Vascular Biology 2023
Platform Presentations from Selected Abstracts

Springer Award Lecture

Hemodynamic regulated genes that alter vascular development
Jihui Lee PhD, Megan E Goeckel MS, Amber N Stratman PhD
Washington University in St. Louis, St. Louis, MO, USA

- CXCR3 in endothelial cells is down regulated by the onset of blood flow
- CXCR3 in endothelial cells helps promote recruitment of mural cells
- Activated CXCR3 inhibits angiogenesis

Hemogenic Endothelium/Endothelial Diversity

01
Deciphering the function of the N-glycan code during the endothelial-to-hematopoietic transition
Taylor S. Turner, Beatriz C. Mercado, Dionna M. Kasper Ph.D.
Dartmouth Geisel School of Medicine, Hanover, NH, USA

- Cell-surface proteins in endothelial cells are decorated with specific N-glycan sugar structures.
- Zebrafish mutants with an altered endothelial N-glycome have more hematopoietic stem cells (HSC).
- Loss of N-glycans from Adam10, a Notch-processing enzyme, alters HSC production.

02
A set of short-lived sprouting vein cells fuels rapid growth of the postnatal liver
D. Berfin Azizoglu Ph.D.[1,2], Roel Nusse Ph.D.[2]
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- The liver forms and vascularizes new functional units, termed lobules, after birth.
- Newly forming liver lobules are vascularized by the sprouting of hepatic vein cells.
- Sprouting rapidly declines and lobule addition ends in the neonate, constraining final liver size.

Pro-Inflammatory Signaling

03
Single cell transcriptional-epigenetic profiling and compartmental cellular proteomics demonstrate that HIV-Nef extracellular vesicles modulate human macrophage heterogeneity to promote atherosclerosis
Sarvesh Chelvanambi PhD[1], Julius Decano MD[1], Yoshihiro Yanagihara DVM[1], Amelie Jule PhD[2], Yuto Nakamura PhD[1], Shin Mukai PhD[1], Takashi Enomoto PhD[1], Constance Delwarde PhD[1], Francesa Bartoli-Leonard PhD[1], Prabhash Kumar Jha PhD[1], Adrien Lupieri PhD[1], Joan T Matamalas PhD[1], Takeshi Tanaka PhD[1], Diego Santinelli-Pestana MD[1], Rile Ge PhD[1], Mary Whelan[1], Katelyn Perez[1], Taku Kasai PhD[1], Shiori Kuraoka[1], Shannon Ho-Sui PhD[2], Abhijeet R Sonawane PhD[1], Sasha A Singh PhD[1], Elena Aikawa MD PhD[1], Masanori Aikawa MD PhD[1]
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- The HIV protein HIV-Nef within extracellular vesicles hijacks macrophage pro-inflammatory signaling.
- Network analysis of single cell multi-omics data to identify dysfunctional macrophages
- Validation studies show HIV-Nef impairs macrophage efferocytosis to accelerates atherosclerosis.

04

Increased endothelial levels of RNA binding protein Elavl1 (HuR) in atherogenic conditions post-transcriptionally defines cell phenotype and supports T cell survival

Sarah-Anne E. Nicholas M.S.[1], Stephen Helming M.S.[1], Jessica Hensel PhD[1], Christopher Pathoulas B.S.[1], Maria M Xu MD/PhD[1], Amy L Kimble B.S.[1], Antoine Menoret PhD[1], Brent Heineman B.S.[1], Evan R Jellison PhD[1], Bo Reese PhD[2], Beiyan Zhou PhD[1], Annabelle Rodriguez-Oquendo MD[1], Anthony Vella PhD[1], Patrick A Murphy PhD[1]
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- Endothelial splice factor Elavl1 reduces atherosclerotic plaque severity and CD8+ T cell numbers.
- Endothelial Elavl1 regulates alternative splicing and ribosomal loading of T cell survival factors.
- Endothelial Elavl1 is required for T cell survival post antigen stimulation.

