22ND INTERNATIONAL VASCULAR BIOLOGY MEETING
OCTOBER 13-17, 2022
SHORT TALK PRESENTATIONS FROM SELECTED ABSTRACTS

VASCULAR MALFORMATIONS

001 Neuroinflammation plays a critical role in brain vascular malformations

Gallego-Gutierrez, Helios[1]; Frias-Anaya, Eduardo[1]; Nelsen, Bliss[1]; Lai, Catherine, C[1]; Orecchioni, Marco[2]; Herrera, Victoria[1]; Ortiz, Elan; Sun, Hao[1]; Mesarwi, Omar[1]; Ley, Klaus[2]; Gongol, Brendan[3]; Lopez-Ramirez, Miguel, A[1]
1. University of California, San Diego, San Diego, California, USA
2. La Jolla Institute for Immunology, San Diego, California, USA
3. University of California, Riverside, Riverside, California, USA

- Neuroinflammatory astrocytes and CCM brain endothelium trigger leukocyte recruitment in CCM lesions
- Leukocyte recruitment into mature active CCM lesions propagate lesion growth and immunothrombosis
- Inhibition of endothelial NFkB activity increases number of lesions and immunothrombosis during CCM

002 The secret agent of endothelial cells - Fibroblasts in PI3K-driven vascular lesions

Laakkonen, Johanna[1]
1. A.I. Virtanen Institute for Molecular Sciences, Kuopio, Finland

- Targeting of intervascular stromal cells can be a potential treatment strategy for vascular lesions
- Oncogenic PI3KCA variant induces growth factor secretion from fibroblasts paracrinally
- Fibroblasts regulate in part PI3K-driven lesion vascularization

SMOOTH MUSCLE CELLS

003 Single-cell and spatially resolved transcriptome analysis reveals cellular heterogeneities and novel regulators of atherosclerotic plaque destabilization

Pauli, Jessica[1]; Wu, Zhiyuan[1]; Yokota, Chika[2]; Paloschi, Valentina[1]; Sachs, Nadja[3]; Winski, Greg[1]; Winter, Hanna[1]; Fasolo, Francesca[1]; Dueck, Anne[4]; Engelhardt, Stefan[4]; Eckstein, Hans-Henning[3]; Maegdefessel, Lars[1]
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4. Institute of Pharmacology and Toxicology, TUM, Munich, Germany

- Establishing a combined workflow for scSeq and total RNA sequencing to identify novel lncRNA targets
- Using spatial transcriptomics approaches to locate novel lncRNA targets in atherosclerotic lesions
- Translate key findings into in vivo models of plaque rupture (ApoE-/- mouse)

004 β-catenin C-terminal signaling induces sphingosine-1-phosphate receptor 1 expression to promote vascular remodeling

Oliveira de Paula, Gustavo[1]; Ressa, Gaia[1]; Almonte, Vanessa[1]; Parikh, Dippal[1]; Valenta, Tomas[2]; Basler, Konrad[2]; Riascos-Bernal, Dario[1]; Sibinga, Nicholas[1]
1. Albert Einstein College of Medicine, New York, USA
2. University of Zurich, Zurich, Switzerland

- The aim of this study was to define the importance of β-catenin C-terminus in vascular remodeling
- We found that β-catenin C-terminus drives neointima formation after injury by up-regulating S1PR1
- Our results define an essential β-catenin C-terminus/S1PR1 axis that promotes vascular remodeling

STEM CELLS

005 Deciphering the function of the N-glycan code during the endothelial-to-hematopoietic transition

Turner, Taylor, S1; Mercado, Beatriz, C1 Binder, Julia, N1; Kasper, Dionna, M[1]
1. Dartmouth Geisel School of Medicine, Hanover, New Hampshire, USA

- Cell-surface proteins in endothelial cells are decorated with specific N-glycan sugar structures
- Zebrafish mutants with an altered endothelial N-glycan code have more hematopoietic stem cells (HSC)
- N-glycan loss from Notch-processing enzyme Adam10 promotes HSC formation from endothelial cells

006 Endoderm-derived endothelial cells constitute a stem cell niche in zebrafish

Nakajima, Hiroyuki[1]; Ishikawa, Hiroyuki[1]; Stainier, Didier[2]; Mochizuki, Naoki[1]
1. National Cerebral and Cardiovascular Research Institute, Suita, Osaka, Japan
2. Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

- We found a novel progenitor population for zebrafish endothelial cells
- We revealed a novel mechanism for endothelial specialization regulated by cell lineage
- We have visualized processes of endothelial differentiation in living zebrafish

VASCULAR CELL-MATRIX INTERACTIONS

007 The integrin inhibitor SHARPIN regulates endothelial permeability via balancing cell-cell and cell-matrix adhesion

Pink, Anne[1]; Kiss, Elina[1]; von Wright, Ylva[1]; Hakanpää, Laura[2]; Peuhu, Emilia[3]; Ivaska, Johanna[4]; Saharinen, Pipsa[1]
1. Translational Cancer Medicine Program, University of Helsinki, Helsinki, Finland
2. Helsinki Institute of Life Science, University of Helsinki, Helsinki, Finland
3. Institute of Biomedicine, University of Turku, Turku, Finland
4. Turku Bioscience Centre, University of Turku and Abo Akademi University, Turku, Finland

- SHARPIN regulates endothelial permeability via balancing cell-cell and cell-matrix adhesion
- SHARPIN deficiency sensitizes the vasculature to VEGF- and inflammation-induced vascular leakage
- Increased integrin activity plays a role in thresholding the endothelial permeability response

008 Structural and functional consequences of deficiency of the elastogenic proteins, fibulin-4 and fibulin-5, on resistance arteries

Lin, Michelle[1]; Roth, Robyn, A[1]; Yanagisawa, Hiromi[2]; Halabi, Carmen, M[1]
1. Washington University School of Medicine in St. Louis, St. Louis, Missouri, USA
2. University of Tsukuba, Tsukuba, Japan

- Fibulin-5, but not fibulin-4, is required for external elastic lamina formation in small arteries
- Either fibulin-4 or fibulin-5 deficiency leads to endothelial dysfunction in resistance arteries
- Fibulin-5, but not fibulin-4, deficiency leads to resistance artery hypercontractility

SYSTEMS APPROACH TO TARGET DISCOVERY

009 Systems approach to evaluate circulating extracellular vesicles containing HIV-Nef as a mechanism for promoting chronic inflammation in cardiac and hepatic monocytes/macrophages

Chelvanambi, Sarvesh, N[1]; Zimmer, Jonas[1]; Ge, Rile[1]; Kasai, Taku[1]; Singh, Sasha, A[1]; Aikawa, Elena[1]; Aikawa, Masanori[1]
1. Brigham And Women's Hospital, Boston, Massachusetts, USA

- HIV-Nef extracellular vesicles contributes towards cardio-metabolic inflammation in mice
- Systems approach shows changes in organ specific signaling in cardiac & hepatic monocyte/macrophage
- Plasma EV proteomics suggests EV cargo contributes towards chronic systemic inflammation

010 Endothelial cell metabolism in heart failure: a gene prioritisation system-level approach

Pasut, Alessandra[1]; Subramanian, Abhishek[1]; Cuijpers, Ilona[1]; Jones, Elizabeth, A[1]; Dewerchin, Mieke[1]; Carmeliet, Peter[1]

1. KULeuven, Leuven, Belgium

- HFpEF is the most common form of HF and it is also characterised by endothelial cell dysfunctions
- Here, we describe a system-level approach for the prioritisation of therapeutically relevant genes
- Oxidative stress, lipids and cholesterol synthesis are major co-regulated pathways in ECs in HFpEF

Translational Approaches to Vascular Pathology and Regeneration

011 Endoluminal biopsy for molecular classification of human brain arteriovenous malformations

Winkler, Ethan, A[1]; Wu, David[1]; Gil, Eugene[1]; Sun, Zhengda[1]; Ross, Jayden[1]; Kim, Helen[1]; Weinsheimer, Shantel[1]; Nowakowski, Tomasz[1]; Lim, Daniel[1]; Abla, Adib[1]; Cooke, Daniel[1]

1. University of California San Francisco, San Francisco, CA, USA

- Endoluminal biopsy allows molecular substratification of human vascular lesions in living patients
- Endovascular biopsy isolates endothelium to perform genomic analyses without need for surgery
- Endoluminal biopsy may allow applications of precision medicine to human cerebrovascular dieseases

Cell-Cell Interactions

012 Endothelial connexin 43 hemichannels promote Ca2+ influx and hyperpolarization in the regulation of arteriolar resistance

Duran, Walter[1]; Lillo, Mauricio, A[1]

1. Rutgers University, Newark, NJ, USA

- New endothelial ion-permeable channels regulating vasomotor tone
- New ion channels play a role in endothelial hyperpolarization in resistant arteries
- Connexin Hemichannels are a new putative target for hypertension disease

013 Normal-to-tumor vascular transition in the periphery of glioblastoma is dependent on VEGFR2 signaling

Kim, Injune[1]; Lee, Eunhyeong[1]; Llaiqui, Melissa[1]; Baek, Seung Eun[1]

