



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

FRIDAY, OCTOBER 14 – 12:00PM TO 2:00PM – WEST HALL

POSTERS: VASCULAR MALFORMATIONS

1001 Preventing stroke from cerebral cavernous malformations by targeting the microbiome

Choi, Jaesung Peter¹

1. Centenary Institute, The University of Technology Sydney (UTS), Newtown, Australia

- Novel therapeutics for cerebral cavernous malformation
- Gut microbiome induced inflammation
- Gut-brain axis

1002 Gain-of-function GNAQ mutation in the endothelium causes aberrant vascular morphogenesis and coagulopathy that are rescued by MEK inhibition

Schrenk, Sandra¹; Goines, Jillian¹; Bischoff, Lindsay¹; Kang, Rachael¹; Boscolo, Elisa¹

1. Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, 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

1003 Essential role of the amino-terminal region of Drosha for the Microprocessor function

Prabhakar, Amit¹; Hu, Song²; Tang, Jin²; Ghatpande, Prajakta²; Lagna, Giorgio¹; Jiang, Xuan²; Hata, Akiko¹

1. CVRI, University of California San Francisco (UCSF), San Francisco, California, USA

2. Sun Yat-Sen University School of Medicine, Shenzhen, Guangdong, China

- Missense mutations in Drosha-NTR are associated with a familial vascular disorder HHT.
- Drosha-NTR is essential for pri-miRNA processing and RP biogenesis.
- Ago2 processes pri-miR-183/96/182 when Drosha is absent or deleted in the NTR.

1004 Bioengineered 3D in vitro strategies to investigate phenotypic and genotypic differences in lymphatic malformation sprouting

Gonzalez-Vargas, Yarelis¹; Spangle, Jennifer M²; Hong, Andrew²; Hawkins, Matthew²; Dixon, J. Brandon¹

1. Georgia Institute of Technology, Atlanta, Georgia, USA

2. Emory University School of Medicine, Atlanta, Georgia, USA

- Use of biomaterial strategies to expand lymphatic malformation cell lines from patient biopsies.
- Reverse engineer a lymphatic malformation organoid from patient biopsies
- Investigate lymphatic malformation organoids sensitivity to inhibitors of signals downstream of VEGF

1005 Lymphedematous extracellular matrix: a new therapeutic target for an unmet medical need.

Morfoisse, Florent¹; Hifdi, Nesrine¹; Benuzzi, Emeline¹; Draia-Nicolau, Tangra¹; Pujol, Françoise¹; Lacazette, Eric²;

Prats, Anne-Catherine¹; Garmy-Susini, Barbara¹

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

2. Université Paul Sabatier, Toulouse 3, Toulouse, France

- Targeting the microenvironment to restore lymphatic vessels in lymphedema
- extracellular matrix remodelling regulators constitute promising therapeutic targets for lymphedema
- Lysyl oxidase (LOX) is a crucial actor of lymphedema-associated fibrosis and lymphatic disruption

1006 Underlying mechanisms in vascular anomalies induced by mutations in RASA1.

Mompeon, Ana¹; Uebelhoer, Melanie²; Iruela-Arispe, M. Luisa¹;

1. Northwestern University, Feinberg School of Medicine, Chicago, Illinois, USA

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

- Neonatal endothelial-specific inactivation of Rasa1 in mice results in hepatic vascular cavernomas.
- RASA1 regulates the subcellular localization of proteins associated with junctional complexes.
- RASA1 is a critical regulator of endothelial junction integrity in response to flow.

1007 Alk1 Controls Endothelial Cx43 to Regulate Vessel Growth

Fang, Jennifer, S¹; Hughes, Christopher, C²

1. Tulane University, New Orleans, Louisiana, USA

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

- Alk1 signaling regulates expression of vascular connexins.
- Silencing of Alk1 upregulates endothelial expression of Cx43.
- Cx43 regulates angiogenic sprouting and vessel formation.

1008 Deciphering the role of the genetic modifier PTPN14 in BMP9-SMAD signaling and vascular malformations in Hereditary Hemorrhagic Telangiectasia

Beleford, Daniah, T¹; Mamai, Ons¹; Basu, Sugandha¹; Del Rosario, Reyno¹; Akhurst, Rosemary, J¹;

1. UCSF, San Francisco, California, USA

- We have developed a novel mouse model for vascular malformations.
- Ptpn14 loss of function causes delayed angiogenesis in developing mouse retinas.
- Ptpn14 localizes to arteries, veins, and lymphatic vessels in adult wild-type mice.

1009 Hypoxia-induced immunothrombosis and exacerbation of brain vascular malformation disease

Frias-Anaya, Eduardo¹; Nelsen, Bliss¹; Gallego-Gutierrez, Helios¹; Weinsheimer, Shantel²; Orecchioni, Marco³; Lai, Catherine, C¹; Hale, Preston¹; Pham, Angela¹; Sun, Hao¹; Shenkar, Robert⁴; Moore, Thomas⁴; Lightle, Ronda⁴; Girard, Romuald⁴; Daneman, Richard¹; Nudleman, Eric¹; Mesarwi, Omar¹; Kim, Helen³; Ley, Klaus³; Awad, Issam, A⁴; Gongol, Brendan⁵; Ginsberg, Mark, H¹; Lopez-Ramirez, Miguel, A¹

1. University of California San Diego, San Diego, California, USA

2. University of California San Francisco, San Francisco, USA

3. La Jolla Institute for Immunology, San Diego, USA

4. The University of Chicago Medicine and Biological Sciences, Chicago, USA

5. University of California Riverside, Riverside, USA

- Hypoxia accelerates CCM disease by increasing lesion burden and neurovascular thrombosis
- Astrocytes and endothelium express genes involved in immune cell recruitment into mature CCM lesions
- Specific variants of hypoxia-related genes are associated with brain hemorrhage and lesion burden

1010 A single-cell atlas of the normal and malformed human brain vasculature

Winkler, Ethan¹; Kim, Chang¹; Ross, Jayden¹; Garcia, Joseph¹; Gil, Eugene¹; Wu, David¹; Catapano, Joshua²; Narsinh, Kazim¹; Kim, Helen¹; Weinsheimer, Shantel¹; Cooke, Daniel¹; Lawton, Michael²; Gupta, Nalin¹; Zlokovic, Berislav³; Chang, Edward¹; Abila, Adib¹; Lim, Daniel¹; Nowakowski, Tomasz¹

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

2. Barrow Neurological Institute, PHOENIX, Arizona, Arizona, USA

3. University of Southern California, Los Angeles, CA, USA

- We provide a cell atlas of the human cerebrovasculature using single-cell RNA-sequencing.
- We define endothelial arteriovenous zonations and expanded perivascular cell diversity in humans.
- We catalog cellular and molecular changes in brain arteriovenous malformations.

1011 Neurovascular dysfunction and behavior changes during brain vascular malformations.

Nelsen, Bliss¹; Frias Anaya, Eduardo¹; Gallego-Gutierrez, Helios¹; Gongol, Brendan²; Conaboy, Liam¹; Anagnostaras, Stephan¹; Lopez Ramirez, Miguel¹

1. University of California, San Diego, San Diego, California, USA

2. University of California, Riverside, Riverside, California, USA

- Activated astrocytes influence CCM disease pathogenesis.
- CCM-activated astrocytes contribute to neuroinflammation.
- This neurovascular dysfunction leads to behavioral changes and neurocognitive impairment.

1012 Endothelial deletion of Rbpj reverses brain arteriovenous malformation induced by constitutively active Notch4 in mice

Nielsen, Corinne¹; Zhang, Xuetao¹; Raygor, Kunal¹; Wang, Shaoxun¹; Wang, Rong¹

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

- Inhibition of endothelial Rbpj from newly formed AVMs reverses Notch4*--induced AVM abnormalities.
- Inhibition of endothelial Rbpj from advanced AVMs reverses Notch4*--induced brain AVM abnormalities.
- Reactivation of Notch4* after full AVM regression did not re-elicite brain AVMs in adult mice.

1013 Pharmacologic rescue of cerebral cavernous malformations (CCMs) by Rapamycin – A pre-clinical study using FDA-approved mTOR inhibitor

Li, Lun¹; Burkhardt, Jan, K¹; Kahn, Mark, L¹

1. University of Pennsylvania, Philadelphia, Pennsylvania, USA

- Inducible adult CCM mouse model that genetically and morphologically more faithful to human disease
- Somatic PIK3CA mutation promotes cavernous malformation growth in the adult brain
- Pharmacologic rescue of CCM by FDA-approved inhibitor using the inducible adult CCM mouse model

1014 Mural cell SRF controls pericyte migration, vessel patterning and blood flow

Orlich, Michael, M¹; Diéguez-Hurtado, Rodrigo²; Muehlfriedel, Regine³; Sothilingam, Vithiyanjali³; Wolburg, Hartwig⁴; Oender, Cansu, E⁵; Woelfling, Pascal⁵; Betsholtz, Christer¹; Gaengel, Konstantin¹; Seeliger, Mathias³; Adams, Ralf, H²; Nordheim, Alfred⁵

1. University of Uppsala, Uppsala, Sweden

2. Max Planck Institute for Molecular Biomedicine, Muenster, Germany

3. Institute for Ophthalmic Research, Tuebingen, Germany

4. Institute of Pathology and Neuropathology, Tuebingen, Germany

5. Interfaculty Institute for Cell Biology, Tuebingen, Germany

- The transcription factor SRF controls pericyte (PC) migration via PDGFB-PDGFRB signalling
- Blockade of SRF signaling in PCs under ischemic conditions mitigates pathologic angiogenesis
- In vSMCs, SRF controls the expression of contractile genes, leading to formation of AV-shunts

1015 Induced-cell cycle arrest prevents arterio-venous malformations in Hereditary Hemorrhagic Telangiectasia

Genet, Gael¹; Genet, Nafiisha¹; Chavkin, Nicholas¹; Cain, Shelby¹; Paila, Uma¹; Sankaranarayanan, Danya¹; Nelson, Elizabeth¹; Hirschi, Karen¹