Stem Cells/Organoids/In vitro models

05

Modeling the multicellular and flow control perspective of the blood-brain barrier

Ian C Harding[1], Nicholas R O'Hare[1], Ira M Herman[2], Eno E Ebong[1]
[1]Northeastern University, Boston, MA, USA. [2]Tufts University School of Medicine, Boston, MA, USA

- A robust blood-brain barrier and its intricate mechanosensitivity are successfully modeled in vitro.
- Pericytes, astrocytes, flow impact blood-brain barrier permeability via endothelial cell junctions.
- Pericytes, astrocytes, and flow impact blood-brain barrier permeability via endothelial glycocalyx.

06

Transcription factor-driven generation of human vascular organoids

Liyan Gong Ph.D.[1,2], Kai Wang Ph.D.[3,2], Allen Chilun Luo Master[3], Rui-Zeng Lin Ph.D.[1,2], Juan M. Melero-Martin Ph.D.[1,2,4]
[1]Department of Cardiac Surgery, Boston Children's Hospital of Cardiac Surgery, Boston, MA, USA. [2]Department of Surgery, Harvard Medical School, Boston, MA, USA. [3]Department of Cardiac Surgery, Boston Children's Hospital, Boston, MA, USA. [4]Harvard Stem Cell Institute, Cambridge, MA, USA

- Generation of vascular organoids by orthogonal activation of two TFs, ETV2 and NKX3.1.
- Our method allowed for the co-differentiation of iECs and iMCs in a 3D configuration, in 5 days.
- The VOs could engraft in vivo and serve as vascular therapeutic agents.

Blood Flow Regulation

07

Exercise training improves coronary vasodilation in the ischemic heart through recruitment of Kv7 channels

Trevor Self, Cristine Heaps
Texas A&M University, College Station, Texas, USA

- Exercise training presents as an effective therapeutic intervention for ischemic heart disease.
- Vascular adaptations to ischemic heart disease converge on voltage-gated potassium channels.
- Exercise training modulates Kv7 function to improve vasodilation in the ischemic heart.

08

Endothelial Pannexin1 overexpression impairs ischemic stroke outcome in a sex-dependent manner

Amanda K Mauro PhD[1], Maria Tomàs Gracia[1], Colleen K Duffy[1], Chris Medina[2], Kodi Ravichandran PhD[3], Brant E Isakson PhD[2], Miranda E Good PhD[1]
[1]Tufts Medical Center, Boston, MA, USA. [2]University of Virginia, Charlottesville, VA, USA. [3]Washington University School of Medicine, St. Louis, MO, USA

- Pannexin1 regulates cerebral vascular reactivity and inflammation and may mediate stroke recovery.
- Overexpression of endothelial Pannexin1 increases myogenic tone and infarct size in females.
- Female cerebrovascular function may be more sensitive to increased levels of endothelial Pannexin1.

Resolution of Inflammation

09

Meningeal lymphatic endothelial cell regulation of T cell function and migration

Aurora Kraus PhD, Daniel Castranova MS, Brant M Weinstein PhD
NIH/NICHD, Bethesda, MD, USA

- Immune-lymphatic interactions
- Lymphocyte migration
- Live-imaging of meninges

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Long noncoding RNA regulation of inflammation in atherosclerosis

Morgane Gourvest Ph.D., Jose Gabriel Barcia Durá Ph.D., Tracy Zhang BSc, Jesse Wang, Alexandra Newman Ph.D., Samantha Dupuis, Chiara Giannarelli MD, Ph.D, Coen van Solingen Ph.D, Kathryn J Moore Ph.D
NYU Cardiovascular Research Center, Leon H. Charney Division of Cardiology, Department of Medicine, New York University Langone Health, NYC, NY, USA

- LncRNA are key regulators of gene expression, prompting interest in their roles/ clinic potential
- The novel lncRNA Caslr is a key regulator of inflammatory signaling in plaque macrophages
- Caslr is evolutionarily conserved. Its targeting may be thus beneficial in treating atherosclerosis.