1. Korea Advanced Institute of Science and Technology, Daejeon, Korea (Republic of)

- New GBM mouse models represent grade IV histopathologic features and peripheral invasion
- Brain vessels undergo normal-to-tumor transition in GBM invading zone
- Pathologic vascular remodeling in GBM is dependent on VEGFR2 signaling

Vascular Heterogeneity

014 Human and murine single-cell RNA sequencing reveals fibroblast heterogeneity in healthy and diseased vasculature and differential regulation by ageing and serum cholesterol

Van Kuijk, Kim[1]; McCracken, Ian[2]; Tillie, Renée[1]; Asselberghs, Sebastiaan[1]; Kheder, Dlzar[1]; Muitjens, Stan[1]; Jin, Han[1]; Taylor, Richard[2]; Wichers Schreur, Ruud[1]; Kuppe, Christoph[3]; Dobie, Ross[2]; Ramachandran, Prakash[2]; Gijbels, Marion[1]; Temmerman, Lieve[1]; Kirkwood, Phoebe[2]; Luyten, Juliën[1]; Li, Yanming[4]; Noels, Heidi[3]; Goossens, Pieter[1]; Wilson-Kanamori, John[2]; Schurgers, Leon[1]; Shen, Ying[4]; Mees, Barend[1]; Biessen, Erik[1]; Henderson, Neil[2]; Kramann, Rafael[3]; Baker, Andy[2]; Sluimer, Judith[1]

1. Maastricht University Medical Center, Maastricht, Netherlands
2. University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland
3. RWTH Aachen University, Aachen, Germany
4. Baylor College of Medicine, Houston, USA

- We validated two adventitial fibroblast markers across human and murine arteries
- Fibroblast heterogeneity is evident in health and cardiovascular disease, in humans and mice
- Fibroblast clusters are differentially regulated by CVD risk factors ageing and hypercholesterolemia

015 Endothelial cell type-specific angiogenesis drives intra-organ vessel phenotypic heterogeneity in the brain

Parab, Sweta[1]; Card, Olivia, A[1]; Buck, Luke, D[1]; Quick, Rachael, E[1]; Horrigan, William[1]; Vanhollebeke, Benoit[2]; Matsuoka, Ryota[1]

1. Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, USA

2. Université Libre de Bruxelles, Gosselies, Belgium

- Endothelial cell type-specific angiogenesis as a mechanism leading to brain vessel heterogeneity
- Regulatory and regional differences of angiogenic mechanisms across fenestrated brain vascular beds
- Identification of key regulators of fenestrated endothelial type-specific angiogenesis in the brain

VASCULAR AGING

016 RGS5 controls heart function by regulating pericyte biology

Tamiato, Anita[1]; Tombor, Lukas, S[1]; Fischer, Ariane[1]; Muhly-Reinholz, Marion[1]; Neitz, Jessica[1]; Guenther, Stefan[2]; John, David[1]; Wettschureck, Nina[2]; Luxan, Guillermo[1]; Dimmeler, Stefanie[1]

1. Institute of Cardiovascular Regeneration, Goethe University Frankfurt, Frankfurt am Main, Germany

2. Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

- RGS5 is an active player regulating pericyte biology and controlling heart function
- Ageing induces microvasculature remodeling in the heart characterized by pericyte coverage reduction
- RGS5 expression is reduced in the old heart and regulates PDGFRb signaling in pericytes

017 The role and regulation of SOX9 in ageing vascular smooth muscle cells

Faleeva, Maria[1]; Cox, Susan[1]; Shanahan, Cathy[1]

1. Kings College London, London, United Kingdom of Great Britain and Northern Ireland

- SOX9 is expressed continuously in the aorta but changes its localisation with ageing
- SOX9 downregulates VSMC contractility and increases synthesised matrix stiffness
- SOX9 regulates its transcriptional activity and nuclear localisation via mechanosignalling

VASCULAR-IMMUNE INTERFACE IN CANCER

018 Notch signaling in tumor endothelial cells programs cancer-associated fibroblasts to suppress anti-tumor T cell immunity

Zhu, Yu[1]; Xiang, Menglan[1]; Brulois, Kevin[1]; Lazarus, Nicole[1]; Pan, Junliang[1]; Butcher, Eugene[1]

1. Stanford University, Palo Alto, California, USA

- ECs in pancreatic cancer (PDAC) upregulate Notch to inhibit T cell immunity & promote tumor growth
- Loss of Notch in ECs reprograms cancer fibroblasts to enhance T cell recruitment via CXCL10/CXCR3
- Loss of Notch in ECs enhances IFNg responses and sensitizes PDAC to PD1-based immunotherapy

019 Endothelial Rap1B mediates T-cell exclusion to promote tumor growth – a novel mechanism underlying vascular immunosuppression

Sharma, Guru Prashad[1]; Kosuru, Ramoji[1]; Lakshmikanthan, Sribalaji[1]; Zheng, Shikan[1]; Chen, Yao[1]; Burns, Robert[1]; Xin, Gang[1]; Cui, Weiguo[1]; Chrzanowska, Magdalena[1]

1. Blood Research Institute, Versiti, Milwaukee, USA

- Endothelial Small GTPase Rap1B promotes pathological angiogenesis and tumor growth
- Rap1B restricts endothelial proinflammatory response and endothelial-leukocyte interactions
- Rap1B is a key mediator of VEGF-dependent endothelial desensitization to proinflammatory stimuli

DYSLIPIDEMIA AS CARDIOVASCULAR RISK

020 Transcriptomic analysis reveals that lipid loading of distinct intimal myeloid cell subpopulations precedes inflammation in early atherogenesis

Scipione, Corey, A[1]; Hyduk, Sharon, J[1]; Polenz, Chanele, K[2]; Althagafi, Marwan, G[1]; Ibrahim, Hisham, M[2]; MacParland, Sonya, A[1]; Cybulsky, Myron, I[1]

1. University Health Network, Toronto, Ontario, Canada

2. University of Toronto, Toronto, Canada

- The normal and atherosclerotic mouse aortic intima contains multiple myeloid cell subsets
- 5-day CRD feeding elevates signatures of lipid loading, but not inflammation in the aortic intima
- In early atherosclerosis, Ccr2+ myeloid cells, rather than foamy macrophages, drive inflammation

021 Pericentrin deficiency in smooth muscle cells leads to augmented phenotypic modulation and atherosclerosis

Majumder, Suravi[1]; Chattopadhyay, Abhijnan[1]; Wright, Jamie, M[1]; Kwartler, Callie, S[1] Milewicz, Dianna, M[1]

1. The University of Texas Health Science Centre at Houston, Houston, Texas, USA

- SMC specific pericentrin loss of function leads to atherosclerosis
- Pericentrin deletion augments HMGCR induced cholesterol synthesis in SMC via HSF1
- Loss of pericentrin induces ER stress induced SMC phenotypic modulation

MECHANOTRANSDUCTION

022 Alignment with flow induces an apical planar polarity to promote endothelial cell resilience via localized signaling domains

Ashby, Julianne, W1; Chattopadhyay, Eesha1; Hong, Soon-Gook1; Kennelly, John, P2; Davidson, Nicholas1; Fang, Jiexuan1; Gallagher-Jones, Marcus3;

Mack, Julia, J[1]

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2. University of California, Los Angeles/ Pathology and Laboratory Medicine, Los Angeles, California, USA

3. University of California, Los Angeles/ QCB, Los Angeles, California, USA

- Laminar flow promotes endothelial resilience via plasma membrane asymmetry and localized signaling
- Endothelial cell body elongation induces an apical planar polarity with respect to flow direction
- Polarity enables localized subcellular signaling to promote vasodilation and suppress inflammation

023 Novel mechanical regulation of angiogenesis: intraluminal pressure restricts wound angiogenesis

Yuge, Shinya[1]; Nishiyama, Koichi[2]; Arima, Yuichiro[3]; Hanada, Yasuyuki[4]; Oguri-Nakamura, Eri[1]; Sanshiro, Hanada[3]; Ishii, Tomohiro[1]; Wakayama, Yuki[5]; Hasegawa, Urara[6]; Tsujita, Kazuya[7]; Yokokawa, Ryuji[8]; Miura, Takashi[9]; Itoh, Toshiki[7]; Tsujita, Kenichi[3]; Mochizuki, Naoki[5]; Fukuhara, Shigetomo[1]

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2. University of Miyazaki, Miyazaki, Japan

3. Kumamoto University, Kumamoto, Japan

4. Nagoya University, Nagoya, Japan

5. National Cerebral and Cardiovascular Center Research Institute, Osaka, Japan

6. The Pennsylvania State University, University Park, Pennsylvania, USA

7. Kobe University, Kobe, Japan

8. Kyoto University, Kyoto, Japan

9. Kyushu University, Fukuoka, Japan

- Live Imaging of angiogenesis in wound healing in the adult zebrafish
- Endothelial cells are stretched by intraluminal pressure
- TOCA family of F-BAR proteins plays a pivotal role in sensors for mechanical cell stretching

ARTERIAL DISEASES

024 Interrogation of the role of androgens and their antagonists in the pathogenesis and treatment of Vascular Ehlers-Danlos Syndrome (VEDS)