1. University of Virginia, Charlottesville, Virginia, USA

- Cell cycle state and associated regulatory genes are dysregulated in endothelial cells forming AVMs.
- Palbociclib, a cell cycle inhibitor, prevents vascular malformations in preclinical models of HHT
- Palbociclib restores endothelial BMP9 signaling, migration and metabolic functions in HHT

1016 Withdrawn

1017 Perturbation of the PGE receptor EP4 Resulting in Mouse Patent Ductus Arteriosus is Dependent on Developmental Timing

Yarboro, Michael, T¹; Boatwright, Naoko²; Hooper, Chris, W²; Wong, Ting²; Poole, Stan, D²; Shelton, Elaine, L²; Reese, Jeff²

1. Vanderbilt University, Nashville, Tennessee, USA

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

- Impaired signaling of the PGE receptor EP4 causes persistent patency of the ductus arteriosus (PDA)
- We detected a critical developmental window when EP4 signaling is required to specify DA identity
- Molecular, pharmacologic, and signaling studies reveal an immature phenotype underlies the EP4 PDA

1018 ZYX is a novel candidate gene in Moyamoya pathogenesis.

Barak, Tanyeri¹; Yalcin, Kanat¹; Gunel, Murat¹

1. Yale University, New Haven, CT, USA

- Rare and damaging mutations ZYX, a focal adhesion molecule are implicated in Moyamoya pathogenesis.
- Loss of function and missense variants identified in patients leads to abnormal cell morphology.
- Mutations identified in patients resulted in impaired cell adhesion.

POSTERS: SMOOTH MUSCLE CELLS

1019 Investigation of Cellular Mechanisms Contributing to Adult Retinal Microvascular Smooth Muscle Cell Loss with Aging and Cav1 Depletion

Gurley, Jami, M¹; Hargis, Elizabeth, H¹; Ballheim, Jennifer, D¹; Pranay, Atul²; Batushansky, Albert²; Schafer, Christopher, M²; Griffin, Tim, M²; Griffin, Courtney, T²; Elliott, Michael, H¹

1. OUHSC, Oklahoma City, Oklahoma, USA

2. OMRF, Oklahoma City, Oklahoma, USA

- Role of Cav1 in retinal smooth muscle cell maintenance
- Retinal microvascular aging
- Role of Cav1 in retinal endothelial metabolism

1020 Regenerating vascular mural cells in zebrafish fin blood vessels are not derived from pre-existing ones and differentially require pdgfrb signaling for their development

Leonard, Elvin, V¹; Figueroa, Ricardo, J²; Bussmann, Jeroen³; Lawson, Nathan, D⁴; Siekman, Arndt, F¹

1. Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA

2. Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Santiago, Chile

3. Leiden Academic Centre for Drug Research, Leiden, Netherlands

4. University of Massachusetts Medical School, Worcester, USA

- Co-expression of pdgfrb and myh11a defines mural cell populations
- Pdgfrb expressing cuboidal-shaped cells are precursors for vascular mural cells
- Pre-existing mural cells are not precursors for regenerating mural cells

1021 sFlt1-Induced Preeclampsia Activates Smooth Muscle Mineralocorticoid Receptors Resulting in Enhanced Post Partum Responsiveness to Hypertensive Stimuli

Biber, Lauren¹; Lu, Qing¹; Ibarrola, Jaime¹; Stepanian, Alec¹; Man, Joshua¹; Carvajal, Brigett¹; Camarda, Nicholas¹; Zsengeller, Zsuzsanna²; Skurnik, Geraldine³; Seely, Ellen³; Karumanchi, S. Ananth⁴; Jaffe, Iris¹

1. Tufts Medical Center, Boston, Massachusetts, USA

2. Beth Israel Deaconess Medical Center, Boston, USA

3. Brigham and Women's Hospital, Boston, USA

4. Cedars Sinai Medical Center, Los Angeles, USA

- Preeclampsia (PE) induces post-partum vascular sensitivity to angiotensin II exposure
- Smooth muscle mineralocorticoid receptor is required for the enhanced hypertensive response after PE
- Mechanistic understanding can lead to strategies to mitigate the high risk of hypertension after PE

1022 The contribution of smooth muscle cells to de novo beige adipogenesis

Tan, Josephine, M¹; Fong, Skylar¹; Cheng, Lan¹; Calhoun, Ryan¹; Seale, Patrick¹

1. University of Pennsylvania, Philadelphia, Pennsylvania, USA

- Smooth muscle cells undergo de-differentiation and transition into different cell types
- Smooth muscle cells can contribute to thermogenic adipogenesis
- SMC-derived thermogenic adipogenesis is heterogeneous between different fat depots

1023 Pericytes, but not vascular smooth muscle cells, invade, recruit to EC-lined tube networks, and induce basement membrane matrix deposition on the EC abluminal tube surface

Yrigoin, Ksenia¹; Davis, George¹

1. University of South Florida, Tampa, Florida, USA

- Pericytes, but not VSMCs, significantly invade collagen matrices with endothelial-derived factors.
- Pericytes, but not VSMCs, recruit to EC-lined vascular tubes under 3D-defined serum-free conditions.
- Pericytes, but not VSMCs, induce basement membrane deposition on EC-lined vascular tubes.

1024 Nuclear smooth muscle α -actin is critical for smooth muscle cell differentiation

Kwartler, Callie¹; Pedroza, Albert, J²; Kaw, Anita¹; Guan, Pujun¹; Ma, Shuangtao³; Duan, Xue-yan¹; Kernell, Caroline¹; Chen, Jiyuan¹; Fischbein, Michael²; Milewicz, Dianna¹

1. University of Texas Health Science Center at Houston, Houston, Texas, USA

2. Stanford University, Stanford, California, USA

3. Michigan State University, East Lansing, Michigan, USA

- α -smooth muscle (SM) actin is found in the nucleus of SM cells on the promoters of SM specific genes
- Mutations affecting Arg. 179 of α -SM actin impair nuclear localization and SM cell differentiation
- Incomplete SM differentiation of Acta2 R179 cells is associated with altered chromatin accessibility

1025 MYH11 rare variant causes aberrant cardiac fibrosis and cardiac hypertrophy and failure with increased biomechanical stress in male mice

Zhou, Zhen¹; Hughes, Kgos²; Saif, Nisha³; Pan, Ping¹; Massett, Michael, P⁴; Zheng, Mingjie¹; Cecchi, Alana, C¹; Guo, Dongchuan¹; Grealley, John, M⁵; Wang, Jun¹; Milewicz, Dianna, M¹

1. UTHealth Science Center at Houston, Houston, Texas, USA

2. Wake Forest University, Winston-Salem, North Carolina, USA

3. The University of Texas at Austin, Austin, Texas, USA

4. Texas Tech University, Lubbock, Texas, USA

- A rare variant in Myh11, c.5676G>C (p.Glu1892Asp) augments stress-induced aortic disease in mice
- SMC-specific myosin heavy chain, p.Glu1892Asp, leads to cardiac fibrosis and pump failure in mice
- Gender difference in stress-induced cardiac remodeling in mice carrying a rare Myh11 mutation

1026 PKC mediates voltage-independent contractile signaling in mouse resistance arteries

Haghbin, Nadia¹; Richter, David, M¹; Kim, Michelle, S¹; Welsh, Donald, G¹

1. Western University, London, Ontario, Canada

- Concentration & mode of agonist application impacts hierarchical arrangement of contractile control.
- voltage-dependent signaling typically precedes voltage-independent contractile signaling.
- PKC mediates voltage-independent contractile signaling.

1027 Vascular smooth muscle cell differentiation on the circle of Willis arteries

Cheng, Siyuan (Lily)¹; Nicoli, Stefania¹

1. Yale University, New Haven, Connecticut, USA

- Endothelial cells in the circle of Willis arteries are specified after migrate from primitive veins
- pdgfrb+ progenitors differentiate into acta2+ vascular smooth muscle cells brain arteries
- Blood flow is required to initiate vascular smooth muscle cell differentiation on brain arteries

POSTERS: STEM CELLS

1028 The EPCR/APC pathway plays an important role in ECFCs vasoreparative function.

Peixoto, Elisa¹; Chambers, Sarah¹; Lechner, Judith¹; Lowry, Amie¹; Pedrini, Edoardo¹; Bertelli, Pietro¹; Medina, Reinhold¹; Stitt, Alan¹

1. Queen's University of Belfast, Belfast, United Kingdom of Great Britain and Northern Ireland

- Endothelial colony-forming progenitor cells (ECFCs) has vasoreparative potential
- Endothelial protein C receptor (EPCR) is progenitor marker and evokes cytoprotective responses
- EPCR/APC pathway regulates progenitor function such as tubulogenesis, clonogenicity and migration

1029 Hedgehog signalling drives EndMT in human resident vascular stem cells, initiating atherogenesis

Nano, Rachel¹; Khosrotehrani, Kiarash²; Richard, Derek¹; Patel, Jatin¹

1. Queensland University of Technology, Brisbane, Australia

2. The University of Queensland, Brisbane, Australia

- Identifying novel mechanisms of resident vascular stem cell dysfunction in atherogenesis
- Hedgehog signalling in the endothelium
- Endothelial to mesenchymal transition driving fibrosis in atherosclerosis

1030 Mechanical Conditioning Prevents Senescence in Mesenchymal Stem Cells from Aged Patients

Massidda, Miles¹; Demkov, Andrei¹; Sices, Aiden¹; Lee, Jason¹; Lee, Muyeoung¹; Kim, Jonghwan¹;

Baker, Aaron¹

1. University of Texas at Austin, Austin, Texas, USA

- Mechanical conditioning of MSCs from aged patients leads to enhanced proliferative capacity.
- Mechanical conditioning of MSCs increases expression of sirtuins, SOD1, and DNA repair proteins.
- Mechanical conditioning acts through an oxidative stress mediated pathway to reduce senescence.