Vascular Malformations

11

Mek inhibition reduced vascular tumor growth and coagulopathy in a mouse model with hyperactive GNAQ

Elisa Boscolo PhD[1], Sandra Schrenk PhD[2]
[1]Cincinnati children's Hospital, Cincinnati, OH, USA. [2]Cincinnati children's Hospital, Cincinnati, OH, USA

- Gain-of-function GNAQ (p.Q209L) mutation in the endothelium causes vascular lesions in mice
- GNAQ (p.Q209L) expression in mouse endothelium increases ERK activation
- The formation of vascular lesions is inhibited by a treatment with a MEK inhibitor

12

Sirolimus in slow-flow vascular malformations: preliminary results of the European multicentric phase III trial

Emmanuel Seront MD, PHD[1], An Van Damme MD, PHD[1], Catherine Legrand[2], Annouk Bisdorff-Bresson MD[3], Philippe Orcel MD[4], Thomas Funck-Brentano MD[4], Marie-Antoinette Sevestre Pietri MD[5], Anne Dompmartin MD, PHD[6], Isabelle Quere MD[7], Nicole Revencu MD, PhD[1], Pascal Brouillard PhD[2], Frank Hammer MD[1], Philippe Clapuyt MD[1], Dana Dimitriu MD[1], Miikka Vikkula MD, PhD[1,8], Laurence Boon MD, PhD[1,2]
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Picardie, Amiens, France. [6]CHU Université Caen Normandie, Caen, France. [7]CHU Montpellier, Hôpital Saint Eloi, Montpellier, France. [8]de Duve Institute, Brussels, Belgium

- Clinical trial
- Venous malformation
- Lymphatic malformation

12a

iPSC-derived EC to model port wine birthmark in a microphysiological system

William Van Trigt PhD Candidate, Chris Hatch, Zee Piermatteo, Kristen Kelly MD, Christopher Hughes PhD
UC Irvine, Irvine, CA, USA

- iPSC-derived endothelial cells with the port wine birthmark GNAQ mutation form dilated microvessels.
- Mutant GNAQ endothelial cells recapitulate disease phenotype in a complex organ-on-chip model.
- Port wine birthmark lesions are formed by intrinsic aberrant angiogenic signaling.

Cardiovascular Cell Biology

13

Obesity in angiogenesis and regenerative lung growth

Tendai Hunyenyiwa, Priscilla Kyi, Tadanori Mammoto, Akiko Mammoto
Medical College of Wisconsin, Milwaukee, Wisconsin, USA

- Post-PNX lung growth is inhibited in obese mice.
- Post-PNX increases in the levels of angiogenic factors are inhibited in obese mouse lungs.
- Twist1 and VEGF signaling may contribute to the inhibition of angiogenesis in an obese condition.

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First proximity proteomic map of vascular CaV1.2

Aaron Rodriques PhD, Jared Kushner
Columbia University, New York, New York, USA

- Calcium channels are essential for generating vascular tone. Still, channel complex is ill-defined.
- Protein interactions are hard to identify for in membranes and in small tissues like microvessels.
- Here we adapt proximity proteomics to identify the Calcium channel domain in rat blood vessels.

Lymphatic Development

15

Inhibiting Foxc2 to dampen epsin expression mitigates obesity and lymphedema

Hong Chen PhD[1], Kui Cui PhD[2]
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- High fat diet induces Foxc2 in LEC which activates epsins expression to downregulate VEGF signaling
- Foxc2 halts capillary to collecting LEC transition and button to zipper conversion to fuel obesity.
- Loss of Foxc2 enhances lymphangiogenesis, improves obesity-associated lymphedema resolution.

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Requirement for lymphatic endothelial Notch4 in murine male livers

Glicella M Salazar-De Simone PhD[1], Joseph D McCarron BS[1], Raine-Monet S Williams[2], Utpal B Pajvani MD[1], June K Wu MD[1], Carrie J Shawber PhD[1]

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- Canonical Notch signaling is enriched in the murine hepatic lymphatic endothelium.
- Loss of postnatal LEC Notch4 was associated with liver fibrosis males, but not females.
- Notch inhibition was associated with reduced portal lymphatic hyperplasia in a murine NASH model.