Juzwiak, Emily[1]; Bowen, Caitlin[1]; Zeng, Anthony[1]; Dietz, Harry, C[1]
1. Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

- Males with VEDS are at a higher risk of arterial rupture and death during puberty than females
- Androgen receptor perturbation improves survival in VEDS mice through ERK signaling inhibition
- Mineralocorticoid receptor inhibition improves survival in VEDS mice

025 Elastin denudation underlies early aortic degeneration in Loeys-Dietz syndrome 3

Yin, Hao[1]; Nong, Zengxuan[1]; Balint, Brittany[1]; Manian, Usha[1]; Wang, Mofei[1]; O'Neil, Caroline[1]; Samsoondar, Joshua, P[1]; Zhao, Pei Jun[1]; Chu, Michael, W[1]; Pickering, J. Geoffrey[1]
1. Western University, London, Ontario, Canada

- Minimally dilated ascending aortas in LDS3 patients have reduced elastin-associated microfibrils
- Minimally dilated LDS3 ascending aortas have aberrant smooth muscle cell-elastin separation
- Transcriptomics of LDS3 aortic SMCs reveals perturbed microfibril expression and assembly profiles

VASCULAR DIFFERENTIATION

026 Differential Etv2 threshold requirement for endothelial and erythropoietic development

Sinha, Tanvi[1]; Lammerts vanBueren, Kelly[1]; Dickel, Diane, E[2]; Zlatanova, Ivana[1]; Thomas, Reuben[3]; Lizama, Carlos, O[1]; Xu, Shan-mei[1]; Zovein, Ann, C[1]; Ikegami, Kohta[4]; Moskowitz, Ivan, P[5]; Pollard, Katherine, S[3]; Pennacchio, Len, A[2]; Black, Brian, L[1]
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3. Gladstone Institutes, San Francisco, California, USA
4. Department of Pediatrics, University of Cincinnati, Cincinnati, Ohio, USA
5. Departments of Pediatrics, University of Chicago, Chicago, Illinois, USA

- Etv2 hypomorphic mutant mouse embryos have profound anemia and normal vasculature
- Higher Etv2 expression is required for erythropoiesis than for vasculogenesis
- Etv2 indirectly regulates the embryonic erythropoietic GRN via Tal1

027 Hemodynamic regulators of vascular development

Goeckel, Megan[1]; Levitas, Alli[1]; Stratman, Amber[1]
1. Washington University, St. Louis, Missouri, USA

- Hemodynamic Regulators of Vascular Development
- Chemokine Signaling
- EC-MC interactions

BLOOD BRAIN BARRIER

028 Monoamine neurotransmitter metabolism at the blood-brain barrier regulates behavior

Munji, Roeben[1]
1. University of California San Diego, La Jolla, California, USA

- The blood-brain barrier regulates behavior
- The blood-brain barrier metabolizes monoamine neurotransmitters
- Blood-brain barrier monoamine metabolism dysfunction may contribute to neuropsychiatric disorders

029 Caveolae mediate leakage and drug delivery at the blood-brain barrier

Chang, Jui-Hsien[1]; Dragoni, Silvia[1]; Futter, Clare[1]; Greene, Chris[2]; Campbell, Matthew[2]; Turowski, Patric[1]
1. University College London, London, United Kingdom of Great Britain and Northern Ireland
2.Trinity College Dublin, Dublin, United Kingdom of Great Britain and Northern Ireland

- Paracellular and transcellular leakage pathways are dissociable and can be targeted in isolation
- Transcellular leakage at the BBB occurs via transport-competent caveolae
- Transport-competent endothelial caveolae can be harnessed to deliver therapeutics across the BBB

Innovative Research on Key Molecule to Regulate Heart, Blood, and Vessel

030 Proteo-genomic identification of endothelial microproteins encoded by non-canonical small open reading frames

Siragusa, Mauro[1]; Graumann, Johannes[2]; Kuenne, Carsten[2]; Günther, Stefan[2]; Jeratsch, Sylvia[2]; Zhou, Xiaozhu[1]; Cho, Haaglim[2]; Müller, Oliver, J[3]; Troidl, Christian[4]; Nef, Holger, M[5]; Looso, Mario[2]; Offermanns, Stefan[2]; Fleming, Ingrid[1]

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3. Department of Internal Medicine III, University of Kiel, Kiel, Germany
4. Department of Cardiology, Kerckhoff Heart & Lung Center, Bad Nauheim, Germany
5. Department of Cardiology & Angiology, University of Giessen, Giessen, Germany

- Thousands of uncharacterized endothelial microproteins exist under (patho)physiological conditions
- Endothelial microproteins regulate essential biological processes
- Endothelial microproteins may become novel biomarkers of/targets against cardiovascular disease

031 Soluble signals to improve vascular integrity in the lung

Yuan, Yifan[1]; Raredon, Micha Sam Brickman[1]; Yuan, Qianying[1]; Obata, Tomohiro[1]; Hong, Qian[2]; Wu, Dianqing (Dan)[1]; Kaminski, Naftali[1]; Niklason, Laura, E[2]

1. Yale University School of Medicine, New Haven, Connecticut, USA
2. Humacyte Inc., Durham, North Carolina, USA

- Connectome revealed strong cell-cell crosstalk signals in the human lung microvascular niche
- The alveolar fibroblast strongly interacts with the microvascular endothelium
- VEGFD secreted from the alveolar fibroblast could potentially improve vascular integrity

Ocular and CNS Vascular Disease

032 Targeting macrophage Slit-Robo signaling prevents ocular neovascularization

Geraldo, Luiz Henrique[1]; Xu, Yunling[2]; Mouthon, Gaspard[1]; Furtado, Jessica[1]; Eichmann, Anne[1]

1. Yale University - Yale Cardiovascular Research Center (YCVRC), New Haven, Connecticut, USA
2. Paris Cardiovascular Research Center (INSERM U970), Paris, France

- Macrophages are key players in physiological angiogenesis and pathological neovascularization
- Slit2-Robo signaling inhibition is a promising therapeutical target for ocular neovascular diseases
- In macrophages, Slit2 induces recruitment and polarization in pathological states via PI3Kgamma

033 Rapid substitution of pericyte subpopulations prevents diabetic retinopathy

Kim, Soo Jin[1]; Lee, Jihye[2]; Park, Jun Hyeong[3]; Kubota, Yoshiaki[4]; Adams, Ralf, H[5]; Koh, Gou Young[6]; Lee, Junyeop[3]

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3. Asan Medical Center, University of Ulsan, College of Medicine, Seoul, Korea (Republic of)
4. Keio University School of Medicine, Tokyo, Japan
5. Max-Planck Institute for Molecular Biomedicine, Münster, Germany
6. Institute for Basic Science (IBS) / KAIST, Daejeon, Korea (Republic of)

- Rapid loss of PDGFRβ+ pericyte in diabetes are filled by the remained TAGLN+ cells in the retina
- Dynamic changes of PDGFB and Ang2 regulate the loss and substitute of pericytes in diabetic retina
- Lack of replacement for the loss of pericytes leads to the development of diabetic retinopathy

TRANSLATIONAL VASCULAR BIOLOGY

034 Rewiring tumor vasculature by endothelial reprogramming to improve immunotherapy

Fan, Yi[1]

1. University of Pennsylvania, Philadelphia, Pennsylvania, USA

- Endothelial transformation drives vascular aberrancy and immunotherapy resistance in cancer
- Single-cell RNAseq reveals that endothelial plasticity induces aberrant vascularity in cancer
- Kinome-wide screen identifies PAK4 as a regulator of abnormal vascularization in tumor

035 Exercise-augmented pulsatile shear stress modulates Stearoyl-CoA Desaturase (SCD1) mediated lipid metabolites for vascular protection

Cavallero, Susana[1]; Roustaei, Mehrdad[1]; Satta, Sandro[1]; Blazquez-Medela, Ana, M[1]; Phan, Henry[1]; Cho, Jae Min[1]; Baek, Kyung In[1]; Gonzalez-Ramos, Sheila[1]; Li, Rongsong[1]; Hsiai, Tzung, K[1]

1. University of California, Los Angeles, Los Angeles, California, USA

- Pulsatile shear stress modulates endothelial metabolomics and increases SCD1 metabolite production
- Endothelial SCD1 is activated by exercise-induced pulsatile shear stress
- Exercise-mediated anti-inflammatory response is mitigated by endothelial Scd1 deletion

AVMS AND SOMATIC VASCULAR MALFORMATIONS

036 Identifying novel therapeutic vulnerabilities in Kras-Driven sporadic brain arteriovenous malformations

Flores Suarez, Carlos[1]; Cerda III, Juan[1]; Younis, Julia, B[1]; Mulhorn, Abby[1]; Ricciardelli, Ashley, R[1]; Wythe, Joshua, D[1]

1. Baylor College of Medicine, Houston, USA

- Kras-induced brain AVMs display altered vessel morphology with increased vessel diameter size
- Treatment with a MEK inhibitor prevents Kras-induced brain AVMs in mice
- Transcriptional profiling of Kras mutant endothelium identifies additional cell processes to target