1031 ABCG2 expressing endothelial stem cells serve to form and maintain blood vessels

Lin, Yang¹; Gil, Chang-Hyun²; Banno, Kimihiko³; Liu, Ying¹; Yokoyama, Masataka⁴; Prasain, Nutan²; Naito, Hisamichi⁵; Wakabayashi, Taku⁶; Sominskaia, Musia¹; Gomez Salinero, Jesus, M¹; Schreiner, Ryan¹; Basile, David, P²; Rafii, Shahin¹; Yoder, Mervin²

1. Weill Cornell Medicine, New York, New York, USA

2. Indiana University School of Medicine, Indianapolis, USA

3. Nara Medical University, Kashihara, Japan

4. Chiba University, Chiba, Japan

5. Kanazawa University School of Medicine, Kanazawa, Japan

6. Thomas Jefferson University, Philadelphia, USA

- ABCG2 expressing EC with endothelial stem cells (VESC) features exist in human and murine vessels
- Abcg2-VESC contribute to vessel growth in development and injury healing
- Abcg2-VESC show transcriptome/epigenetic signature involved in vessel development and self-renewal

POSTERS: VASCULAR CELL-MATRIX INTERACTIONS

1032 Identification of unique cell populations associated with thoracic aortic aneurysm of Marfan syndrome mice

Asano, Keiichi¹; Sun, Yifei¹; Cantalupo, Anna¹; Sedes, Lauriane¹; Walsh, Martin, J¹; Ramirez, Francesco¹

1. Icahn School of Medicine at Mount Sinai, New York, New York, USA

- Characterization of cellular heterogeneity of thoracic aortic aneurysm of Marfan syndrome mice.
- Identification of unique EC and SMC populations associated with aneurysm of Marfan syndrome mice.
- Elimination of the unique cell populations following treatment with At1r antagonist, losartan.

1033 c-Src activity induces vascular malformations and breakdown of the extracellular matrix

Essebieer, Patricia, J¹; Schimmel, Lillian¹; Yordanov, Teodor¹; Keyser, Mikaela¹; Yu, Alexander¹; Hill, Brittany¹;

Stehbens, Samantha¹; Noordstra, Ivar¹; Yap, Alpha¹; Lagendijk, Anne¹; Gordon, Emma¹

1. Institute for Molecular Bioscience, Brisbane, Australia

- The non-receptor tyrosine kinase c-Src is a driver of blood vessel growth and cell adhesion
- A constitutively active form of c-Src induces vascular malformations and loss of vessel integrity
- c-Src activity drives blood vessel defects by increasing matrix degradation at focal adhesions

1034 Context-dependent integrin activation regulates vascular stability and permeability

Kiss, Elina, A¹; Ganesh, Keerthana¹; von Wright, Ylva¹; Halme, Aleksis¹; Peuhu, Emilia²; Miinalainen, Ilkka³; Eklund, Lauri³; Ivaska, Johanna²; Pink, Anne¹; Saharinen, Pipsa¹

1. University of Helsinki, Helsinki, Finland

2. University of Turku, Turku, Finland

3. University of Oulu, Oulu, Finland

- β 1- and β 3-integrins protect blood capillaries
- Balance of EC-EC and EC-matrix adhesions thresholds EC permeability
- Inflammatory signals regulate context-dependent functions of EC integrins

1035 Protective role of endothelial fibulin-4 in valvulo-arterial integrity

Nguyen, Tram Anh, Vu¹; Lino, Caroline, A²; Hang, Huynh, T¹; Alves, Juliano, V³;

Thang, Bui, Q¹; Shin, SeungJae¹; Sugiyama, Kaori⁴; Matsunaga, Hiroko⁴; Takeyama, Haruko⁴; Yamashiro, Yoshito¹; Yanagisawa, Hiromi¹

1. University of Tsukuba, Tsukuba, Ibaraki, Japan

2. University of Sao Paulo, Sao Paulo, Brazil

3. University of Sao Paulo, Ribeirao Preto, Brazil

4. Waseda University, Tokyo, Japan

- Knockdown of FBLN4 in endothelial cells (ECs) induced mesenchymal cell-like changes.
- EC and SMC- specific knockout for fibulin-4 (DKO) showed worsening aortic aneurysms.
- DKO mice displayed thickening aortic valves with altered transcriptome profiles suggestive of EndMT.

POSTERS: CELL-CELL INTERACTIONS

1036 Identification of novel VE-cadherin binding proteins that regulate the endothelial barrier

Schoon, Rianne, M¹; Malinova, Tsveta, S¹; van Alphen, Floris, P²; van den Biggelaar, Maartje²; van Buul, Jaap, D²; Huvencers, Stephan¹

1. Amsterdam UMC, University of Amsterdam / Academic Medical Center, Amsterdam, Netherlands

2. Sanquin Landsteiner Laboratory, Amsterdam, Netherlands

- Using mass-spectrometry after VE-cadherin pull-down from HUVECs we found novel interacting proteins
- shRNA knock-down experiments show association of these proteins with different cellular processes
- Our novel VE-cadherin-binding proteins are potent regulators of the vascular endothelial barrier

1037 Endothelial cells secrete extracellular vesicles in a polarized fashion to participate in cell-cell communication: Implications for atherosclerotic plaque development

Raju, Sneha¹; Prajapati, Kamalben²; Ho, Tse Wing Winnie³; Blaser, Mark⁴; Botts, Steven, R¹; Ching, Crizza¹; Singh, Sasha, A⁴; Galant, Natalie, J²; Fiddes, Lindsey⁵; Wu, Ruilin³; Stark, Jamie⁶; Veitch, Shawn³; Aikawa, Elena⁴; Lee, Warren³; Fish, Jason, E¹; Howe, Kathryn, L¹

1. Institute of Medical Sciences, University of Toronto, Toronto, Ontario, Canada

2. University Health Network, Toronto, Ontario, Canada

3. Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada

4. Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

5. Temerty Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada

6. University of Toronto, Toronto, Ontario, Canada

- ECs increase EV release, and alter EV-miRNA and -protein content upon activation.
- EVs from activated ECs modulate inflammatory and atherogenic pathways in VSMCs and CD14+ monocytes.
- ECs secrete EVs bidirectionally to participate in cell-cell communication.

1038 How VE-PTP strengthens VE-cadherin adhesion

Fröhlich, Deborah¹; Braun, Laura, J¹; Vestweber, Dietmar¹

1. Max Planck Institute for Molecular Biomedicine, Münster, Germany

- VE-PTP strengthens VE-cadherin adhesion via its phosphatase activity in endothelial junctions.
- Using a specific adhesion assay we exclude EphB4 and VE-cadherin Y685 from the strengthening effect.
- The link to the actin cytoskeleton presents key for VE-PTP to strengthen VE-cadherin adhesion.

1039 Systems-Mechanobiology of Endothelial Dynamics

Keshavanarayana, Pradeep¹; Moeendarbary, Emad²; Spill, Fabian¹

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

2. UCL, London, United Kingdom of Great Britain and Northern Ireland

- Gaps in endothelium are regulated by forces and molecules
- Forces affect molecular pathways, and molecular pathways affect forces
- Systems-level understanding requires models to integrate mechanical and molecular features

1040 Notch Pathways Regulate Expression of Angiostatic Factor Activin A in Heterotypic Endothelial - Pericyte-like Mesenchymal Cell Interactions

Merfeld-Clauss, Stephanie¹; March, Keith, L¹; Traktuev, Dmitry, O¹

1. University of Florida, Gainesville, Florida, USA

- Endothelial cells induce Activin A expression in perivascular cells through juxtacrine signaling
- Notch2 induces and Notch3 inhibits Activin A expression in perivascular cells
- Silencing Notch3 induces spontaneous acquisition of smooth muscle phenotype in perivascular cells

1041 Role of endothelial- and neural-expressed Cx43 in retinal vascular development.

Genet, Nafiisha¹; Genet, Gael¹; Chavkin, Nicholas, W¹; Hirschi, Karen¹

1. University of Virginia, Charlottesville, Virginia, USA

- Investigate the role of Cx43 in EC and NSC during postnatal mouse retinal vascularization.
- In Cx43ECiKO P7 retina, vascular progression is impaired and density is increased.
- In Cx43GlastiKO, arterial branchpoints and general vascular density were significantly increased.

1042 Connexin 43-mediated neurovascular interactions regulate neurogenesis in the adult brain subventricular zone.

Genet, Nafiisha¹; Genet, Gael¹; Fang, Jennifer²; Chavkin, Nicholas, W¹; Vasavada, Hema²; Joshua, Goldberg, S²; Bhatt, Neha²; Baker, Kasey²; McDonnell, Stephanie, P¹; Huba, Mahalia¹; Ma, Gerry, Z³; Anne, Eichmann²; Thomas, Jean-Leon²; French-Constant, Charles³; Hirschi, Karen¹

1. University of Virginia, Charlottesville, Virginia, USA

2. Yale University, New Haven, Connecticut, USA

3. University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland

- In a transwell system, when NSC is co-cultured with EC, Cx43 mRNA expression is upregulated in NSC.
- In vivo, in the adult brain SVZ, vascular EC-expressed Cx43 regulates NSC activation.
- The EC maintenance of NSC quiescence is dependent on Cx43 and ERK activity.

POSTERS: VASCULAR HETEROGENEITY

1043 Defining the Transcriptional and Epigenetic Basis of Organotypic Endothelial Diversity in the Developing and Adult Mouse

Cantu Gutierrez, Manuel¹; Hill, Matthew, C¹; Largoza, Gabrielle¹; Martin, James, F¹; Wythe, Joshua, D¹

1. Baylor College of Medicine, Houston, Texas, USA

- ATAC-seq identified common and unique epigenetic signatures in the endothelium of six organs.
- scRNA-seq and ATAC-seq identified novel early and late transcriptional regulators of BBB maturation.
- These novel BBB regulators are evolutionarily conserved and may control BBB maturation.