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Piezo2 regulation of lymphangiogenesis

Zuzanna J Juśkiewicz MS[1,2], Melissa A Luse MS[1,2], Luke S Dunaway PhD[1], Skylar A Loeb BS[1,2], Brant E Isakson PhD[1,2]

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- Piezo2 is a marker of lymphatic capillary vessels.
- Piezo2 regulates expression of Vegfr3 in lymphatic capillary endothelium.
- Piezo2 affects weight gain.

18

Rictor induces AKT signaling to regulate lymphatic valve formation and maintenance

Richa Banerjee MS[1], Luz A Knauer[1], Drishya Iyer PhD[1], Sara E Barlow[1], Joshua P Scallan PhD[2], Ying Yang PhD[1]

[1]University of South Florida, Tampa, Florida, USA. [2]University of South Florida, Tampa, Florida, USA

- Rictor regulates the formation and maintenance of lymphatic valves
- Rictor deletion increases nuclear Foxo1 expression in lymphatic endothelial cells.
- Foxo1 deletion rescues lymphatic valve defects by promoting the growth of new valves.

Systemic Inflammatory Networks

19

Pro-inflammatory macrophage IL-12 and IL-23 modulate vascular smooth muscle cell differentiation via the histone methyltransferase SETD4

Kevin D Mangum MD, PhD, Amrita Joshi PhD, Sonya Wolf PhD, Emily Barrett MD, Bethany B Moore PhD, Frank M Davis MD, Katherine A Gallagher MD

University of Michigan, Ann Arbor, MI, USA

- Diabetes is associated with increased risk of vascular disease (e..g, restenosis).
- The histone methyltransferase SETD4 is increased in diabetic SMC and inhibits SMC gene expression
- IL-12 and IL-23 upregulate SETD4 expression and negatively regulate SMC gene expression

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Adipocyte extracellular vesicles mediate obesity-accelerated atherosclerosis

Dharti Shantaram MS, Valerie P Wright BA, Joey Liu PhD, Xilal Y Rima PhD, Jacob Doon-Ralls BS, Eduardo Reategui PhD, Willa Hsueh MD

The Ohio State University, Columbus, OH, USA

- Adipose tissue inflammation accelerates atherosclerosis in obesity.
- Extracellular vesicles mediate metabolic complications like atherosclerosis and insulin resistance.
- Adipocyte extracellular vesicles activate immune cells that mediate inflammation in obesity.

Mechanical Forces and the Vasculature

21

DLC1 promotes mechanotransductive feedback for YAP via Rho GAP-mediated focal adhesion turnover

Aukie Hooglugt[1], Miesje van der Stoel[1], Apeksha Shapeti[2], Hans van Oosterwyck[2], Reinier Boon[1], Stephan Huveneers[1]
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- DLC1 is a direct target of YAP/TAZ signaling and drives collective migration and sprouting.
- DLC1 provides mechanotransductive feedback for YAP transcriptional activity.
- Signaling through the RhoGAP domain of DLC1 limits intracellular tension at focal adhesions

22

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

Emerging Topics in Mircocirculation

23

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

Shinya Ishiko M.D., Ph.D, 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.

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

Jamie E Meegan PhD, 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).

Aging, Metabolism and the Vasculature

25

Nucleoporin93 (Nup93) limits YAP activity to prevent endothelial cell senescence and dysfunction

Tung D Nguyen[1,2], Mihir K Rao[1], Shaiva P Dhyani[1], Justin M Banks[1], Michael A Winek[1], Monica Y Lee PhD[1,2]
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- Nucleoporin93 (Nup93) expression is critical for endothelial cell health by limiting YAP activity
- Inhibiting YAP activity in Nup93-null ECs attenuates aspects of cell senescence and inflammation
- Aging may involve the loss of endothelial Nup93 as a mechanism of EC senescence and dysfunction

26

The VEGF-A isoforms switch and opposing VEGF receptors binding as mechanisms of impaired inflammatory angiogenesis in the context of advanced aging.