037 Localized conditional induction of brain arteriovenous malformations in an HHT mouse model

Scherschinski, Lea[1]; Han, Chul[1]; Kim, Yong, H[1]; Lawton, Michael, T[1]; Oh, Paul, S[1]

1. Barrow Neurological Institute, Phoenix, Arizona, USA

- To develop a novel experimental HHT mouse model with localized, conditional induction of brain AVMs
- Intracerebral delivery of hydroxytamoxifen in Alk1-inducible knockout mice induces bAVMs reliably
- Localized induction of brain AVMs in Alk1-iKO mice produces a robust longitudinal HHT mouse model

BIOENGINEERING

038 Generation of vascular malformations in a novel HHT-on-a-Chip microphysiological model

Fang, Jennifer, S[1]; Hatch, Christopher, J[2]; Matsumoto, Satomi[2]; van Trigt, William[2]; Andrejecsk, Jillian[2]; Hughes, Christopher, C[2]

1. Tulane University, New Orleans, LouisianaLouisiana, USA

2. University of California-Irvine, Irvine, California, USA

- A novel microphysiological disease model of HHT recapitulates vascular malformations of patients
- Vascular malformations are mosaic structures comprised of both Alk1-intact and -deficient EC
- Pazopanib prevents abnormal vascular lesions in the HHT-on-a-chip platform

039 Modeling intussusceptive angiogenesis in a vessel-on-a-chip

Staples, Sabrina[1]; Yin, Hao[1]; Prescott, Emma[1]; Poepping, Tamie[2]; Pickering, J. Geoffrey[1]
1. Robarts Research Institute, Western University, London, ON, Canada
2. Western University, London, ON, Canada

- We developed the first live-cell model of transluminal endothelial bridging using microfluidics
- A reduced VEGFR2-NO axis promoted transluminal endothelial bridging
- Time-lapse imaging revealed flow-orthogonal protrusions that transform into endothelial bridges

LYMPHANGIOGENESIS

040 VEGFR3 is required for button junction development in lymphatic capillaries

Jannaway, Melanie[1]; Iyer, Drishya[1]; Mastrogiacomo, Diandra[1]; Li, Kunyu[1]; Sung, Derek[2]; Yang, Ying[1]; Kahn, Mark[2]; Scallan, Joshua[1]
1. University of South Florida, Tampa, Florida, USA
2. University of Pennsylvania, Philadelphia, Pennsylvania, USA

- VEGFR3 signaling is required for the formation of button junctions in lymphatic capillaries
- Loss of VEGFR3 decreases DLL4 and NOTCH1 expression, and reduces NOTCH1 activation
- Overexpression of NOTCH1 rescues button formation and function in VEGFR3-deficient mice

041 Engineering functional biomaterials with stem cells for therapeutic lymphangiogenesis

Alderfer, Laura[1]; Saha, Sanjoy[1]; Jeong, Donghyun, P[1]; Hanjaya-Putra, Donny[1]
1. University of Notre Dame, Notre Dame, Indiana, USA

- Robust and efficient differentiation of hPSCs-derived LECs that express mature lymphatic markers
- Matrix stiffness primes hPSC-LECs to undergo lymphatic tube formation directed by VEGF-C
- Engineered human lymphatic networks matured and integrated with the murine lymphatic system in vivo

MYELOID CELLS, VASCULATURE, AND CANCER PROGRESSION

042 Myocardial infarction increases metastatic outgrowth in the lung

Newman, Alexandra[1]; Kolewyn, Graeme[2]; Bozal, Fazli[1]; Cyr, Yannick[1]; Lim, Brian[3]; Von Itter, Richard[1]; Moore, Kathryn[1]
1. New York University, New York, New York, USA
2. SFU, Burnaby, BC, Canada
3. Cedar's Sinai, Los Angeles, USA

- Reverse Cardio-oncology
- Cardiovascular and cancer crosstalk
- MI promotes pre-metastatic niche formation

043 Spatial and temporal vascular remodelling in triple-negative breast cancer lung metastases

Lin, Salwa[1]; Carroll, Thomas[1]; Elshenawy, Badran[1]; Bridgeman, Victoria[2]; Malanchi, Ilaria[2]; Harris, Adrian[1]; Banham, Alison[1]; De Val, Sarah[1]
1. University of Oxford, OXFORD, United Kingdom, United Kingdom of Great Britain and Northern Ireland
2. Francis Crick Institute, London, United Kingdom, United Kingdom of Great Britain and Northern Ireland

- understanding how TNBC acquire access to blood vessels to metastasize to lungs
- Investigating the molecular cues from neighboring (niche) stromal cells driving metastasis
- interrogate the transcriptome profile of tumour vascular endothelium

ATHEROSCLEROSIS

044 Lgi3 deficiency ameliorated atherogenesis via attenuating lesional DC accumulation

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2. Severance Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Korea (Republic of)
3. Department of Biochemistry, Chung-Ang University, College of Medicine, Seoul, Korea (Republic of)

- Plasma LGI3 level is highly correlated with atherosclerosis severity
- Lgi3 deficiency reduces vascular inflammation, alleviating plaque formation
- LGI3 antagonist peptide effectively attenuates atherosclerosis

045 Selective delivery of nanoparticle encapsulated Nrf2 Activator, CDDO-Methyl, for the treatment of atherosclerosis

Maiocchi, Sophie[1]; Cartaya, Ana[1]; Buglak, Nicholas[1]; Torzone, Sarah[1]; Peterson, Andrew[1]; Akerman, Adam[1]; Bahnson, Edward[1]

1. University of North Carolina at Chapel Hill, United States, Durham, North Carolina, USA

- Oxidative stress and inflammation are well-established drivers of atherosclerotic progression
- The clinical translation of anti-inflammatory, redox-based therapies is lacking
- Selective delivery of Nrf2 activators may prevent atherosclerotic progression

Vascular Cell Differentiation and Plasticity

046 O-GlcNAcylation enhances transdifferentiation and vascular regeneration

Lu, Alexander1; Carter, Kaylee1; Cooke, John1; Lai, Li[1]

1. Houston Methodist Research Institute, Houston, TexasTexas, USA

- Angiogenic transdifferentiation directly contributes to the vasculature repair after limb ischemia
- UDP-GlcNAc and O-GlcNAcylation are required for transdifferentiation and vascular recovery
- O-GlcNAcylation of H3.3 chaperon HIRA is essential for transdifferentiation

047 Role of Smad4 in coronary vascular growth

Szumska-Bilska, Dorota[1]; Payne, Sophie[1]; Bruche, Susann[1]; Neal, Alice[1]; Smart, Nicola[1]; De Val, Sarah[1]

1. University of Oxford, Oxford, United Kingdom of Great Britain and Northern Ireland

BMP-Smad signaling directly targets a number of genes involved in coronary vessel formation

- Multiple regulatory pathways combine to form the coronary vasculature
- Analysis of different enhancers provides key information about the regulation of coronary vessels

Vascular Cell-Blood Interaction

048 TMEM16 phospholipid scramblases regulate endothelial cell procoagulant activity and thrombosis

Schmaier, Alec[1]; Anderson, Papa[1]; Chen, Siyu[1]; El-Darzi, Emale[1]; Sack, Kelsey[1]; Hartzell, Criss[2]; Parikh, Samir[3]; Flaumenhaft, Robert[1]; Schulman, Sol[1]

1. Beth Israel Deaconess Medical Center, Boston, USA

2. Emory School of Medicine, Atlanta, USA

3. University of Texas Southwestern Medical Center, Boston, USA

- The vessel wall exposes phosphatidylserine to support thrombosis in vivo
- Endothelial cell phosphatidylserine externalization is regulated by both TMEM16E and TMEM16F
- TMEM16 inhibitors protect against thrombosis without exacerbating bleeding

049 Why are HEV high? Role of the Ire1-Xbp1 pathway in the morphology and function of high endothelial venules

Bi, Yuhan[1]; Pan, Junliang[1]; Brulois, Kevin[1]; Xiang, Menglan[1]; Butcher, Eugene[1]

1. Stanford University, Palo Alto, California, USA

- The IRE1α-XBP1 pathway is enriched in and maintains the health of lymphocyte-recruiting HEV
- EC-specific Xbp1 ablation flattens HEV with loss of ER & Golgi, and reduces lymphocyte recruitment
- The Xbp1-dependent 'highness' of HEV supports HEV survival and function in lymphocyte recruitment

ENDOTHELIAL ORGAN HETEROGENEITY AND STEM CELLS

050 Mouse placenta fetal macrophages are tissue resident macrophages that do not arise from placenta endothelium

Chen, Xiaowen[1]; Kahn, Mark[1]; Tang, Alan[1]; Speck, Nancy[1]; Tober, Joanna[1]
1. University of Pennsylvania, Philadelphia, USA

- We generated a Hoxa13Cre allele that specifically labels all placental endothelial cells (ECs)
- Lineage tracing using Hoxa13Cre and others show that mouse placenta fetal Macs do not arise de novo
- Mouse placenta fetal Macs share a common origin and location to human Hofbauer cells (HBCs)

Reconstructing organotypic vasculature from iPSCs to study pulmonary vascular disease