1044 IL-1R1 in Endothelial-to-Mesenchymal Activation

Koppada, Satya-Priya¹; Pea, Meleah²; Cheng, Siyuan³; Xu, Xiuping³; Shen, Xinggui⁴;

Alfaidi, Mabruka¹

1. Department of Internal Medicine, LSU Health Shreveport, Shreveport, Louisiana, USA

2. Grambling State University, Shreveport, Louisiana, USA

3. Department of Urology, LSU Health Shreveport, Shreveport, Louisiana, USA

4. Department of Pathology, LSU Health Shreveport, Shreveport, Louisiana, USA

- Endothelial-to-mesenchymal transition (EndMT) identified in vivo and in vitro under d-flow areas.
- Both interleukin-1 and d-flow are involved in EndMT, the upstream pathways are largely unknown.
- We identified IL-1R1 as a direct driver to EndMT under d-flow in vivo and in vitro

1045 Mechanosensitive vascular Wnt signalling shapes hepatic vascular resilience and sustains zoned metabolic liver function

Lee, Ki Hong¹; Jakab, Moritz¹; Uvarovskii, Alexey²; Papageorgiou, Dimitris³; Inverso, Donato¹; Shi, Jingjing¹; Kulkarni, Shubhada¹; Ali, Adnan³; Gallage, Suchira³; Buettner, Michael⁴; Poschet, Gernot⁴; Heikenwalder, Mathias³; Boutros, Michael⁵; Niehrs, Christof⁶; Krijgsveld, Jeroen³; Anders, Simon²; Augustin, Hellmut, G¹

1. European Center for Angioscience/German Cancer Research Center, Mannheim, Germany

2. Center for Molecular Biology Heidelberg, Heidelberg, Germany

3. German Cancer Research Center, Heidelberg, Germany

4. Metabolomics Core Technology Platform, Centre for Organismal Studies, Heidelberg, Germany

5. Medical Faculty Mannheim/German Cancer Research Center, Heidelberg, Germany

6. Institute of Molecular Biology, Mainz/German Cancer Research Center, Heidelberg, Germany

- Blood flow is a crucial milieu factor that governs the vascular Wnt expression in the liver
- Spatial deconvolution of multiomic data unveils zoned self-feeding autocrine Wnt loop in liver EC
- Autocrine Wnt regulates the expression of junctional molecules and the shear sensing machinery

1046 Transcriptional landscape of adipose tissue derived endothelial cells

*Hasan, Sana*¹; *John, David*²

1. German Cancer Research Center, Heidelberg, Germany

2. Institute for Cardiovascular Regeneration, Frankfurt, Germany

- Endothelial heterogeneity in white adipose tissue vasculature.
- Depot specific difference in vasculature in subcutaneous vs visceral white adipose tissue
- Obesity driven alterations in transcriptional profile of white adipose tissue endothelium

1047 Evidence for P53 protection of Car4+ lung endothelial cells in neonatal hyperoxia

*Vila Ellis, Lisandra*¹; *Bywaters, Jonathan*¹; *Chen, Jichao*¹

1. MD Anderson Cancer Center, Houston, Texas, USA

- Lung Car4+capillaries (Cap2) arise from Plvap+Cap1; absence of Cap2 leads to alveolar simplification
- Hyperoxia treated neonatal lungs show Cap1 stall in their transition to Cap2, activating p53 genes
- Deletion of p53 showed that Cap2 are preferentially reduced upon hyperoxia treatment

1048 Nova2 regulated alternative splicing controls lineage fate and network morphogenesis in vascular development

*Rondon, Maria, C*¹; *Okuda, Kazuhide, S*¹; *Dudczig, Stefanie*¹; *Hogan, Benjamin, M*¹; *Wickramasinghe, Vihandha*¹

1. Peter MacCallum Cancer Center, Melbourne, Australia

- Cell differentiation and fate are key for successful development.
- Formation of a functional vasculature requires accurate specification and cell signalling control.
- We have identified an RNA binding protein that has a mechanism that regulates gene expression.

1049 VSMC contribution to neointimal lesions arises from the clonal expansion of few primed cells

*Worssam, Matt, D*¹; *Lambert, Jordi*¹; *Oc, Sebnem*¹; *Chappell, Joel, D*¹; *Bennett, Martin, R*¹; *Jorgensen, Helle, F*¹

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

- Activation of VSMC proliferation is a rare event in vascular disease.
- Regions where VSMC proliferation is activated display VSMC death and immune cell recruitment.
- Activated VSMCs show global opening of chromatin, including at genes relating to proliferation.

1050 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

1051 The Role of Endothelial PARs in Modulating Insulin Signaling

*Rajala, Rahul*¹; *Griffin, Courtney, T*²

1. University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA

2. Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA

- The Role of the Vasculature in Controlling Insulin Sensitivity
- The Role of PARs in Endothelial Insulin Signaling
- The Role of Endothelial PARs in Diabetes

1052 ATF3 promotes endothelial cell response to acute lung injury

Niethamer, Terren, K¹; Levin, Lillian, I¹; Morley, Michael, P¹; Babu, Apoorva¹; Zhou, Su¹; Morrissey, Edward, E¹;

1. *University of Pennsylvania, Philadelphia, Pennsylvania, USA*

- ATF3 promotes pulmonary endothelial cell proliferation after viral lung injury
- Loss of ATF3 results in failure of pulmonary ECs to mount a robust injury response
- ATF3 may mediate pulmonary EC injury response through the Wnt signaling pathway

1053 Distinct morphogenetic processes coordinate the stepwise assembly of the zebrafish tail fin vasculature

Leonard, Elvin¹; Hasan, Sana²; Siekmann, Arndt, F¹

1. *University of Pennsylvania, Philadelphia, Pennsylvania, USA*

2. *Deutsches Krebsforschungszentrum Heidelberg, Heidelberg, Germany*

- Distinct morphogenetic mechanisms coordinate the stepwise assembly of an organ specific vascular bed
- Different types of vascular mural cells associate with distinct regions of the vascular tree
- Mural cells have a limited capacity for self renewal

1054 Pericyte heterogeneity identified by 3D ultrastructural analysis of the microvessel wall

Nolan, Kyle¹; Abdelazim, Hanaa²; Payne, Laura Beth²; Paralkar, Karan²; Bradley, Vanessa²; Kanodia, Ronak²; Gude, Rosalie²; Ward, Rache²; Monavarfeshani, Aboozar²; Fox, Michael, A²; Chappell, John, C²

1. *Virginia Tech Carilion School of Medicine, Roanoke, Virginia, US*

2. *Fralin Biomedical Research Institute at Virginia Tech-Carilion, Roanoke, Virginia, USA*

- Pericyte morphology is likely more diverse than the colloquial characterization of "bumps on a log."
- Datasets of mouse brain tissue imaged by serial block face-scanning electron microscopy.
- Data shows pericyte phenotypes described in past literature are unique on an ultrastructural scale.

POSTERS: VASCULAR AGING

1055 Alteration in VWF levels and expression pattern in response to aging

Alavi, Parnian¹; Brown, Douglas²; Bourque, Stephane³; Lewis, John²; Jahroudi, Nadia¹

1. *Department of Medicine, University of Alberta, Edmonton, Canada*

2. *Department of Oncology, University of Alberta, Edmonton, Canada*

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

- VWF mRNA and protein are upregulated in aged mice in an organ-specific manner
- Increasing microvessels exhibit VWF expression in select organs of aged mice
- Increased VWF expression is accompanied with increased platelet aggregate formation in target organs

1056 Role of stress response and its modulation mechanisms in the age-related decrease in microvascular density

Kobayashi, Miho¹; Hirose, Honoka¹; Nakayama, Masanori²; Watabe, Tetsuro¹;

1. *Dept. of Biochem., Tokyo Medical and Dental University, Tokyo, Japan*

2. *Lab. for Cell Polarity and Organogenesis, MPI for Heart and Lung Research, Bad Nauheim, Germany*

- Age-related reduction of microvascular density (MVD) is associated with longevity.
- We identified the mechanism that reduced stress tolerance in vascular endothelial cells with aging.
- This molecular mechanism may play a role in the age-related reduction of MVD.

1057 A role for extracellular vesicles in the deposition of amyloid proteins in the cerebrovasculature

Shanahan, Catherine, M¹; Whitehead, Meredith¹; Antonazzi, Marco¹

1. *King's College London, London, United Kingdom of Great Britain and Northern Ireland*

- Senescent vascular smooth muscle cells might be implicated in cerebrovascular amyloidosis
- EVs from senescent VSMC could enhance the aggregation of Abeta in the cerebrovasculature
- The disruption of endosomal lysosomal pathways during senescence might be a possible mechanism

1058 Senescence drives changes in vesicle secretion and extracellular matrix organisation to enhance vascular amyloidosis

Whitehead, Meredith¹; Yusoff, Syabira¹; Ahmad, Sadia¹; Shanahan, Cathy¹

1. King's College London, London, United Kingdom of Great Britain and Northern Ireland

- VSMC-derived extracellular vesicles mediate extracellular accumulation of the medin amyloid peptide
- VSMC senescence induces vesicle secretion and changes in vesicle cargo to enhance medin aggregation
- Changes to extracellular matrix composition with VSMC senescence stimulates medin fibril formation

1059 Vimentin shields the endothelial nucleus from the deleterious effects of turbulent flow

Salvador, Jocelynda¹; Abrahamson, Cyrus, W¹; Mompeon-Campos, Ana¹; Hernandez, Gloria²; Ridge, Karen, M¹; Goldman, Robert¹; Iruela-Arispe, M. Luisa¹

1. Northwestern University, Chicago, USA

2. Genentech, South San Francisco, California, USA

- Oscillatory flow progressively deforms endothelial nuclei with age in vivo.
- Vimentin forms a unique juxtannuclear cage protecting endothelial nuclei under shear stress.
- Vimentin antagonizes EC aging and chromatin damage associated with turbulent flow.