Chris S Mantsounga PhD, Sheila Sharma Master, Julia Pierce BS, Jade C Neverson BS, Rachel Carley Pharm D, Crystal Perry BS, Olivya Caballero BS, Elizabeth Amelotte PhD, Elizabeth O Harrington PhD, Frank Sellke MD, Gaurav Choudhary MD, Alan R Morrison MD PhD
Providence VA Medical Center, Providence, RI, USA

- Uncoupling of IL-1beta and VEGF-A in inflammatory angiogenesis in the context of Aging
- VEGF-A isoforms switch
- VEGF-A receptors signal differently based on VEGF-A or VEGF-A isoforms involved in the signaling.

Adv. Engineering Models & Imaging Techniques

27

Advancing custom patterned vessels in engineered human myocardium as a revascularization co-therapy for heart regeneration

Rajeev J Kant PhD, Stephanie M Roser ScM, Kiera D Dwyer BS, Anaya Kaul, Evan Ren, Collin Polucha BS, Kareen LK Coulombe PhD
Brown University, Providence, RI, USA

- New therapies for heart failure with reduced ejection fraction are urgently needed.
- We developed patterned arteriole-scale channels in vascularized engineered human myocardium (vEHM).
- Host vessels connect to perfused vEHM to increase vessel and cardiomyocyte density in the MI heart.

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Perfusable vascular organoids for blood-brain barrier modeling

Yu Jung Shin, Ying Zheng
University of Washington, Seattle, Washington, USA

- Utilizing vascular organoids and microfluidic vessels for modeling perfusable vasculature in vitro.
- Investigating blood vessel development and remodeling under defined pressure and flow.
- Understanding acquisition of blood-brain barrier phenotype in vascular organoids.

3D Imaging and Organotypic Vasculature

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Defining the cellular complexity of the zebrafish bipotential gonad

Michelle E Kossack PhD, Lucy Tian BS, Kealyn Bowie BS, Jessica S Plavicki PhD
Brown University, Providence, RI, USA

- The zebrafish bipotential gonad is vascularized
- Vascular and lymphatic endothelial cells are present in the zebrafish biopotential gonad.
- The gonadal artery supplies blood to the zebrafish biopotential gonad.

30

Human bone-specific endothelial cells mediate osteogenesis via KIT ligand

Xiang Li Ph.D.[1,2], Hwan D. Kim Ph.D.[1,2,3], Allen C. Luo M.S.[1], Nathaniel S. Hwang Ph.D.[4], Ruei-Zeng Lin Ph.D.[5,2], Juan M. Melero-Martin Ph.D.[5,2,6]
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- Human bone arteriole endothelial cells (ECs) are endowed with unique osteoinductive properties.
- KITLG of bone ECs enables the recruitment of hematopoietic progenitor cells to mediate osteogenesis.
- The mechanism of osteogenesis via tissue-specific EC can benefit effort for bone tissue engineering.

Vascular Biomaterials and Bioengineering

31

Growth of an engineered vascular graft in simulated repair of absent pulmonary artery branch

Zeeshan H Syedain PhD[1], Gurumurthy Hiremath MD[1], John P Carney[1], Jill Schappa Faustich DVM[1], Tate Shannon BS[1], Andrea Rivera[1], Richard Bianco[1], Robroy MacIver MD[2], John Mayer MD[3], Robert T Tranquillo PhD[1]
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- The growing TEVG implanted into a pulmonary artery allows for near-normal vascular growth.
- The non-growing ePTFE graft implanted into a pulmonary artery causes abnormal vascular growth.
- Perturbation of hemodynamic growth signals associated with a 50-50 flow split is OK if transient.

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Sex differentiating factors in the pathophysiology of human ascending aortic disease

Soheila AA Ghavimi PhD[1,2], Ryan N Martinez MS[1], Colin Flaherty[1], Lana Vogler[1], Arianna Antigua[1], Amarri Harrison BS[1], Kim I de la Cruz MD[1,2], Marie Billaud PhD[1,2]
[1]Brigham & Women's Hospital, Boston, MA, USA. [2]Harvard Medical School, Boston, MA, USA

- Ascending aortic aneurysms affect more men than women, yet kill more women than men.
- The proteomic profile of aneurysmal aortic specimens from men is distinct from that of women.
- Primary SMC isolated from men and women aneurysmal aortas respond differently to ECM substrates.

