>, Evan Jellison PhD<sup>2</sup>, Bo Reese PhD<sup>3</sup>, Xiangyou Hu PhD<sup>4</sup>, Rigiang Yan PhD<sup>4</sup>, Patrick Murphy PhD<sup>1</sup>

<sup>1</sup>University of Connecticut Medical School, Center for Vascular Biology, Farmington, Connecticut, USA. <sup>2</sup>University of Connecticut Medical School, Department of Immunology, Farmington, Connecticut, USA. <sup>3</sup>University of Connecticut, Center for Genome Innovation, New Britain, Connecticut, USA. <sup>4</sup>University of Connecticut Medical School, Department of Neuroscience, Farmington, Connecticut, USA

- ALS/FTD-associated mutations in TDP-43 reduce nuclear levels in brain ECs as well as neurons
- Reduction or endothelial-specific deletion of TDP-43 disrupts RNA splicing, impairs EC-junctions
- Brain EC TDP-43 deletion mimics ALS/FTD: BBB loss, fibrin, glial activation, and cognitive issues

#### W-36

# Wnt-directed specialization of endothelial colony forming cells to generate a perfusable blood brain barrier microphysiological system

<u>Makena L Ewald</u>, Christopher J Hatch, Amber R Keith, Sarah J Hernandez PhD, Duc TT Phan PhD, Leslie M Thompson PhD, Christopher CW Hughes PhD

University of California, Irvine, Irvine, Ca, USA

- Advances in CNS related disease treatments require advanced human-derived in vitro BBB models.
- Endothelial cells specialize into organotypic vasculature based on environmental cues.
- We developed a blood brain barrier model by mimicking natural developmental processes in vitro

#### W-37

### Netrin-1 binding to Unc5B regulates BRB integrity via Norrin/ $\beta$ -catenin

Jessica Furtado BS<sup>1</sup>, Kevin Boyé PhD<sup>2</sup>, Anne Eichmann PhD<sup>3</sup>

<sup>1</sup>Yale University, New Haven, CT, USA. <sup>2</sup>Inserm, Paris, France. <sup>3</sup>Yale University, New Haven, USA

- Unc5B regulates blood retina barrier permeability.
- Netrin1 binding to Unc5B regulates the Wnt-related Norrin/β- catenin signaling via pLRP5.

Endothelial cell and pericyte Unc5B may have opposing roles.

### 3D Imaging and Organotypic Vasculature

#### W-38

# Creating vascularized gut tube organoid to recapitulate organotypic endothelium and mesenchyme

<u>Yifei Miao PhD</u><sup>1,2</sup>, Cheng Tan MD<sup>1,2</sup>, Nicole Pek BA<sup>1</sup>, Zhiyun Yu BA<sup>1</sup>, Kentaro Iwasawa MD<sup>1</sup>, Daniel Kechele PhD<sup>1</sup>, Nambirajan Sundaram PhD<sup>1</sup>, Victor Pastrana-Gomez BA<sup>1</sup>, Kyle McCracken MD/PhD<sup>1</sup>, Jason Tchieu PhD<sup>1</sup>, Jeffrey Whitsett MD<sup>1</sup>, Michael Helmrath MD<sup>1</sup>, Aaron Zorn PhD<sup>1</sup>, James Wells PhD<sup>1</sup>, Takanori Takebe MD/PhD<sup>1</sup>, Darrell Kotton MD<sup>3</sup>, Ya-Wen Chen PhD<sup>4</sup>, Minzhe Guo PhD<sup>1</sup>, Mingxia Gu MD/PhD<sup>1,2</sup>

<sup>1</sup>Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA. <sup>2</sup>University of Cincinnati College of Medicine, Cincinnati, OH, USA. <sup>3</sup>Boston University and Boston Medical Center, Boston, MA, USA. <sup>4</sup>Icahn School of Medicine at Mount Sinai, New York, NY, USA

- Gut epithelium, mesenchyme, and endothelium simultaneously co-develop from iPSC-derived organoids.
- Vascularized organoid provides a proper niche to pattern organotypic endothelium and mesenchyme.
- Organotypic endothelium and mesenchyme generated from organoids are similar to human fetal organs.

#### W-39

#### Multimolecular ultrasound imaging for vascular regeneration at centimeter depths

<u>G. Edward W. Marti Ph.D.</u>, Cheng Liu Ph.D., Kaitlyn Liang M.S., James D. Brooks M.D., Jeremy J. Dahl Ph.D., Steven Chu Ph.D.