1060 Drug Compound A attenuates cellular senescence and maintains CD34+ progenitor population of Endothelial Progenitor Cells by reducing ROS generation

Lim, Hyeji¹

1. School of Medicine, Pusan National University, Yangsan, Korea (Republic of)

- Drug A enhanced the survival, proliferation, migration and tube-forming capacity of senescent EPCs.
- Drug compound A maintains CD34+ population and their characteristics in EPCs.
- Drug A improved angiogenic potential of EPCs by rescuing them from replicative cellular senescence.

1061 Interaction of Inorganic Phosphate and Unfolded Protein Response (UPR) in Placenta

Correia-Branco, Ana¹; Joe, Andrew¹; Hinderer, Eugene¹; Jayaraman, Nirmala¹; Kashpur, Olga¹; Blaser, Mark, C²; Higashi, Hideyuki²; Kuraoka, Shiori²; Mahmoud, Taysir¹; O'Tierney-Ginn, Perrie¹; Singh, Sasha, A²; Aikawa, Elena²; Wallingford, Mary, C¹

1. Tufts Medical Center, Boston, Massachusetts, USA

2. Brigham and Women's Hospital, Boston, Massachusetts, USA

- In this study we evaluated the role of Slc20a2 in placental health at the molecular level.
- We identified an increase in eIF2 α and downstream target PDI in calcified Slc20a2 null tissue.
- We propose that Slc20a2 maintains homeostatic Pi levels in balance with UPRER.

1062 Endothelial Nup93 regulates YAP activity to limit features of endothelial cell senescence

Nguyen, Tung, D¹; Rao, Mihir, K¹; Dhyan, Shaiva, P¹; Winek, Michael, A¹; Lee, Monica, Y¹

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

- Nup93 expression is reduced in severely aged vessels and in vitro models of endothelial senescence.
- Loss of endothelial Nup93 leads to features of endothelial senescence and consequent dysfunction.

- Nup93 expression is crucial for endothelial health by limiting features of endothelial senescence.

POSTERS: VASCULAR-IMMUNE INTERFACE IN CANCER

1063 Desmoglein-2, an unsuspected regulator of tumour vasculature and immune response in melanoma

Cockshell, Michaelia¹; Tan, Lih¹; Myo Min, Kay Khine¹; Holst, Jeff²; Ebert, Lisa¹; Bonder, Claudine¹

1. Centre for Cancer Biology, Adelaide, South Australia, Australia

2. School of Medical Sciences, University of New South Wales, Sydney, Select State, Australia

- Low DSG2 expression in mice reduced melanoma growth and altered leukocyte content and vasculature
- Melanoma cells can mediate leukocyte recruitment via classical endothelial adhesion molecule, ICAM1
- DSG2 plays a role in regulating tumour vasculature and infiltration of leukocytes

1064 Inhibition of angiotensin-2 reverses T-cell exclusion and enhances anti-PD-1 therapy in melanoma

Shiva, Anahita¹; Cummings, Portia¹; Carvajal, Richard¹; Thurston, Gavin²; Yang, Hee Won¹; Kim, Minah¹

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

2. Regeneron Pharmaceuticals Inc, Tarrytown, USA

- Mechanism underlying the vascular regulation of immune evasion and checkpoint blockade efficacy
- Promoting vascular normalization to suppress T-cell exclusion in melanoma
- Ang2/Tie2 signaling regulation of immune evasion and resistance to checkpoint blockade.

1065 Comparison of endothelial cell toxicity of established and novel BCR-ABL tyrosine kinase inhibitors

Travers, Richard, J¹; Wang, Evon²; Stepanian, Alec³; Liu, Qing³; Jaffe, Iris, Z³

1. Tufts Medical Center, Department of Hematology/Oncology, Boston, Massachusetts, USA

2. Tufts University, Medford, Massachusetts, USA

3. Tufts Medical Center, Molecular Cardiology Research Institute, Boston, Massachusetts, USA

- BCR-ABL tyrosine kinase inhibitors improve outcomes in Philadelphia chromosome positive leukemias
- Newer BCR-ABL TKIs have significantly increased risk of arterial thrombosis
- Endothelial cell toxicity of TKIs is a possible mediator of their cardiovascular toxicity

1066 Single Cell Transcriptomic Analysis of Breast Tumor Endothelial Cell Populations Reveal Distinct Phenotypes of Tumor Vascular Subpopulations

Phoenix, Kathryn, N²; Singh, Vijender³; Claffey, Kevin, P¹

1. UConn Health, Burlington, USA

2. UConn Health, Farmington, Connecticut, Connecticut, USA

3. University of Connecticut, Storrs, Connecticut, USA

- Analysis of tumor endothelial cells reveals distinct populations with diverse gene profiles.
- Tumor endothelial cells cluster in groups across various breast tumor phenotypes.
- Defining tumor endothelial cell phenotypes may identify novel targets for cancer therapies.

1067 A large-scale microfluidic system to study the tumor microenvironment and the tumor-EC-immune cell interactions in the context of immunotherapy

Sominskaia, Musia¹; Lin, Yang¹; Yang, Yanping¹; Schreiner, Ryan¹; Jin, Moonsoo¹; Rafii, Shahin¹

1. Weill Cornell Medicine, New York, New York, USA

- Vascularized tumors in vitro mimic the pathological tumor microenvironment in vivo
- Large size of microfluidic device allows for transcriptome studies of tumor-EC coculture
- Our model accounts for tumor-EC-immune cells interaction during immunotherapy testing

1068 The Rho GAP DLC1 acts as a negative feedback sensor for YAP in angiogenic sprouting

Hooglugt, Aukie¹; van der Stoep, Miesje, M¹; Neep, Beau, F¹; de Haan, Annett, J¹; Huvneers, Stephan¹

1. Amsterdam UMC, Amsterdam, Noord-Holland, Netherlands

- DLC1 expression promotes the nuclear-to-cytoplasmic shuttling of endothelial YAP
- YAP cytoplasmic retention by DLC1 requires its functional Rho GTPase-activating protein (GAP) domain
- The GAP activity of DLC1 is needed to rescue the sprouting defects of YAP-depleted endothelial cells

1069 Junctional mechanotransduction in angiogenesis

Huvneers, Stephan¹

1. Amsterdam UMC, University of Amsterdam, Amsterdam, Netherlands

- There are unique mechanotransduction responses at the endothelial junctions
- Junctional forces propagate directional cues by polarized VE-cadherin trafficking
- Vinculin in strengthening of the endothelial barrier during vascular development

1070 A novel model for the study of flow-dependent endothelial cell-cardiomyocyte interactions

Blazeski, Adriana¹; Kamm, Roger, D²; García-Cardeña, Guillermo¹

1. Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA

2. Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

- Our microfluidic device integrates cardiac spheroids, microvascular networks and transluminal flow.
- Application of flow activates a KLF2-GFP endothelial cell sensor and leads to vascular remodeling.
- We study the effects of flow on cardiac contraction and gene expression in our integrated model.

1071 Delineating the transcriptional regulators of KLF2 using enhancer analysis

Fleisinger, Lucija¹; Bruche, Susann¹; De Val, Sarah¹; Jain, Mukesh²; Vinayachandran, Vinesh²; Sparrow, Duncan¹

1. Department of Physiology, Anatomy and Genetics; University of Oxford, Oxford, United Kingdom of Great Britain and Northern Ireland

2. School of Medicine, Case Western Reserve University, Cleveland, Ohio, USA

- Endothelial KLF2 is developmentally regulated by distal enhancers in addition to the core promoter.
- KLF2 enhancers are regulated by a number of transcription factors in addition to MEF2 factors.
- A novel highly conserved motif is required for activity of all KLF2/4 regulatory regions.

1072 Cyclic strain regulates Notch signaling to mediate phenotypic switching of vascular smooth muscle cells

Karakaya, Cansu¹; van Turnhout, Mark, C¹; Visser, Valery, L¹; Ristori, Tommaso¹; Bouten, Carlijn¹; Sahlgren, Cecilia, M²; Loerakker, Sandra¹

1. Eindhoven University of Technology/Department of Biomedical Engineering, Eindhoven, Netherlands

2. Abo Akademi University/Faculty of Science and Engineering, Turku, Finland

- Growth and remodeling are mediated by cells and mechanical cues play a pivotal role in this process
- Mechanosensitive cell signaling pathways can be the link between mechanical cues and cell behavior
- Notch signaling can directly regulate VSMC phenotype in response to mechanical stress

1073 Mechanical tension-induced vascular morphogenesis during lung regeneration

Mammoto, Akiko¹; Hunyenyiwa, Tendai¹; Kyi, Priscilla¹; Matus, Kienna¹; Mammoto, Tadanori¹

1. Medical College of Wisconsin, Milwaukee, Wisconsin, USA

- Vascular formation is stimulated at the peripheral region of the post-pneumonectomy mouse lungs.
- Cellular stretching increases the expression of paxillin and angiogenic factors in vitro.
- Paxillin senses mechanical stretch after pneumonectomy and controls regenerative lung growth.

1074 Pulmonary endothelial cells uniquely respond to flow in vitro

Spearman, Andrew, D¹; Goberman, Katherine¹; Merbach, Monica¹; Ramchandran, Ramani¹

1. Medical College of Wisconsin, Milwaukee, Wisconsin, USA

- Primary human pulmonary endothelial cells uniquely respond to flow in vitro.
- Data from one endothelial cell sub-type should be cautiously extrapolated to other endothelial cells
- Variability in endothelial flow responses may provide insight into acquired vascular malformations.