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Precision nanomedicine targeting novel endothelial mechano-sensing mechanisms to treat vascular diseases

Yun Fang

University of Chicago, Chicago, IL, USA

- Precision nanomedicine platforms to target dys-regulated endothelial mechano-sensing mechanisms.
- Polymer or liposome-based nanoparticles to deliver therapeutic nucleotides .
- VCAM1-targeting liposomes effectively delivered functional mRNAs to promote vascular health.

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Biophysical rejuvenation of mesenchymal stem cells for enhancing vascular regeneration

Miles Massidda PhD, Andrei Demkov, Aiden Sices, Jason Lee PhD, Muyoung Lee, Jonghwan Kim PhD, Aaron Baker PhD

University of Texas at Austin, Austin, TX, USA

- Mechanical conditioning leads to a increase in proliferation and expansion potential in MSCs.
- Mechanical conditioning reduces senescence in MSCs from elderly patients.
- Mechanical conditioning leads to rapid enhancement of DNA damage repair mechanisms.

Neurovascular Unit and Disease

35

Hypoxia acts as an accelerant of Cerebral Cavernous Malformations disease through neuroinflammation signaling

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- Hypoxia accelerates CCM by increasing angiogenesis, neuroinflammation, and vascular thrombosis
- CX3CR1-CX3CL1 signaling pathway contributes to heterogeneity in CCM
- CX3CR1 could be a potential marker for CCM aggressiveness

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Moderately advanced age exacerbates neuroinflammation, blood-brain barrier leakage, and behavioral deficits in a mouse model of COVID-19

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- Patients with Long Covid experience neurological defects such as delirium, confusion, and headaches.
- Acute, mild SARS-CoV-2 infection and age exacerbates blood-brain barrier leakage and gliosis.
- Using MA10 SARS-CoV-2, mice exhibited motor-coordination and neurological deficits.

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Combined single-cell and intranuclear CITE-seq reveals transcriptional association of reduced TDP-43 in brain vascular endothelial cells

Omar Fathy MS[1], Amy Kimble MS[1], Ashok Cheemala PhD[1], Swati Pandey BA[1], Qian Wu MD[1], Evan Jellison PhD[1], Bo Reese PhD[2], Patrick Murphy PhD[1]

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- A novel technique for enriching endothelial cell nuclei for single-nucleus profiling.
- Co-measurement of nuclear proteins and transcriptomes at the single-cell level
- A reactive capillary population associated with low TDP-43 and inflammatory signaling

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Targeting metabolic alterations to prevent moyamoya-like cerebrovascular disease

Callie Kwartler PhD[1], Anita Kaw MD/PhD[1], Jose Emiliano Esparza Pinelo BS[1], Amelie Pinard PhD[2], Hannah Krenz[1], Caroline Kernell BA[3], Dianna Milewicz MD/PhD[1]

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- Acta2 p.R179 variants cause moyamoya-like disease and lead to immature smooth muscle cells (SMCs)
- Nicotinamide riboside (NR) restores differentiated SMC phenotype in Acta2 p.R179 SMCs
- An RNF213 variant that causes moyamoya disease leads to similar SMC phenotypes that respond to NR

Inflammation in Cancer

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The oral bacterium *Streptococcus mutans* promotes tumor metastasis by inducing vascular inflammation and thrombosis

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- Oral bacteria invade the blood circulation and induce inflammation in endothelial cells
- Endothelial inflammation disrupts vascular integrity and pro-thrombosis formation
- Vascular inflammation and thrombosis promote tumor cell metastasis to distant organs

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Circulating factors as key contributors to endothelial dysfunction following anticancer therapy

Stephen T Hammond PhD[1], Janée D Terwoord PhD[2,1], Yoshinori Nishijima PhD[1], Shelby N Hader MS[1], Erin Birch BS[1], Andreas M Beyer PhD[1]

[1]Medical College of Wisconsin, Milwaukee, WI, USA. [2]Rocky Vista University, Ivins, UT, USA

- Anticancer therapy (CTx) induces microvascular dysfunction via unestablished mechanisms.
- We found that circulating nucleotides contribute to the onset of these abnormalities.
- Pretreatment with a nucleotide scavenger reversed CTx-induced microvascular dysfunction.