Miao, Yifei[1]; Pek, Nicole[1]; Pastrana-Gomez, Victor[1]; Guo, Minzhe[1]; Yu, Zhiyun[1]; Whitsett, Jeffrey[1]; Kitzmiller, Joseph[1]; Kotton, Darrell[2]; Gu, Mingxia[1]
1. Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA
2. Boston University, Boston, USA

- Via a co-differentiation strategy, we generated lung organoids with organotypic vasculature
- The vascularized lung organoids derived from patient iPSCs recapitulated phenotypes in ACD/MPV
- The vascularized lung organoids provide a human platform to study endothelial-epithelial crosstalk

051 Temporally-restricted patterns of endothelial cell collagen IV expression determined with a novel knockin Col4a1-GFP mouse line

van der Ent, Martijn[1]; Lartey, Nathaniel, L[1]; Saunders, Thomas, L[1]; Hughes, Elixabeth, D[1]; Alonzo, Roxann[1]; King, Philip, D[1]
1. University of Michigan Medical School, Ann Arbor, Michigan, USA

- Which EC types actively engage in collagen IV synthesis in the vasculature is largely unknown
- Using a Col4a1-GFP mouse we found that Col4a1 expression is largely limited to mid to late gestation
- Findings are consistent with temporally-restricted phenotypes in EPHB4- or RASA1-deficient mice

STRATEGIES TO UNDERSTAND AND TREAT COVID-19

Multistep attenuation reveals broad fitness tradeoff for the SARS-CoV-2 Omicron variant

Taha Y. Taha[1]; Irene P. Chen[1,3]*; Takako Tabata[1]*; Abdullah M. Syed[1,2]; Alison Ciling[1,2]; Rahul Suryawanshi[1]; Hannah Martin[1,2]; Bryan Bach[2]; Chia-Lin Tsou[1]; Mir M. Khalid[1]; Bharath K. Sreekumar[1]; G. Renuka Kumar[1]; Jennifer M. Hayashi[1]; Frank W. Soveg[1]; Stacia Wyman[2]; Jennifer A. Doudna[1,2,4-8]; and Melanie Ott[1,3,9]*
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4. *Department of Molecular and Cell Biology, University of California, Berkeley, CA, USA*
5. *Howard Hughes Medical Institute, University of California, Berkeley, Berkeley, CA, USA*
6. *Department of Chemistry, University of California, Berkeley, Berkeley, CA, USA*
7. *Molecular Biophysics and Integrated Bioimaging Division, Lawrence Berkeley National Laboratory, Berkeley, CA, USA*
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9. *Chan Zuckerberg Biohub, San Francisco, CA, USA*

**These authors contributed equally to this work*

052 Investigate COVID-19-associated vascular dysfunction by using novel mouse models

Gao, Siqi[1]; Kahn, Mark[1]
1. University of Pennsylvania, Philadelphia, USA

- New hACE2 mouse model is susceptible to SARS-CoV-2 infection and develops vascular dysfunction
- Deletion of hACE2 in endothelial cells or pericytes did not ameliorate lethal phenotype
- Olfactory epithelial and neuronal infection confer lethal phenotype in the absence of lung infection

053 An engineered ACE2 decoy receptor can be administered by inhalation and targets omicron variants of SARS-CoV-2

Zhang, Lianghui[1]; Rong, Lijun[2]; Rehman, Jalees[3]; Malik, Asrar, B[3]; Procko, Erik[4]
1. University of Pittsburgh Medical Center, Pittsburgh, USA
2. Department of Microbiology at University of Illinois at Chicago, Chicago, IL, USA
3. Department of Pharmacology at University of Illinois at Chicago, Chicago, Illinois,Illinois, USA
4. Department of Biochemistry, University of Illinois, Urbana, Illinois, USA

- An engineered ACE2 decoy receptor blocks replication of SARS-CoV-2 omicron variants
- The catalytic activity of the engineered ACE2 decoy is required for its therapeutic efficacy
- The decoy receptor is therapeutically effective via intravenous infusion and inhalation routes

054 SARS-CoV-2-induced blood-brain barrier leakage, T cell infiltration, and neuropsychiatric dysfunction are worsened by age-related declines in cerebrovascular Wnt/beta-catenin

Niladhuri, Seshadri, B[1]; Trevino, Troy, N[1]; Almousawi, Ali, A[1]; Robinson, KaReisha, F[1]; Richner, Justin, M[1]; Lutz, Sarah, E[1]
1. University of Illinois at Chicago, Chicago, Illinois, USA

- Middle age worsens BBB leakage and compulsivity after SARS-CoV-2 infection in mice
- Infection triggers BBB-protective Wnt/beta catenin response in young adults
- Cerebrovascular Wnt or downstream effectors could be therapeutic targets in long COVID

Angiogenesis and Vascular Remodeling

055 OPN5 light sensing regulates hyaloid vessels regression through Hippo-YAP signaling pathway

Sakabe, Masahide[1]; Odaka, Yoshinobu[2]; Chen, Nong[1]; Vemaraju, Shruti[1]; Lang, Richard[1]; Xin, Mei[1]
1. Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

- PN5 light sensing regulates hyaloid vessel regression through the Hippo-YAP signaling pathway
- Inactivation of YAP is functionally required for the hyaloid vascular regression process
- How light stimulation is translated into biological effects to regulate hyaloid vessel regression

056 Angiogenesis in ischemic muscle is dominated by low-flow intussusception, not sprouting, and launched by flow-seeking endothelial cells

Arpino, John-Michael1; Yin, Hao1; Prescott, Emma, K1; Staples, Sabrina, C1; Nong, Zengxuan1; Li, Fuyan1; Chevalier, Jacqueline1; Balint, Brittany1; O'Neil, Caroline1; Mortuza, Rokhsana1; Milkovich, Stephanie1; Lee, Jason, J1; Lorusso, Daniel1; Sandig, Martin1; Hamilton, Douglas, W1; Holdsworth, David, W1; Poepping, Tamie, L1; Ellis, Christopher, G1; Pickering, J. Geoffrey[1]
1. Western University, London, Ontario, Canada

- The dominant mode of angiogenesis in regenerating muscle is intussusception, not sprouting
- Primordial vessels with ultralow flow are the first conduits to form in ischemia-injured muscle
- Endothelial cells with low VEGFR2 activity and shear-seeking behavior may underlie pillar formation

New Therapeutics

057 Use of Oxygel for the ambient transportation of endothelial colony forming cells (ECFCs) for cell therapy applications

Mcloughlin, Kiran, J[1]; Domingo-Lopez, Daniel, A[2]; Eyre, Jessica, J[1]; Bertelli, Pietro, M[1]; McDonnell, Shannon[1]; Duffy, Garry, P[2]; Medina, Reinhold, J[1]
1. Queen's University Belfast, Belfast, County Antrim, United Kingdom of Great Britain and Northern Ireland
2. National University of Galway, Ireland, Galway, Ireland

- To transport ECFCs at ambient temperatures using Oxygel as an alternative to cryopreservation
- To optimise Oxygel for longer term viability to allow a wider range of transportation options
- To enhance recovery of ECFCs for further downstream applications, such as in vivo studies

058 Targeted CD39 as a therapy for ischaemic stroke and global hypoxic ischaemic brain injury

Lee, Natasha, T[1]; Selan, Carly[1]; Chia, Joanne, S[1]; Willcox, Abbey, E[1]; Brkljaca, Robert[1]; Wright, David, K[1]; Medcalf, Robert, L[1]; Nandurkar, Harshal, H[1]; Sashindranath, Maithili[1]

1. Monash University, Melbourne, VIC, Australia

- Preclinical data for targeted CD39 as a therapy for stroke and global hypoxic ischaemic brain injury
- CD39 protects the endothelium which promotes neurovascular integrity and protects the brain
- CD39 has the potential to rescue the ischaemic penumbra and can synergise with current thrombolytics

VASCULAR PLASTICITY

059 Mechanisms of vascular maturation and maintenance captured by longitudinal imaging of live mouse skin

Kam, Chen Yuan[1]; Singh, Ishani, D[1]; Matte-Martone, Catherine[1]; Gonzalez, David, G[1]; Sola, Paloma[2]; Solanas, Guiomar[2]; Bonjoch, Julia[2]; Marsh, Edward, D[1]; Hirschi, Karen, K[3]; Greco, Valentina[1]

1. Yale University, New Haven, CT, USA

2. IRB Barcelona, Barcelona, Spain

3. University of Virginia, Charlottesville, Virginia, USA

- Skin plexus maturation is mediated by coordinated regression and rearrangement of existing ECs
- Adult but not neonatal ECs preferentially survive damage via a plasmalemmal self-repair mechanism
- Neonatal regression and adult maintenance are orchestrated by temporally restricted VEGFR2 signaling

060 A novel mouse model for Hereditary Hemorrhagic Telangiectasia (HHT) and pulmonary vascular abnormalities

Schimmel, Katharina[1]; Ichimura, Kenzo[1]; Andruska, Adam, M[1]; Ali, Md, K[1]; Spiekerkoetter, Edda[1]