1075 Flow-sensitive endothelial protein HEG1 mediates stable flow-induced KLF2/KLF4 expression and functional responses, and protects against atherosclerosis

Tamargo, Ian¹; Xu, Chenbo²; Baek, Kyung In²; Kang, Dong-Won²; Kumar, Sandeep²; Andueza, Aitor²; Demos, Catherine²; Villa-Roel, Nicolas²; Williams, Darian¹; Kim, Yerin²; Kim, Juyoung²; Choi, Rachel³; Tsuji, Shoutaro⁴; Jo, Hanjoong²

1. Molecular and Systems Pharmacology, Emory University, Atlanta, Georgia, USA

2. Biomedical Engineering, Georgia Tech and Emory University, Atlanta, Georgia, USA

3. Biochemistry, Georgia Tech, Atlanta, Georgia, USA

4. Med. Technology & Clin. Engineering, Gunma University of Health and Welfare, Maebashi, Japan

- HEG1 is a stable flow-induced endothelial protein.
- Endothelial HEG1 expression is required for KLF2 and KLF4 induction by stable flow.
- HEG1 expression prevents endothelial dysfunction and protects against atherosclerosis.

1076 ARHGEF18: A new mechanosensitive player in endothelial cell biology ?

Batta, Surya¹; Rio, Marc¹; Lebot, Corentin¹; Le Ruz, Robin¹; Loirand, Gervaise¹;

Vion, Anne-Clémence¹

1. Nantes Université, CHU Nantes, CNRS, INSERM, l'institut du thorax, Nantes, France

- ARHGEF18 expression and activity is regulated by shear stress in endothelial cells
- ARHGEF18 interacts with RhoA and ZO-1 but not with Rac1
- ARHGEF18 contributes in tight junctions and focal adhesions formation under shear stress

1077 Endothelial cell elongation in response to shear stress requires post-translational modifications in microtubules

Moise, Katiannah¹; Vattulainen-Collanus, Sanna²; Salvador, Jocelynda¹; Ashfar, Yalda³; Iruela-Arispe, Luisa, M¹

1. Northwestern University, Chicago, Illinois, USA

2. Blueprint Genetics, Helsinki, Finland

3. University of California-Los Angeles, Los Angeles, California, USA

- Endothelial cell elongation requires acetylation of microtubules to respond to shear stress
- Acetylated tubulin are found central downstream while polyglutamylated microtubules are peripheral.
- Mutations that disrupt incorporation of acetyl groups to microtubules results in impaired elongation

1078 Cytoskeletal alignment and cellular elongation induces an anti-inflammatory endothelial transcriptome independent of fluid shear stress

Fallon, Meghan, E¹; Barnes, Anthony, P¹; Hinds, Monica, T¹

1. Oregon Health & Science University, Portland, Oregon, USA

- We identified 1302 mechanosensitive genes differentially expressed by micropatterned ECs by RNA-seq.
- Cytoskeletal alignment induces YAP deactivation under basal and inflammatory conditions.

- Cytoskeletal alignment downregulates YAP target genes and inflammatory cytokine expression.

1079 Assessing endothelial cell mechanosensory response to multi-directional wall shear stress

Moore, Kevin¹; Grol, Matthew, W²; Holdsworth, David, W¹; Pickering, Geoffrey¹; Poepping, Tamie, L³

1. *Robarts Research Institute, Western University, London, Ontario, Canada*

2. *Department of Physiology & Pharmacology, Western University, London, Ontario, Canada*

3. *Department of Physics & Astronomy, Western University, London, Ontario, Canada*

- Atherosclerotic plaque tends to develop in regions of disturbed/multi-directional blood flow
- A novel microfluidic device has been created to simulate disturbed blood flow over endothelial cells
- The results suggest endothelial cells exhibit a unique mechanosensory response under disturbed flow

1080 Integration of multi-layer omics to identify mechano-sensitive super-enhancers in vascular endothelial cells

Li, Jin¹; Gray, Olivia¹; Sobreira, Débora¹; Wu, David¹; Huang, Ru-Ting¹; Sakabe, Noboru Jo¹; Krause, Matthew, D¹; Romanoski, Casey, E²; Nobrega, Marcelo¹; Di Rienzo, Anna¹; Fang, Yun¹

1. *The University of Chicago, Chicago, Illinois, USA*

2. *University of Arizona, Tucson, USA*

- Super-enhancer architectures in human aortic endothelium are dynamically regulated by hemodynamics
- Endothelial super-enhancers are enriched with EC transcription factor binding sites and CVD SNPs
- Mechano-sensitive super-enhancers preferentially contact the promoters of mechano-sensitive genes

1081 Enhanced matrix stiffness induces VSMC hypertrophy: How calcium signalling and microtubule stability regulate vascular compliance during ageing.

Johnson, Robert, T¹; Ahmed, Sultan¹; Solanki, Reesha¹; Wostear, Finn¹; Afewerki, TecLino¹; Warren, Derek, T¹

1. *University of East Anglia, Norwich, United Kingdom of Great Britain and Northern Ireland*

- Enhanced matrix stiffness perturbs VSMC contractility and promotes VSMC swelling.
- Enlarged VSMC area and volume contributes to reduced aortic compliance during ageing and CVD onset.
- Aberrant regulation of calcium signalling and microtubule stability promote VSMC swelling.

1082 Resolving temporal dynamics of mechanotransduction via Notch1

Whitworth, Chloe, P¹; Aw, Wen¹; Bautch, Victoria¹; Polacheck, William¹

1. *University of North Carolina at Chapel Hill, Chapel Hill, USA*

- Endothelial cells (EC) respond to laminar shear stress
- Evidence suggests that Notch1 may be a master regulator of the flow response in EC
- Notch1 is temporally regulated relative to the initiation and maintenance of flow in EC

1083 Central nervous system pericytes constrict in response to intraluminal pressure

Klug, Nicholas, R¹; Sancho, Maria¹; Gonzales, Albert, L²; Heppner, Thomas, J¹; O'Brien, Rochelle Irene, C¹; Hill-Eubanks, David¹; Nelson, Mark, T¹

1. *University of Vermont, Burlington, Vermont, USA*

2. *University of Nevada, Reno, Reno, Nevada, USA*

- Pressure-induced constriction of central nervous system pericytes
- Functional expression of voltage-dependent calcium channels in pericytes
- Mechanisms of pressure sensing in central nervous system pericytes

POSTERS: VASCULAR DIFFERENTIATION

1084 Oxidative Pentose Phosphate Pathway Controls Vascular Mural Cell Coverage By Regulating Extracellular Matrix Composition

Facchinello, Nicola¹; Arce, Cristina¹; Mitro, Nico²; Crisan, Mihaela³; Santoro, Massimo¹

1. University of Padua, Padua, Italy

2. University of Milan, Milan, Italy

3. University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland

- Pentose Phosphate Pathway drives vascular maturation and mural cell recruitment
- oxPPP controls ELASTIN expression and deposition in EC
- Hemodynamic forces promote ELASTIN synthesis and vMC coverage in a PPP-dependent manner

1085 CDH6 connects the heart and great vessel by organizing collective cell-adhesion between endocardial ECs and vascular EC

Fukumoto, Moe¹; Mochizuki, Naoki¹

1. NCVV, Suita-City, Osaka, Japan

- We performed live imaging to understand how heart and vessels connect each other.
- We analyzed scRNA-seq. data set for molecular screening.
- We established CDH6-EGFP knock-in lines to understand the localization of CDH6 protein.

1086 Stroke-associated intergenic variants are located in a transcriptional enhancer of the vascular stability-promoting transcription factor FOXF2

Ryu, Jae-Ryeon¹; Ahuja, Suchit¹; Arnold, Corey, R¹; Potts, Kyle, G¹; Mishra, Aniket²; Yang, Qiong³; Sargurupremraj, Muralidharan⁴; Mahoney, Douglas, J¹; Seshadri, Sudha⁴; Dobbie, Stephanie²;

Childs, Sarah, J¹

1. University of Calgary, Calgary, AB, Canada

2. University of Bordeaux, Bordeaux, France

3. Boston University, Boston, Massachusetts, USA

4. University of Texas Health Sciences Center, San Antonio, Texas, USA

- A SNP in a FOXF2 enhancer is associated with stroke in humans and modulates FOXF2 expression
- FoxF2 is expressed in pericytes and controls pericyte number and vascular stabilization in zebrafish
- A SNP affecting FOXF2 expression is located in an ETS1 binding site. RbpJ binding is also important

1087 In vivo analysis of collective endothelial cell migration

Hubert, Marvin¹; Herzog, Wiebke¹

1. University of Erlangen-Nuremberg, Erlangen, Germany

- VE-Cadherin regulates collective cell migration and polarization during angiogenesis.
- The Rho Kinase ROCK acts downstream of VE-Cadherin during collective endothelial cell migration.
- Loss of VE-Cadherin function during collective cell migration can be rescued by activating ROCK.

1088 Rab family members regulate vWF secretion in the subintestinal vascular bed and thereby contribute to angiogenesis

Wakayama, Yuki¹; Margadant, Coert²; Herzog, Wiebke¹

1. University of Erlangen-Nürnberg, Erlangen, Germany

2. Sanquin Research, Amsterdam, Netherlands

- Rab27A is highly expressed in the vessels.
- Knockdown of vwf and rab27a using MO inhibited SIV formation.
- Rab27A mediated secretion of vWF enhanced Vegfa signaling to promote intestinal angiogenesis.

1089 The role of macrophages in the perivascular space

Yamamoto, Seiji¹; Azuma, Erika¹; Okuno, Noriko¹; Hamashima, Takeru¹; Sasahara, Masakiyo¹

1. University of Toyama, Toyama, Japan

- CD206-positive M2-like macrophages promote neovascularization in the skin wound healing area
- CD206-positive M2-like macrophages secrete ANG1 and modulate filopodia formation of endothelial cells
- Endothelial cells supplemented with ANG1 markedly accelerate glycolysis and energy generation

1090 Lats1/2 are required for endothelial cell remodeling and stability

Cowdin, Mitzy, A¹; Cleaver, Ondine¹

1. UT Southwestern Medical Center, Dallas, Texas, USA

- Lats1/2 are required for embryonic endothelial cell remodeling
- Lats1/2 help regulate cell shape under shear stress
- Lats1/2 are required for stability of embryonic blood vessels

1091 Primary cilia as potential mechanosensing regulators of vascular stability during embryonic development

Collin, Sarah¹; Sviben, Sanja¹; Roth, Robyn¹; Halabi, Carmen¹; Stratman, Amber¹

1. Washington University in St. Louis, St. Louis, Missouri, USA

- Zebrafish cluap1 mutants display a decrease in klf2a/klf4a expression and SMC mistargeting to veins.
- Endothelial cilia in the main axial vessels are primarily abluminal in early development.
- This study links primary cilia, mechanosensing, Klf2/4, and SMC biology.