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Endothelial cell-selective adhesion molecule alters tumor microenvironment and promotes tumor growth in a mouse model of diastolic heart failure

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[1]Augusta University, Augusta, GA, USA. [2]Augusta, University, GA, USA. [3]Augusta University, Augusta, GA, USA

- Incidence of multiple types of cancer is significantly higher in heart failure
- In heart failure pro-inflammatory tumor microenvironment promotes tumor growth.
- ESAM may act to promote tumor angiogenesis, neutrophil and MDSCs tumor infiltration.

Plasticity of the Vasculature

43

Cell cycle-dependent regulation of endothelial cell chromatin availability and transcription factor activity during arterial-venous specification

Nicholas W Chavkin PhD, Karen K Hirschi PhD
University of Virginia, Charlottesville, VA, USA

- Endothelial cell chromatin availability is regulated in a cell cycle-dependent manner.
- E2F and SOX binding motifs are differentially available in cell cycle states of endothelial cells.
- E2F and SOX family members are predicted to activate arterial and venous genes, respectively.

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Evolutionarily conserved mechanisms drive ontogeny and arterial endothelial *heterogeneity of the lung vasculature*

Prashant Chandrasekaran PhD[1], MinQi Lu MB[1], Hongbo Wen BS[1], Nigel Michki PhD[1], Annabelle Jin[1], Wenli Yang PhD[2], David B Frank MD, PhD[1]
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- Cardiopulmonary progenitor cells give rise cardiac lineages and all mesodermal lineages of the lung.
- Single cell transcriptomics deciphers arterial endothelial heterogeneity and early CPP commitment.
- CPP differentiation is evolutionarily conserved.

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Hematopoietic potential of the endocardium in zebrafish embryos

Suman Gurung, Nicole K. Restrepo, Saulius Sumanas
University of South Florida, Tampa, FL, USA

- Endocardium gives rise to neutrophils in zebrafish
- Endocardial hematopoiesis is not dependent on Etv2/Etsrp or Scl/Tal1 function
- Hedgehog signaling and Gata5/6 function are required for endocardial hematopoiesis

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Non-canonical telomerase reverse transcriptase controls osteogenic reprogramming of aortic valve cells through STAT5

Rolando A Cuevas PhD[1], Luis Hortels PhD[2], Claire Claire Chu Bs[1], Ryan Wong Bs[1], Alex Crane Bs[1], Camille Boufford Bs[1], Cailyn Regan Bs[1], William J Moorhead Bs[1], Michael J Bashline MD[1], Aneesha Parwal Bs[1], Angelina M Parise Bs[1], Parya Behzadi PhD[1], Mark J Brown Bs[1], Aditi Gurkar PhD[1], Dennis Bruemmer MD[3], John Sembrat[1], Ibrahim Sultan MD[1], Thomas Gleason MS[1], Marie Billaud PhD[4], Cynthia St. Hilaire PhD[1]
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- Calcific aortic valve disease is the most prevalent form of aortic valve pathology.
- Genetic loss or depletion of telomerase reverse transcriptase blocks calcification.
- Telomerase TERT and STAT5 are novel initiators of osteogenic reprogramming in valve cells.

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Molecular signature of smooth muscle cell expansion in hypoxia-induced pulmonary hypertension: identification of Cthrc1 as a possible target

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- Pulmonary hypertension (PH) involves excess smooth muscle cell (SMC) proliferation and migration.
- Single cell RNA sequencing delineates molecular signature of SMC expansion during PH progression.
- Cthrc1 is a potential target for PH, regulating pulmonary arteriole hypermuscularization.

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Longitudinal mapping of lung regeneration reveals the emergence of injury-associated endothelial cell states

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- Pulmonary endothelial cells respond strongly to interferon signaling after viral lung injury
- The pulmonary endothelium is highly plastic, with multiple cell states arising during regeneration
- Endothelial cell proliferation is important for lung regeneration