1. Stanford University School of Medicine, Palo Alto, California, USA

- Modeling focal occurrence of pulmonary arteriovenous malformations in HHT faithfully in the mouse
- Replicating a focal bi-allelic loss of HHT genes as seen in vascular abnormalities of HHT patients
- Bi-allelic deletion of Alk1 in a subset of endothelial cells of mouse pulmonary capillaries

NEUROVASCULAR CROSSTALK

061 Electro-Calcium signaling in the brain endothelium: A higher order mechanism to control cerebral blood flow

Mughal, Amreen[1]; Heppner, Thomas[1]; Hennig, Grant, W[1]; Nelson, Mark, T[1]

1. University of Vermont, Burlington, Vermont, USA

- Capillary endothelial cells in control of Cerebral blood flow
- A novel neurovascular coupling mechanism linked with electrical and calcium signaling
- Electro-calcium signaling to maintain brain homeostasis

062 Inhibition of Notch signaling in endothelial cells preserves cognitive function in a model of familial Alzheimer's disease

Villa-Niemczyk, Stephanie, R[1]; Naiche, L A[1]; Arowolo, Jumobi[1]; Kitajewski, Jan, K[1]

1. University of Illinois at Chicago, Chicago, Illinois, USA

- Brain endothelial Notch signaling changes with age and is altered in Alzheimer's disease
- Endothelial Notch inhibition preserves cognitive function in a model of Alzheimer's disease
- Microglial activation is influenced by endothelial Notch inhibition

Innovative Research on Mechanism for Variant Angina or Diabetic Cardiomyopathy

063 Altered coronary artery function, arteriogenesis and endothelial YAP signaling in postnatal hypertrophic cardiomyopathy

Langa, Paulina[1]; Marszalek, Richard, J1; Warren, Chad, M1; Chowdhury, Shamim1; Halas, Monika1; Batra, Ashley1; Rafael-Clyke, Koreena1; Thompson, Walter1; Goldspink, Paul, H1; Solaro, John, R1; Wolska, Beata, M1
1. University of Illinois at Chicago, Chicago, Illinois, USA

- Altered coronary artery function in early onset Hypertrophic Cardiomyopathy in TnT-R92Q mouse model
- Endothelial YAP signaling imbalance in Hypertrophic Cardiomyopathy in TnT-R92Q mouse model
- Perivascular fibrotic remodeling in early postnatal Hypertrophic Cardiomyopathy mouse model

064 The regulatory role of Sirtuin 6 in coronary microvascular dysfunction

Wang, Yang[1]; Enrick, Molly[1]; Juguilon, Cody[1]; Gadd, James[1]; Clark, Alyssa[1]; Yin, Liya[1]
1. Northeast Ohio Medical University, Rootstown, Ohio, USA

- Microvascular aging and development
- The Vasculature in Metabolic Disease
- Pathophysiology of Vascular Disease

Imaging and Computational Approaches

065 Increased hemoglobin oxygenation detected by photoacoustic imaging suggests altered microvascular function in chronic ischemia

Tarvainen, Santeri[1]; Wirth, Galina[1]; Laitinen, Tomi[2]; Mäkinen, Kimmo[1]; Ylä-Herttuala, Seppo[3]; Korpisalo, Petra[1]
1. Heart Center, Kuopio University Hospital, Kuopio, Finland
2. Imaging Center, Kuopio University Hospital, Kuopio, Finland
3. Dept. of Mol. Medicine, A.I.Virtanen institute, UEF, Kuopio, Finland

- Photoacoustic imaging used to study microvascular hemoglobin oxygenation in ischemic muscle
- A translational study with chronic limb threatening ischemia patients, healthy volunteers and mice
- Paradoxically non-decreased muscle hemoglobin oxygenation suggests altered microvascular function

066 A novel vasculature-centric method for mapping In vivo blood oxygen saturation in preclinical applications

Ren, Yunke[1]; Senarathna, Janaka[2]; Chu, Xinying[1]; Pathak, Arvind[2]
1. Dept of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, USA
2. Dept of Radiology, Johns Hopkins University, Baltimore, Maryland, USA

- Absolute intravascular oxygenation can be mapped in vivo using intrinsic optical signal imaging
- Vascular-centric quantification enhances accuracy of in vivo oxygen saturation measurements
- Our novel oxygen saturation mapping method can be utilized in a range of preclinical applications

Tumor Biology

067 Targeting the cerebrovasculature to combat glioblastoma multiforme

Hudson, Nicholas[1]; Calderon, Sebastian[1]; Ruiz, Oscar[1]; Deneen, Benjamin[1]; Rao, Ganesh[1]; Samee, Hassan[1]; Wythe, Joshua, D[1]
1. Baylor College of Medicine, Houston, TexasTexas, USA

- GBM features extensive heterogeneity in the endothelium and tumor microenvironment
- A VEGF-MAPK-ETS-BRD4 angiogenic signature distinguishes high grade glioma from low grade glioma
- Targeting the VEGF-MAPK-ETS-BRD4 axis may disrupt glioma progression

068 Lung endothelium instructs dormancy of susceptible metastatic tumor cells

Jakab, Moritz[1]; Lee, Ki Hong[1]; Uvarovskii, Alexey[2]; Ovchinnikova, Svetlana[3]; Kulkarni, Shubhada, R[1]; Rostalski, Till[1]; Anders, Simon[3]; Augustin, Hellmut, G[1]

1. German Cancer Research Center, Heidelberg, BW, Germany

2. Center for Molecular Biology Heidelberg University, Heidelberg, BW, Germany

3. Bioquant Center Heidelberg University, Heidelberg, Germany

- Lung endothelium serves as an instructor of metastatic behavior of arrested circulating tumor cells
- Metastatic niche-derived angiocrine Wnt ligands induce quiescence in responsive tumor cells
- Tumor cell responsiveness towards angiocrine Wnt is predetermined epigenetically

The Vasculature in Health and Disease

069 Impact of the gut microbiome on vascular development

Dreger, Sally, A[1]; Robinson, Stephen, D[1]

1. Quadram Institute Bioscience, Norwich, United Kingdom of Great Britain and Northern Ireland

- Antibiotic use perturbs the gut microbiome affecting retinal vascular development in neonate pups
- The maternal microbiome impacts the developing vasculature in neonates
- Use of a live biotherapuetic product (LBP) restores angiogenesis

Epigenetic Regulation

070 Distal regulatory elements control angiogenic and homeostatic endothelial state

Gehrs, Stephanie[1]; Gu, Zuguang[2]; Weichenhan, Dieter[3]; Hey, Joschka[3]; Díaz-Jiménez, Alberto[4]; Breuer, Kersten[3]; Lutsik, Pavlo[3]; Kulkarni, Shubhada[1]; Schlesner, Matthias[5]; Sotillo, Rocio[4]; Plass, Christoph[3]; Augustin, Hellmut[1]; Schlereth, Katharina[1]

1. European Center for Angioscience, Heidelberg University, Mannheim, Germany

2. Molecular Precision Oncology Program, National Center for Tumor Diseases, Heidelberg, Germany

3. Division of Cancer Epigenomics, German Cancer Research Center, Heidelberg, Germany

4. Division of Molecular Thoracic Oncology, German Cancer Research Center, Heidelberg, Germany

5. Biomedical Informatics, University of Augsburg, Augsburg, Germany

- Epigenetic driven cell state transition in angiogenic vs. homeostatic EC
- Selective chromatin accessibility focuses on enhancers in state-specific EC
- Integrity of endothelial enhancers is ensured via peripheral DNA methylation

071 A novel epigenetic regulator of arterial specification and development in zebrafish

Marvel, Miranda[1]; Gore, Aniket, V[1]; Greenbaum, Jordyn[1]; Castranova, Daniel[1]; Davis, Andrew[1]; Taimatsu, Kiyohito[1]; Weinstein, Brant, M[1]

1. NICHD/NIH, Bethesda, Maryland, USA

- A novel epigenetic reporter zebrafish line is a powerful tool to discover novel epigenetic mutants
- Kdm4ab is a novel epigenetic regulator of arterial specification and development
- Ectopic expression of venous genes in arteries may result in the loss of arterial sprouting

Stem Cells and Regenerative Medicine

072 Stacking perfusable human microvascular networks for thick and dense vascularity and rapid integration into infarcted rat heart

Frey, Ariana[1]; Zeinstra, Nicole[1]; Xie, Zhiying[1]; Wang, Ruikang[1]; Murry, Charles[1]; Zheng, Ying[1]

1. University of Washington, Seattle, USA

- Heart attacks lead to permanent loss of cardiac muscle, requiring cardiac regenerative therapies
- We developed perfusable thick multilayer microvessels which support vascular remodeling in vitro
- These microvessels support early vascular remodeling and host vascular integration in vivo

073 Hematopoietic stem and progenitor cell heterogeneity is inherited from the embryonic hemogenic endothelium

Ghersi, joey, J[1]; Baldissera, Gabriel[1]; Hintzen, Jared[1]; Luff, Stephanie[2]; Xia, Ivan Fan[1]; Sturgeon, Christopher[2]; Nicoli, Stefania[1]
1. Yale University, New Haven, Connecticut, USA
2. Icahn, New York, New York, USA