Stanford University, Palo Alto, CA, USA

- Molecular ultrasound imaging will enable deep tissue, long-term observations of vascular changes.
- This modality uses ligand- or antibody-labeled microbubbles to localize surface markers.
- We are developing a multi-molecular approach to track several molecular markers simultaneously.

#### W-40

### Investigating the role of endothelial Rac1 towards regulation of vascular and organ homeostasis

<u>Chen Yuan Kam PhD</u><sup>1</sup>, Ishani D Singh BS<sup>1</sup>, Karen K Hirschi PhD<sup>2</sup>, Valentina Greco PhD<sup>1</sup> Yale University, New Haven, CT, USA. <sup>2</sup>University of Virginia, Charlottesville, VA, USA

- Neonatal endothelial Rac1 impairs angiogenesis but not vessel regression in maturing skin
- In adulthood, Rac1 mutant capillaries and venules are perturbed while arterioles are protected
- Endothelial Rac1 mutants display hair growth defects with delayed entry into hair cycle

#### W-41

### Dissecting cutaneous wound healing in zebrafish

<u>Leah Greenspan PhD</u>, Keith Ameyaw BS, Daniel Castranova MS, Van Pham, Gennady Margolin, Caleb Mertus, Brant Weinstein PhD

NICHD, Bethesda, MD, USA

- Delays in vessel regrowth are a major contributor to defects in wound closure.
- Our new rotary tool injury system can be used to study cutaneous wound healing in zebrafish.
- Live imaging reveals insights into immune and endothelial cell behavior during wound healing.

#### W-43

# Discovery of a new external immune surveillance organ in the zebrafish, an exciting model to study immune and endothelial cells

<u>Daniel Castranova  $MS^1$ </u>, Madeleine Kenton  $MS^1$ , Aurora Kraus  $PhD^1$ , Jong Park  $PhD^1$ , Marina Venero Galanternik  $PhD^2$ , Gilseung Park  $PhD^1$ , Daniel Lumbantobing  $PhD^3$ , Miranda Marvel  $PhD^1$ , James Iben  $PhD^1$ , Louis Dye  $PhD^1$ , Lucas Blevins<sup>4</sup>, John K Frazer  $PhD^4$ , Brant Weinstein  $PhD^1$ 

<sup>1</sup>NIH, Bethesda, MD, USA. <sup>2</sup>University of Utah, Salt Lake City, UT, USA. <sup>3</sup>Smithsonian Institution, Washington, DC, USA. <sup>4</sup>University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

- Zebrafish have an external organ (lobe) behind their operculum that fully regenerates when removed.
- The lobe is teaming with immune cells and believed to be involved in immune surveillance.
- The lobe can be imaged in vivo and ex vivo, making it great to study immune and endothelial cells.

#### W-44

#### A zebrafish gill model of mammalian lung endothelium

<u>Jong S Park Ph.D.</u>, Celia Martinez-Aceves, Daniel Castranova, Louis Dye, Madeline Kenton, Gennady Margolin, Van Pham, Brant Weinstein NICHD, Bethesda, MD, USA

- Many cell types found in lungs are also present in gills.
- scRNAseq revealed aerocyte-like cell population in the zebrafish gill endothelium.
- Gill aerocyte-like cells localize to the lamella of the gill where gas-exchange takes place.

#### **Endothelium in Health and Disease II**

#### W-45

# Endothelial protease-activated receptors modulate hepatic vascular permeability during acetaminophen overdose

Rahul Rajala B.A., B.S.<sup>1,2,3</sup>, Audrey C.A. Cleuren Ph.D.<sup>1,2</sup>, Courtney T Griffin Ph.D.<sup>1,2</sup>

<sup>1</sup>Oklahoma Medical Research Foundation, Oklahoma Clty, OK, USA. <sup>2</sup>University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA. <sup>3</sup>Harold Hamm Diabetes Center, Oklahoma City, OK, USA

- Endothelial PARs promote hepatic vascular permeability following APAP overdose.
- Endothelial PARs can reciprocally regulate their activating proteases.
- Translating Ribosome Affinity Purification can identify novel PAR targets following APAP Overdose.