POSTERS: BLOOD BRAIN BARRIER

1092 Endothelial heterogeneity and its association with vascular function in the inner and outer blood-retinal barrier

Lee, Junyeop¹; Kim, Soo Jin²; Park, Jun Hyeong¹; Lee, Jihye³

1. Asan Medical Center, University of Ulsan, College of Medicine, Seoul, Korea (Republic of)

2. AMIST, Asan Medical Center, University of Ulsan, College of Medicine, Seoul, Korea (Republic of)

3. Inha University, Incheon, Korea (Republic of)

- Retina and choroid have organotypic vasculature with distinct cellular and molecular heterogeneities
- Retinal ECs are angiogenic with high migratory, faster sprouting, and more responsive to VEGF.
- The choroid has quiescent and tight ECs but is specialized for trans-endothelial molecular transport

1093 The role of Znhit1 is a key regulator of vascular permeability within the CNS vasculature

Verba, Mark, J¹

1. Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

- Znhit1 is a regulator of vascular permeability within the CNS vasculature.
- Znhit1 is a critical component of Blood-Brain barrier integrity and vascular homeostasis
- Znhit1 could be important for other vascular diseases and should be looked at more closely.

1094 Neuronally secreted Spock1 induces blood-brain barrier function

O'Brown, Natasha, M¹; Patel, Nikit¹; Klein, Allon, M¹; Gu, Chenghua¹; Megason, Sean, G¹

1. Harvard Medical School, Boston, USA

- BBB properties are induced by signals from the brain microenvironment.
- Neuronal Spock1 signals to the vasculature at close range to induce BBB properties
- A single exogenous dose of SPOCK1 protein can partially restore BBB function

1095 Vascular and perivascular cell profiling reveals the molecular and cellular bases of blood-brain barrier heterogeneity

Pfau, Sarah, J¹; Langen, Urs, H¹; Fisher, Theodore, M¹; Prakash, Indumathi¹; Nagpurwala, Faheem¹; Lozoya, Ricardo, A¹; Lee, Wei-Chung, A¹; Wu, Zhuhao²; Gu, Chenghua³

1. Harvard Medical School, Boston, Massachusetts, USA

2. Icahn School of Medicine at Mount Sinai, New York, New York, USA

3. Howard Hughes Medical Institute, Harvard Medical School, Boston, Massachusetts, USA

- We compared two brain regions with different BBB properties, the median eminence and cortex.
- We found key molecular differences in endothelial cells and perivascular astrocytes and pericytes.
- We identified unique physical interactions of perivascular cells and endothelial cells in each area.

1096 Longitudinal studies of cerebrovascular response following ischemic stroke in the living mouse

Protzmann, Jil¹; Fredriksson, Linda¹

1. Karolinska Institute, Stockholm, Sweden

- In vivo 2-photon imaging can be used to dissect stroke progression in the living animal in real time
- Transgenic reporter mouse lines can be used to follow cell fate during blood-brain barrier breach
- Reducing blood-brain barrier breakdown is beneficial in ischemic stroke

1097 Employing a Microfluidic Neurovascular Model to Assess Pathological Alterations of the BBB in Alzheimer's Disease

Ko, Eunkyung¹; Spitz, Sarah²; Pavlou, Georgios¹; Jorfi, Mehdi³; Choi, Sehoon³; Kamm, Roger, D¹

1. Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

2. Vienna University of Technology, Vienna, Austria

3. Massachusetts General Hospital, Harvard Medical School, Charlestown, USA

- Development of a 3D neurovascular model system co-cultured with neurons
- A BBB microphysiological model system to study Alzheimer's disease pathology
- Pre-cultured neurosphere in a 3D neurovascular model system to reduce co-culture time

1098 Prox1 misexpression disrupts the blood-brain barrier integrity and lymphatic avascularity in the central nervous system

Gonzalez-Hernandez, Sara¹; Mukoyama, Yoh-suke¹

1. National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland, USA

- Prox1 expression is repressed in the CNS vasculature to maintain the blood-brain barrier
- Prox1 ectopic expression in the CNS vasculature induces blood-brain barrier breakdown
- Prox1 ectopic expression in the CNS vasculature induces a hybrid blood-lymphatic phenotype

1100 Inhibition of Abl Kinase by Imatinib Can Restore the Compromised Blood-Brain Barrier in 22q11.2DS Patients

Li, Yunfei¹; Sun, Yan²; Zhu, Huixiang²; Leong, Kam, W²; Xu, Bin²; Fu, Bingmei, M¹

1. The City College of the City University of New York, New York, New York, USA

2. Columbia University, New York, New York, USA

- compromised blood-brain barrier in patients with 22q11.2 deletion syndrome
- inhibition of abl kinase by imatinib can restore the compromised BBB in 22q11.2DS patients
- TEER and permeability to Dex-70k as well as glycocalyx and tight junctions are restored by imatinib

1101 Impaired blood brain barrier integrity in Col4a1 mutant mice

Wang, Xiaowei¹; Smith, Megan¹; Labelle-Dumais, Cassandre¹; Gould, Douglas¹

1. UCSF, San Francisco, CA, USA

- Col4a1 mutant mice have allele-dependent BBB impairment which correlates with seizure susceptibility
- BBB impairment is dynamic and largely resolves between 1.0 and 1.5 months.
- Treatment with 4PBA or reducing TGF β signaling improves BBB integrity in Col4a1 mutant mice.

1103 Protein Atlas of the Adult Mouse Brain Vasculature

He, Liqun¹; Johansson, Henrik²; Vazquez-Liebanas, Elisa¹; Vanlandewijck, Michael¹; Betsholtz, Christer¹; Andaloussi Mäe, Maarja¹

1. Uppsala University, Uppsala, Sweden

2. Karolinska Institute, Stockholm, Sweden

- We created a resource of quantitative protein atlas of the adult mouse brain vascular cells.
- We report protein copy numbers per cell in all principal brain vascular cell-types.
- We reveal general and protein-class-specific correlation between mRNA and protein expression.

1104 Mechanisms of Blood Retinal Barrier Development

Furtado, Jessica¹; Boyé, Kevin²; Eichmann, Anne¹

1. Yale University School of Medicine, New Haven, Connecticut, USA

2. Université de Paris, Paris, France

- Unc5B regulates blood retina barrier permeability.
- Netrin1 binding to Unc5B regulates the Wnt-related Norrin/ β -catenin signaling via pLRP5.
- Endothelial cell and pericyte Unc5B may have opposing roles.

POSTERS: TRANSLATIONAL RESEARCH

1105 Targeting the Long Non-Coding RNA SMILR Using Small Interfering RNA for Therapeutic Intervention in Vein Graft Failure

Brown, Simon, D¹; Malinowska, Anna, L²; Roux, Loic²; Lam, Amy³; Correa-Sánchez, Andrés²; Lench, Nick²; Webster, Scott, P¹; Barton, Anna¹; Newby, David, E¹; Baker, Andrew, H¹

1. BHF Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland

2. MRC/UKRI Nucleic Acid Therapy Accelerator, Oxford, United Kingdom of Great Britain and Northern Ireland

3. Edinburgh Innovations, University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland

- We aim to develop an siRNA therapeutic for use in the cardiac theatre to prevent vein graft failure.
- We have synthesised a pool of siRNA against the lncRNA SMILR, which regulates proliferation in vSMCs
- We have identified 3 lead siRNA that reduce SMILR expression and proliferation in vSMCs.

1106 Exosomal MicroRNAs 486-5p is a predictable biomarker for human coronary atherosclerosis progression

Kim, Hyung-Seok¹; Lee, Sujin¹; Park, Jong-Tae¹; Lee, Sunmin¹; Kim, Soyeon¹

1. Chonnam National University Medical School, Gwangju, Korea (Republic of)

- The Features of Exosome in the post-mortem body fluid
- Exosomal RNA Profiling for Post-mortem Acute Myocardial Infarction Diagnosis
- Exosomal RNA Profiling can be used to evaluate human coronary atherosclerosis severity

1107 Role of Matrix Gla protein in vascular regulation in Brown Adipose Tissue

Zhang, LI¹; Cai, XinJiang¹; Wu, XiuJu¹; Qiao, XiaoJing¹; Yao, Yucheng¹; Boström, Kristina, I¹

1. Division of Cardiology, David Geffen School of Medicine at UCLA, Los Angeles, CaliforniaCA, USA

- Lipoproteins in Vascular Disease
- The Vasculature in Metabolic Disease
- Angiogenesis and Vascular Remodeling

1108 Withdrawn

POSTERS: VASCULATURE IN DISEASE I

1109 scRNAseq Reveals Sex-Dependent Endothelial Responses to Hyperoxia in a Neonatal Mouse Model of Experimental BPD

Vila Ellis, Lisandra²; Menden, Heather¹; Mabry, Sherry¹; Chen, Jichao²; Sampath, Venkatesh¹; Xia, Sheng¹

1. Children's Mercy Kansas City, Kansas City, Missouri, USA

2. The University of Texas M. D. Anderson Cancer Center, Houston, Texas, USA

- Car4+ Cap2 and Car4 expression in Cap1 increased after HOX, indicating a reparative response.
- A new subpopulation of Car4+ Cap2 endothelial cells emerged in hyperoxia.
- These findings suggest that HOX programs distinct sex-specific cellular reparative responses.