- Dysregulation of HSC heterogeneity is associated with poor outcomes of autologous transplants
- Endothelial Cells (ECs) form different primed hematopoietic stem cells (HSCs)
- HSCs heterogeneity is inherited in ECs by activities of distinct signaling pathways

ORGAN CROSSTALK

074 Regulation of blood pressure by adipocyte identity

Koenen, Mascha[1]; Becher, Tobias[1]; Halix, Sarah1; delGaudio, Ilaria[2]; Butler, Scott[3]; DiLorenzo, Annarita[4]; Cohen, Paul[1]
1. Rockefeller University, NEW YORK, NY, USA
2. Paris Cardiovascular Research Center, Université Paris Cité, Inserm, Paris, France

- Thermogenic adipose tissue affects blood pressure regulation
- Adipose tissue identity can shape response to angiotensin II
- Adipocyte derived secreted factors affect vascular smooth muscle cell contraction

075 Advancing knowledge on the effects and pathogenesis of hereditary hemorrhagic telangiectasia in pregnancy

Mathew, Vineetha[1]; Mei, Ariel[1]; Mann, Molly[1]; Jayaraman, Nirmala[1]; Joe, Andrew[1]; O'Tierney Ginn, Perrie[1]; Alvarado-Flores, Fernanda[1]; Bhave, Shreyas, A[1]; Hirschi, Karen[2]; Kapur, Navin[1]; Good, Miranda, E[1]; Wallingford, Mary, C[1]
1. Tufts Medical Center, Boston, USA
2. University of Virginia School of Medicine, Boston, Virginia, USA

- This study aims to explore placental vascular health and pathogenesis in HHT
- Morphology of placental vessels was evaluated in clinical biopsies and HHT mouse model tissues
- Multiple placental vascular abnormalities were observed, including maternal-fetal interface defects

IMMUNE-VASCULAR CROSSTALK IN NON-NEOPLASTIC DISEASES

076 Prox1 haploinsufficiency promotes immunosuppression by enhancing anti-inflammatory macrophage polarization

Herrada, Andres, A1; Olate-Briones, Alexandra[1]; Lazo-Amador, Rodrigo[1]; Hernandez-Rojas, Bairon[2]; Riadi, Gonzalo[2]; Escobedo, Noelia[1]
1. Universidad Autonoma de Chile, Talca, Chile
2. Universidad de Talca, Talca, Chile

- lymphatic vasculature
- inflammation and inflammatory bowel disease
- Macrophages

077 Diminished vasculogenesis under inflammatory conditions is mediated by Activin A

Manohar-Sindhu, Sahana[1]; Merfeld-Clauss, Stephanie[1]; March, Keith, L1; Traktuev, Dmitry, O[1]
1. University of Florida, Gainesville, Florida, USA

- Inflammatory cells induce Activin A secretion in endothelial and perivascular cells
- Inhibition of Activin A improves endothelial cells tubulogenesis in inflammatory environment
- Activin A promotes acquisition of myofibroblast phenotype in mural cells and CTGF secretion

SIGNALING IN VASCULAR DISEASE

078 Endothelial cell immunoproteasome expression contributes to neo-antigen presentation and immune activation in hypertension

de la Visitación, Néstor[1]; Ao, Mingfang[1]; Krishnan, Jaya[1]; Hennen, Elizabeth, M[2]; Van Beusecum, Justin, P[3]; Chen, Wei[1]; Saleem, Mohammad[1]; Harrison, David, G[1]; Patrick, David, M[1]

1. Vanderbilt University Medical Center, Nashville, Tennessee, USA

2. Vanderbilt University, Nashville, Tennessee, USA

3. Medical University of South Carolina, Charleston, South Carolina, USA

- ROS production results in isolevuglandin adduct presentation by MHC-I in endothelial cells
- Loss of immunoproteasome function in endothelial cells prevents hypertension and immune infiltration
- Endothelial cell proteasome expression is isoLG-dependent and mediated by the cGAS/STING pathway

079 Human milk oligosaccharide attenuates angiotensin II-induced vascular smooth muscle dysfunction and vascular remodeling

Nguyen, Le Lam Thuy[1]; Jin, Yujin[1]; Nguyen, Van Dung[1]; Kim, Lila[2]; Myung, Chang-Seon[1]; Heo, Kyung-Sun[1]

1. College of Pharmacy, Chungnam National University, Daejeon, Korea (Republic of)

2. GeneChem Inc., Yuseong-gu, Daejeon, Korea (Republic of)

- HMO reduces Ang II-induced proliferation and migration by inhibiting p90RSK/Akt and NF-kB pathway
- HMO inhibits osteogenic switching by abolishing p90RSK- and JNK-mediated AP-1 activity
- HMO attenuates Ang II-induced abdominal aortic aneurysm formation in vivo

THE VASCULATURE IN METABOLIC DISEASE

080 Endothelial lipid droplets link metabolic syndrome to blood pressure elevation

Kim, Boa[1]; Tang, Soon, Y[1]; Zhao, Wencao[1]; Ibrahim, Ayon[1]; Yang, Yifan[1]; Roberts, Emilia[1]; Li, Jian1; Assoian, Rick[1]; FitzGerald, Garret, A[1]; Arany, Zoltan[1]

1. University of Pennsylvania, Philadelphia, USA

- High fat consumption leads to the accumulation of lipid droplets in the endothelium
- Lipid droplet accumulation in endothelium leads to endothelial dysfunction and hypertension
- Lipid droplets activates an inflammatory signaling cascade that suppresses eNOS and NO production

081 Obesogenic diet promotese endothelial-to-mesenchymal transition in adipose tissue

Chavkin, Nicholas, W[1]; Hirschi, Karen, K[1]; Gokce, Noyan[2]; Walsh, Kenneth, K[1]

1. University of Virginia, Charlottesville, USA

2. Boston University School of Medicince, Boston, USA

- Obesogenic diet induces EndoMT in adipose tissue of endothelial cell lineage-traced mice
- EndoMT occurs in cultured human adipose-derived endothelial cells after induction
- Single cell RNA sequencing datasets from obese human adipose tissues contain pre-EndoMT clusters

CARDIOVASCULAR REGENERATIVE MEDICINE

082 Intramyocardial application of CCL24, novel macrophage-derived angiocrine factor, promotes cardiac repair following injury

Perez, Dahlia, E[1]; Petrover, Zachary[1]; Miyara, Shoval[1]; Zhang, Ling Ling[1]; Sarusi-Portuguez, Avital[1]; Petrovich, Ekaterina[1]; Baruch Umansky, Kfir[1]; Tzahor, Eldad[1]

1. Weizmann Institute of Science, Rehovot, Israel

- A pro-regenerative chemokine, CCL24, coordinates angiogenic processes after myocardial infarction
- Direct application of CCL24 to damaged myocardium improves cardiac functional parameters

- CCL24 may integrate the angiogenic, mitogenic and anti-inflammatory requirements of scar repair

083 Dynamic endothelial plasticity spatiotemporally induces vascular aberrancy during cardiac repair

Gong, Yanqing Anna[1]; Huang, Menggui[1]; Yang, Fan[1]; Zhang, Duo[1]; Mitchell, Michael[1]; Rader, Daniel[1]; Fan, Yi[1]
1. University of Pennsylvania, Philadelphia, USA

- Newly formed vessels in injured heart after myocardial infarction (MI) are not fully functional
- Endothelial cells undergo mesenchymal activation and drives vascular abnormalities after MI
- PDGF/NF-kB axis induces mesenchymal activation in ECs , culminating in aberrant vascularization

LYMPHATICS

084 Modular HA-Hydrogels to generate lymphatic networks for tissue engineering applications

Alderfer, Laura[1]; Fan, Fei[1]; Hanjaya-Putra, Donny[1]
1. University of Notre Dame, Notre Dame, Indiana, USA

- Matrix stiffness and growth factor supplementation can control lymphatic endothelial cell behavior
- We can generate lymphatic capillaries in a synthetic hydrogel and implant into a mouse model
- Our hydrogel system can be used for advanced mechanistic studies in vitro

085 Impact of Lymphatic Injury on Contractility and Mitochondrial Bioenergetics of Lymphatic Vessels

Nepiyushchikh, Zhanna[1]; Chin, Rachel[1]; Mavris, Sophia[2]; Jang, Young[3]; Dixon, Brandon[1]
1. Georgia Institute of Technology/School of Mechanical Engineering, Atlanta, Georgia, United States of America;
2. Georgia Institute of Technology/Department of Biomedical Engineering, Atlanta, Georgia, USA
3. Emory School of Medicine /Department of Orthopaedics, Atlanta, Georgia, USA

- How mitochondrial bioenergetics of collecting lymphatic vessels impacted after surgical intervention
- How collecting lymphatic metabolize energy source after injury
- Correlations between impacted contractility of lymphatics and their metabolic state after injury