#### W-47

# Loss of GATA6 in human pulmonary artery endothelial cells shuts down interferon signaling

<u>Vrinda Dambal Graduate Student</u>, Maria Trojanowska Professor Boston University, Boston, MA, USA

- Endothelium loses response to dsRNA and viral infection with knockdown of GATA6 in HPAECs
- Loss of GATA6 in HPAECs leads to inhibition of interferon signaling.
- Loss of interferon response in GATA6 knockdown HPAECs contributes to PAH development

#### W-48

# Activation of endothelial GCN2 kinase contributes to pulmonary vascular remodeling and pulmonary arterial hypertension

Maggie M Zhu M.S<sup>1,2</sup>, <u>Mohammad Shafiq Ph.D.</u><sup>1,2</sup>, Jingbo Dai Ph.D.<sup>1</sup>, Yi Peng Ph.D.<sup>1,2</sup>, You Yang Zhao Ph.D.<sup>1,2,3,4</sup>
<sup>1</sup>Program for Lung and Vascular Biology, Section for Injury Repair and Regeneration, Stanley Manne Children's Research Institute, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois, USA. <sup>2</sup>Department of

Pediatrics, Division of Critical Care, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA. <sup>3</sup>Departments of Pharmacology, and Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA. <sup>4</sup>Feinberg Cardiovascular and Renal Research Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

- Loss of GCN2 kinase activity in mice inhibited hypoxia-induced PH.
- GCN2 was activated in response to hypoxia to mediate ET1 expression through GCN2/HIF2a/ET1.
- GCN2 activity was highly induced in pulmonary vascular lesions in iPAH patients.

#### W-49

### Gadolinium blocks histone-induced endothelial calcium events and plasma membrane activation

<u>Jade H Cleary</u>, Sophia H Piffard BS, Carlos Lecuier-Garcia, Grant Hennig PhD, Kalev Freeman MD, PhD University of Vermont, Burlington, VT, USA

- Extracellular histones trigger rapid cytosolic Ca2+ events in endothelial cells.
- Histones activate endothelial membranes causing blebbing and dye internalization within minutes.
- Ca2+ events and membrane effects of histones were completely abrogated by Gd3+.

#### W-50

#### The cerebrovasculature in a mouse model of Alzheimer's disease

<u>Lauren R Miller PhD</u><sup>1</sup>, Sharon Negri PhD<sup>2,3</sup>, Debra Saunders<sup>1</sup>, Michael J Beckstead PhD<sup>1</sup>, Stefano Tarantini PhD<sup>2,3</sup>, Audrey C A Cleuren PhD<sup>1</sup>

<sup>1</sup>Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA. <sup>2</sup>University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA. <sup>3</sup>Semmelweis University, Budapest, Hungary

- Endothelial-specific transcriptomics
- Vascular components of Alzheimer's disease
- Cerebrovascular function

#### W-51

# Single nucleus sequencing reveals vascular microheterogeneity in acute rejection of human cardiac transplants

<u>Christopher Pathoulas</u><sup>1</sup>, Amy Kimble<sup>1</sup>, Omar Omar<sup>1</sup>, Giulia Protti<sup>2</sup>, Gregory Fishbein M.D.<sup>3</sup>, Ryan Lau M.D.<sup>3</sup>, Matteo Pellegrini Ph.D.<sup>2</sup>, Patrick Murphy Ph.D.<sup>1</sup>, Nicole Valenzuela Ph.D.<sup>3</sup>

<sup>1</sup>University of Connecticut Health Center, Farmington, CT, USA. <sup>2</sup>Department of Molecular, Cell and Developmental Biology, University of California, Los Angeles, CA, USA. <sup>3</sup>Department of Pathology and Laboratory Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA, USA

- There is a need for increased understanding of the processes that promote heart transplant rejection
- Endothelial cells become activated and could play an important role in graft rejection
- Longitudinal endothelial gene expression analysis of patient biopsies offers insight into rejection

#### W-52

### Mechanobiology of vascular dysfunction in early age-related macular degeneration

<u>Irene Santiago Tierno</u><sup>1,2</sup>, Sathishkumar Chandrakumar PhD<sup>1,2</sup>, Mahesh Agarwal PhD<sup>1,2</sup>, Kaustabh Ghosh<sup>1,2</sup>
<sup>1</sup>UCLA, Los Angeles, CA, USA. <sup>2</sup>Doheny Eye Institute, Pasadena, CA, USA

- Endothelial cells from AMD eyes exhibit significantly impaired neovascularization.
- AMD ECs presented significant increase in FAK activity that was localized to disrupted EC junctions.
- Transcriptomics data revealed 16% of all DEG-enriched pathways were related to mechanotransduction.

### Mechanical regulation of retinal vascular inflammation and degeneration in diabetes

Sathishkumar Chandrakumar PhD<sup>1,2</sup>, <u>Irene Santiago Tierno MS</u><sup>1,2</sup>, Mahesh Agarwal PhD<sup>1,2</sup>, Timothy S Kern PhD<sup>3,4</sup>, Kaustabh Ghosh PhD<sup>1,2</sup>

<sup>1</sup>UCLA, Los Angeles, CA, USA. <sup>2</sup>Doheny Eye Institute, Pasadena, CA, USA. <sup>3</sup>UC Irvine, Irvine, CA, USA. <sup>4</sup>Gavin Herbert Eye Institute, Irvine, CA, USA

- Diabetes leads to lysyl oxidase (LOX)-mediated retinal capillary stiffening
- Stiffer retinal capillaries undergo inflammation-mediated degeneration in diabetes
- Diabetes-induced LOX upregulation is mediated by AGE/RAGE

### Diseases (Vascular and Cardiovascular) II

#### W-54

#### Cardiovascular safety of nanoparticle vs conventional Doxorubicin

<u>Lukas Brandt</u>, Shelby N. Hader, Laura E. Norwood Toro PhD, Radha Vaddavalli PhD, Venkateswara Gogineni PhD, Sarah B. White MD, Andreas M. Beyer

Medical College of Wisconsin, Milwaukee, Wisconsin, USA

- Endothelial Dysfunction
- Cardio-Oncology
- Cardio-toxicity

#### W-55

# The pH-sensing G protein-coupled receptor GPR68 promotes the contractile phenotype in vascular smooth muscle cells

<u>Madison D Williams MS</u><sup>1</sup>, Joshua S Morgan PhD<sup>1</sup>, Michael T Bullock MS<sup>2</sup>, Kristen Carraway<sup>1</sup>, Tonya N Zeczycki  $PhD^1$ , Kyle D Mansfield  $PhD^1$ , David A Tulis  $PhD^1$ 

<sup>1</sup>East Carolina University, Greenville, NC, USA. <sup>2</sup>Edward Via College of Osteopathic Medicine, Carolinas Campus, Spartanburg, SC, USA

- Decreased abundance of contractile and cytoskeletal proteins in GPR68 KO versus WT thoracic aortae
- Decreased expression of contractile and cytoskeletal proteins in GPR68 KO versus WT cells in hypoxia
- GPR68 may signal through the small GTPases Rap1A/1B and Rab5a to control VSMC phenotype

#### W-57

### The liver as an inflammatory mediator of pulmonary arterial hypertension

<u>Navneet Singh MD</u><sup>1,2</sup>, Amy Princiotto<sup>2</sup>, Corey E Ventetuolo MD, MS<sup>1</sup>, Elizabeth O Harrington PhD<sup>2,1</sup>

Brown University, Providence, RI, USA. <sup>2</sup>Providence VA Medical Center/CPVB COBRE, Providence, RI, USA

- The liver may mediate inflammation that drives the pathobiology of pulmonary arterial hypertension
- Livers of Sugen-Hypoxia rats may demonstrate an inflammatory infiltrate compared to controls
- Increased GDF2 expression in SuHx livers may be a compensatory response to nonfunctional BMP9

#### W-58

### MicroRNA loss drives tumor development in murine models of angiosarcoma

Annaleigh Benton, Ant Murphy, <u>Jason A Hanna PhD</u>

Purdue University, West Lafayette, IN, USA

- MicroRNA loss results in aggressive tumor development in mouse models of angiosarcoma.
- MiRNA-497 is a key tumor suppressing miRNA in angiosarcoma.
- We have identified several genes regulated by miR-497 that are upregulated in human angiosarcoma.