IMMUNE VASCULAR CROSSTALK FOR CANCER THERAPY

086 Losartan prevents immunotherapy-associated edema and enhances survival in glioblastoma

Datta, Meenal[1]; Chatterjee, Sampurna[2]; Perez, Elizabeth[2]; Gritsch, Simon[2]; Roberge, Sylvie[2]; Duquette, Mark[2]; Chen, Ivy[2]; Naxerova, Kamila[2]; Kumar, Ashwin[2]; Ghosh, Mitrajit[2]; Emblem, Kyrre[3]; Ng, Rosa[2]; Ho, William[2]; Kumar, Pragya[2]; Krishnan, Shanmugarajan[2]; Dong, Xinyue[2]; Speranza, Maria[2]; Neagu, Martha[2]; Reardon, David[2]; Sharpe, Arlene[2]; Freeman, Gordon[2]; Suva, Mario[2]; Xu, Lei[2]; Jain, Rakesh, K[2]
1. University of Notre Dame, Notre Dame, Indiana, USA
2. Harvard Medical School, Boston, USA
3. Oslo University Hospital, Oslo, Norway

- Immune checkpoint blockade disrupts glioblastoma endothelial barrier and increases cerebral edema
- Losartan overcomes immunotherapy-induced edema and reprograms the glioblastoma microenvironment
- Bihemispheric mouse model reveals predictive tissue-based biomarkers of variable therapy response

087 Priming a vascular-selective cytokine response permits CD8+ T-cell entry into tumors

Dudley, Andrew[1]
1. University of Virginia, Charlottesville, Virginia, USA

- Dysfunctional tumor vasculature is non-permissive to anti-tumor immune cells.
- "Normalizing" tumor vessels can improve immune cell trafficking and checkpoint blockade efficacy.
- Targeting epigenetic effectors primes endothelial cells for optimal tumor immune surveillance.

Leukocyte Transendothelial Migration

088 The role of Sphingosine-1-Phosphate (S1P) in the Reverse Transendothelial Migration (RTM) of aortic intimal Myeloid Cells (MCs)

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- RTM of intimal MCs into the circulation is a protective immune response triggered by LPS stimulation
- RTM is dependent on S1P signaling; specifically, sensing of S1P via myeloid S1PR1 and likely S1PR3
- S1P production by SPHK1 in hematopoietic cells contributes to maintaining the MC population and RTM

089 Mechanotransduction across endothelial PECAM initiates transmigration and reveals a ligand-independent role for VEGFR2 in diapedesis

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- Leukocytes signal through a VEGFR2/PECAM/VE-cadherin mechanosensory complex during TEM
- The cytoplasmic tail of PECAM transmits the tension signal
- The mechanosensory complex signals to TRPC6 through PLCgamma1

Vasculature in the Inflammatory Response

090 15-Lipoxygenase drives inflammation resolution and Treg trafficking in lymphedema

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1. INSERM Institute of Metabolic and Cardiovascular Diseases, Toulouse, France

- Lymphedema chronic inflammation is promoted by a defect of resolution
- Decrease in arachidonic acid-derived lipid mediators generated by the 15-lipoxygenase in lymphedema
- 15-LOX is involved in selective adipose tissue Treg recruitment in lymphedema

091 Regeneration of the pulmonary vascular endothelium after severe viral pneumonia

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- The lung vascular endothelium undergoes robust regeneration after severe viral pneumonia
- TGF-B signaling impact lung endothelial repair and cell type specification
- Failure of vascular repair after influenza infection prevents physiologic recovery of lung function

Pathophysiology of Vascular Disease

092 Genome-wide analysis reveals epigenetic coordinated endogenous FOXO1 stimulates tissue-specific and Tip-marked gene expression in endothelium

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- FOXO1-expressed many cells, but unique function may have in ECs from the general knockout study

- Endogenous FOXO1 ChIP-seq unexpectedly identified the regulation of EC-specific and tip-marked genes
- Global FOXO1 systems approach may find de novo promoter/enhancer regions during vessel maturation

093 The novel "microbiome-oral-gut-brain axis" in the mechanism of stroke

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2. Dept. of Vascular Physiology, National Cerebral and Cardiovascular Center, Suita, Osaka, Japan

- Microbiome research held in acute stroke cohort
- Oral and gut microbes coordinately contributed on the dysbiosis in stroke
- Clinical relevance proposed novel oral-gut-brain axis

Impact of Microvascular Aging in Development and Progression of Cardiovascular Pathology

094 In utero exposure of delta-9-tetrahydrocannabinol (THC) affects cardiovascular tissues in rhesus macaques

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- Cannabis use is increasing in pregnant women
- THC can cross the placenta and bind to cannabinoid receptors on the fetus including the heart
- Our group developed a rhesus macaque model of chronic prenatal edible THC use

095 Impairment of vascular mitochondrial metabolism accelerates vascular aging, promotes endothelial dysfunction, vascular hypertrophy and hypertension

Dikalov, Sergey[1]; Gutor, Sergey[1]; Polosukhin, Vasiliy[1]; Dikalova, Anna[1]
1. Vanderbilt University Medical Center, Nashville, Tennessee, USA

- Vascular dysfunction contributes to pathogenesis of cardiovascular disease which is linked to aging
- Risk factors impair mitochondrial deacetylase Sirt3 which leads to accelerated vascular aging
- Sirt3 deficiency promotes vascular disease and hypertension and targeting Sirt3 can be beneficial

New -omics Approaches

096 Peroxidase proximity biotinylation: a valuable tool in understanding the regulation of endothelial proteins and vascular function

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2. Cell Signalling & Proteomics Group, Queen Mary University of London, London, United Kingdom of Great Britain and Northern Ireland

- Endothelial protein trafficking is a key regulator of angiogenesis
- Peroxidase proximity biotinylation allows the unbiased identification of co-localised proteins
- Proteins co-localised with angiogenic mediators are potential regulators and therapeutic targets

097 Integrated single cell molecular analysis of pericytes reveals the cis-regulatory logic governing their identity

Idrizi, Feston[1]; Lawson, Nathan1; Shih, Yu-Huan1; Goodman, Aliece1
1. University of Massachusetts Chan Medical School, Worcester, Massachusetts, USA

- Single Cell RNA seq reveals pericyte specific gene signature
- Single Cell ATAC seq reveals pericyte specific enhancer signature

- Integrated "omics" data suggest the Notch signaling pathway drives pericyte specific gene expression

HETEROGENEITY OF VASCULAR AND IMMUNE CELLS

098 Macrophages support healing of ischemic injury by initiating transdifferentiation towards mural cells to adopt functions important for vascular support

Parv, Kristel[1]; Herrera-Hidalgo, Carmen[1]; Xu, Feifei[1]; Amoedo-Leite, Catarina[1]; Giraud, Antoine[1]; Holl, Daniel[2]; Seignez, Cedric[1]; Göeritz, Christian[2]; Christoffersson, Gustaf[1]; Phillipson, Mia[1]

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2. Karolinska Institute, Stockholm, Sweden

- Macrophages of adult, injured tissue induce transdifferentiation towards mural cells
- Induction of PDGFRβ-expression is required for the fate switch of the perivascular macrophages
- The transdifferentiation of macrophages into mural cells support healing of ischemic injury

099 Single-cell transcriptomic profiling of endothelial cells reveals novel sub-populations of capillary cells involved in PH pathogenesis

Rafikova, Olga[1]; James, Joel[1]; Dekan, Alexander[1]; Varghese, Mathews[1]; Niihori, Maki[1]; Yi, Dan[2]; Dai, Zhiyu[2]; Rafikov, Ruslan[1]

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2. University of Arizona, Phoenix, Arizona, USA

- Single-cell transcriptomics of lung endothelium showed four novel subpopulations of capillary cells
- Each subphenotype has a characteristic function in the capillary
- Mitochondrial dysfunction induces senescence in capillary cells and involves in PH pathogenesis

100 Targeting Epsins by nanotherapy promotes cholesterol efflux and lipid metabolism to fortify atheroma regression

Cui, Kui[1]; Gao, Xinlei[1]; Wang, Beibei[1]; Wu, Hao[1]; Dong, Yunzhou[1]; Xiao, Yuling[1]; Jiang, Xingya[2]; Malovichko, Marina, V[3]; Li, Kathryn[1]; Shan, Dan[1]; Peng, Qianman[1]; Lu, Yaowei[1]; Zhu, Bo[1]; Zheng, Rongbin[1]; Wong, Scott[1]; Cowan, Douglas[1]; Linton, MacRae[4]; Srivastava, Sanjay[3]; Shi, Jinjun[2]; Chen, Kaifu[1]; Chen, Hong[1]

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3. University of Louisville, Louisville, Kentucky, USA

4. Vanderbilt University Medical Center;, Nashville, USA

- Macrophage Epsins regulate lipid metabolism
- Macrophage Epsins promote cholesterol efflux
- Targeting Epsins in lesional macrophages may offer therapeutic benefits for atherosclerosis

101 Molecular mechanisms linking LIPA CAD GWAS variants to increased myeloid expression and atherosclerosis

Zhang, Hanrui[1]

1. Columbia University Irving Medical Center, New York, New York, USA

- Connecting variant-to-function is essential for GWAS translation
- CAD GWAS variants in LIPA lead to increased macrophage LIPA expression and enzyme activity
- Myeloid-specific overexpression of Lipa exacerbates atherosclerosis