#### W-59

### The slow progression of diabetic retinopathy is associated with transient protection of retinal vessels from death

Yanliang Li MD/PhD, Basma Baccouche PhD, Norma Del-Risco BS, Jason Park PhD, Amy Song BS, J. Jason McAnany PhD, Andrius Kazlauskas PhD

University of Illinios at Chicago, Chicago, IL, USA

- There is compelling evidence for protection from diabetic retinopathy in patients and animal models.
- Diabetes induced transient protection of the retinal vasculature in both T1D and T2D mice.
- As the duration of DM was prolonged, protection waned and vulnerability developed.

### **Cardiovascular Cell Biology II**

#### W-60

## STING inhibitors allow plasmid gene expression in primary vascular cells: an easy protocol for gene delivery in hard-to-transfect cells

Shuai Yuan, Adam Straub

University of Pittsburgh, Pittsburgh, PA, USA

- STING inhibitors enhance plasmid transfection in endothelial and smooth muscle cells.
- The inhibitor's effect is transient while protein expression sustains.
- Overexpressed protein retains normal functionality.

#### W-62

## The role of COL8A1 in endothelial phenotypic modulation during inflammatory endothelial-to-mesenchymal transition

<u>Qian Li</u>, Sriharsha Talapaneni, Yonghong Meng, Linda L Demer, Yin Tintut, Jeffrey J Hsu UCLA, Los Angeles, CA, USA

- COL8A1 mediates the endothelial cell transition during inflammatory EndMT.
- COL8A1 maintains normal endothelial function.
- TNF-a decreases COL8A1 expression to facilitate the loss of the endothelial phenotype.

#### W-63

#### Nuclear functions of smooth muscle $\alpha$ -actin

<u>Callie Kwartler PhD</u><sup>1</sup>, Jose Emiliano Esparza Pinelo BS<sup>1</sup>, Anita Kaw MD/PhD<sup>2</sup>, Dianna Milewicz MD/PhD<sup>1</sup>

<sup>1</sup>UTHouston McGovern Medical School, Houston, TX, USA. <sup>2</sup>UTHouston McGovern Medical School, Houston, TX, USA

- Smooth muscle (SM) α-actin associates with the INO80 and BAF chromatin remodeling complexes
- SM α-actin p.Arg 179 variants alter histone modifications on critical SM-specific promoters
- Genetic evidence says altered chromatin remodeling may be a common pathway to moyamoya disease

#### W-64

Endothelial cell-targeted nanoparticle delivery of CRISPR/Cas9 plasmid DNA causes robust genome editing of endothelial HIF-2a in adult rats and inhibits experimental pulmonary arterial hypertension: Towards precision gene therapy of vascular diseases

Jingbo Dai PhD, Yi Peng PhD, Youyang Zhao PhD

Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, IL, USA

- Endothelium-targeted nanoparticle delivery of the genome editing system in adult rats.
- Targeting vascular bed-specific ECs for modulation of gene expression.
- Selective disruption of Hif2a in lung EC inhibits pulmonary hypertension with minimal off-targets.

#### W-65

# Variant-to-function of coronary artery disease: identifying novel regulation of the notch pathway in endothelial cells

Vivian S Lee-Kim Ph.D., Rajat M. Gupta M.D.

Brigham and Women's Hospital, Boston, MA, USA

- Human genetics to identify novel disease pathways
- Notch signaling pathway regulation
- Endothelial dysfunction in coronary artery disease

#### W-66

#### How does Dach1 promote vascularization?

Wen-Chuan Hsieh Ph.D., Kristy Red-Horse Ph.D.

Stanford, Stanford, CA, USA

- Assess FDA-approved drugs and small molecules that increase Dach1 level in artery endothelial cells.
- Investigate the molecular mechanism of Dach1 in artery maturation.
- Identify novel regulators and targets of Dach1.

#### W-67

### A chemical biology approach for functional perturbation studies in the vasculature

Joseph Lim Bachelor of Science<sup>1,2</sup>, Jorge Andrade PhD<sup>1,2</sup>, Michael Potente MD<sup>1,2</sup>

<sup>1</sup>Angiogenesis and Metabolism Laboratory, Berlin Institute of Health at Charité – Universitätsmedizin Berlin, Berlin, Germany. <sup>2</sup>Max Delbrück Center for Molecular Medicine in the Helmholtz Association, Berlin, Germany

- A highly efficient, specific, and reversible means to manipulate protein levels in blood vasculature
- Potentially overcoming inherent limitations of conventional genetic tools
- Gaining novel mechanistic insights by leveraging high(er)- temporal resolution of perturbation