1110 Inhibition of p90RSK ameliorates PDGF-BB-induced vascular smooth muscle cell phenotypic change and neointimal hyperplasia

Hwang, Ae Rang¹; Hong, Changui¹; Lee, Haegyul¹; Lee, Suyeon¹; Woo, Chang-Hoon¹

1. Department of Pharmacology, College of Medicine, Yeungnam University, Daegu, Korea (Republic of)

- Various vascular diseases are initiated and aggravated by the abnormal proliferation of VSMCs.
- PDGF-BB is one of the most potent stimulants of VSMC proliferation and migration.
- Activated p90RSK interacts with several substrates and is involved in proliferation and migration.

1111 Primary tumor-derived, systemic nANGPTL4 inhibits metastasis

Grieshaber, Denise¹; Hübers, Corinne²; Abdul Pari, Ashik Ahmed¹; Augustin, Hellmut¹; Felcht, Moritz²

1. European Center for Angioscience, Medical Faculty Mannheim, Heidelberg, BW, Germany

2. University Medical Centre Mannheim, Mannheim, BW, Germany

- Proteolytic processing of ANGPTL4 converts a pro-tumorigenic into an anti-tumorigenic molecule.
- nANGPTL4 acts as a novel anti-metastatic therapeutic agent in preclinical tumor experiments.
- nANGPTL4 serves as predictive biomarker for metastatic disease progression in melanoma patients.

1112 Differential response to doxorubicin-induced cardiac dysfunction and remodeling in endothelial c-Myc overexpressing mice

Freire Machi, Jacqueline¹; Tang, Joshua, K¹; Menzie-Suderam, Janet¹; Rodrigues, Claudia, O¹

1. Florida Atlantic University, Boca Raton, Florida, USA

- Anthracyclines are highly effective chemotherapeutic agents broadly used in the treatment of cancer
- Cancer survivors experience serious chronic and life-threatening effects due to its cardiotoxicity.
- Antioxidant therapy has shown little efficacy in clinical settings.

1113 Pressure-overload induced cardiac hypertrophy is associated with vascular malformations via up-regulation of Notch4 in endothelial cells.

Glaser, Simone-Franziska¹; Luxan, Guillermo¹; Cheng, Feng²; Fischer, Ariane¹; Klangwart, Marius¹; Muhly-Reinholz, Marion¹; Nicin, Luka¹; Schulze-Brüning, Ralf¹; Yekelchik, Michail³; Kawase, Haruya³; Wettschurek, Nina³; Braun, Thomas³; Meder, Benjamin⁴; Reich, Christoph⁴; Kempf, Tibor⁵; Klintschar, Michael⁶; David, John¹; Zeiher, Andreas¹; Wang, Rong²; Dimmeler, Stefanie¹

1. Institute for Cardiovascular Regeneration, Goethe University Frankfurt, Frankfurt, Germany

2. Laboratory for Accelerated Vascular Research, San Francisco, California, USA

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

4. University Hospital Heidelberg, Heidelberg, Germany

5. Clinic for Cardiology and Angiology, Hannover, Germany

6. Legal Medicine Hannover, Hannover, Germany

- To use single nuclear RNA sequencing to characterize the cardiac microcirculation.
- To reveal the effects of pressure-overload induced cardiac hypertrophy on endothelial cells.

- To identify molecular pathways being affected during chronic pressure overload.

1114 Vascular targeting of Tie2 for the prevention of brain metastasis and epilepsy

Reiss, Yvonne¹; Macas, Jadranka¹; Sommer, Kathleen¹; Fidan, Elif¹; Willems, Laurent²; Rosenow, Felix²; Spitzer, Daniel²; Liebner, Stefan¹; Devraj, Kavi¹; Plate, Karl, H¹

1. Institute of Neurology, Goethe University Hospital Frankfurt, Frankfurt, Germany

2. Center of Neurology and Neurosurgery, Goethe University Hospital Frankfurt, Frankfurt, Germany

- Vasculature in Disease
- Vascular Beds and Cells
- Vascular Diseases

1115 Effect of androgens on vasomotor responses in arteries with vascular dysfunction. Role of nitric oxide.

Sánchez, David¹; Mateo, Alicia²; Rodríguez, Penélope¹; Martínez, Begoña¹; Eguibar, Aritz³; Gómez-Rivas, Juan⁴; Ferrer, Mercedes¹

1. Universidad Autónoma de Madrid, Madrid, Spain

2. Universidad Complutense de Madrid, Madrid, Madrid, Spain

3. Hospital Universitario La Paz, Madrid, Madrid, Spain

4. Hospital Clínico San Carlos, Madrid, Madrid, Spain

- Regulation of the vascular tone by male sex hormones.
- Analyze the effect of androgens in aorta from aged rats and spontaneously hypertensive rats.
- Potentiation of endothelial-dependent vasodilation by androgens.

1116 Beneficial effect of Spirulina extract on aging-associated alterations in vasodilation

Ferrer, Mercedes¹; Majewski, Michal²; Klett-Mingo, Mercedes¹; Vendasco-Martín, Carlos³; Otero, Cristina³

1. Universidad Autónoma de Madrid, Madrid, Spain

2. University of Warmia and Mazury, Olsztyn, Poland

3. Consejo Superior de Investigaciones Científicas, Madrid, Madrid, Spain

- Analyze the effect of an aqueous Spirulina extract on the vasodilation of aorta from aged rats.
- Antioxidant properties of Spirulina extract.
- Investigate the effect of Spirulina extract on the release of nitric oxide.

1117 Impact of cigarette smoking on the lymph node vasculature and stroma at single cell resolution

Xiang, Menglan¹; Ocón, Borja¹; Butcher, Eugene, C¹

1. Stanford University, Palo Alto, USA

- Cigarette smoking (CS) has systemic effects on the immune system and vasculature
- scRNAseq of immune organ stroma reveals prominent effects of CS on the endothelium
- CS suppresses EC DNA repair and may trigger immune changes through common transcriptional pathways

1118 Uveal melanoma activates VEGFR2 trafficking in endothelial cells to open the endothelial barrier for uveal melanoma cells metastasis

Nguyen, Thi Thanh Nhan¹; Cho, Hyun-dong¹; Yamada, Kaori¹

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

- Endothelial junction integrity is disrupted by uveal melanoma-induced VEGFR2 trafficking activation
- Uveal melanoma cells generate VEGF to promote their transendothelial migration
- Inhibition of VEGFR2 trafficking prevented uveal melanoma cells transendothelial migration

1119 Pulmonary vascular regeneration via venous endothelial progenitors following viral lung injury.

Wong, Joanna¹; Zhao, Gan¹; Frank, David, B²; Vaughan, Andrew, E¹

1. University of Pennsylvania, Philadelphia, Pennsylvania, USA
2. Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

- The venous endothelium is highly proliferative and enriched in progenitor potential.
- Venous endothelial cells have the capacity to branch into the microvasculature following influenza.
- Endothelial plasticity underlies pulmonary vascular regeneration.

1120 Sterol regulatory element-binding protein 2 (SREBP2) reduces TNF α -induced interferon-stimulated genes

Horikami, Daiki¹; Fowler, Joseph Wayne, M¹; Boutagy, Nabil, E¹; Iwakiri, Yasuko¹; Sessa, William, C¹

1. Yale University School of Medicine, New Haven, Connecticut, USA

- Knockdown of SREBP2 significantly elevated TNF α mediated stimulation of ISGs.
- Knockdown of HMGR also significantly elevated TNF α mediated stimulation of ISGs.
- Knockdown of IRF1 suppressed TNF α -induced ISGs expression even in SREBP2 silenced HUVECs.

POSTERS: VASCULAR PHYSIOLOGY

1121 Activation of the orphan GPCR, T1R3, promotes the release of barrier-protective extracellular vesicles – a novel role for endothelial sweet taste sensing

Chichger, Havovi¹

1. Anglia Ruskin University, Cambridge, United Kingdom of Great Britain and Northern Ireland

- Lipopolysaccharide results in the release of barrier-disruptive extracellular vesicles
- Activation of T1R3 attenuates the barrier disruptive effects of pathogenic extracellular vesicles
- The protective effect of T1R3 activation acts directly through the release of extracellular vesicles

1122 Role of Endothelial Cell-Selective Adhesion Molecule in the Development of Left Ventricle Diastolic Dysfunction

Buncha, Vadym¹; Fopiano, Katie Anne¹; Tiann, Yanna¹; Lang, Liwei¹; Bagi, Zsolt¹

1. Augusta University, Augusta, GA, USA

- Mice lacking ESAM develop left ventricular diastolic dysfunction, compared to wild type mice
- ESAM knock-out mice have decreased myocardial tissue vascularization levels compared to wild types
- ESAM knock-out mice pulmonary vasculature, but not aorta has impaired vasodilator function

1123 PAK2 and septins are essential for exocytosis of Von Willebrand factor from endothelial cells.

El-Mansi, Sammy¹; Robinson, Chris¹; Mitchell, Tom¹; Mostowy, Serge²; Nightingale, Tom¹

1. Centre of Microvascular Research, Queen Mary University of London, London, United Kingdom of Great Britain and Northern Ireland
 2. London School of Hygiene and Tropical Medicine, London, United Kingdom of Great Britain and Northern Ireland
- APEX2 proximity proteomics in endothelial cells reveals novel proteins associated with VWF release.
 - Two siRNA sub-screens identify putative actomyosin ring machinery involved in regulated VWF release.
 - PAK2 silencing or inhibition prevents septin-mediated VWF release from endothelial cells.

1124 Using the blood vasculature as a coordinate system to map the human body, from whole organs down to microvasculature

Gustilo, Katherine, S¹; Weber, Griffin, M²

1. Indiana University, Bloomington, Indiana, USA
2. Harvard Medical School, Boston, Massachusetts, USA

- The Human Reference Atlas (HRA) brings together 17 consortia mapping the cells in the human body.
- The HRA's Vasculature Common Coordinate Framework (HRA-VCCF) is a database of 900+ blood vessels.
- We present our work mapping these vessels to anatomic and cellular structures across all organs.

1125 Vascular lipid droplets as a source of COX-2 derived eicosanoids from endogenous AA

Sternak, Magdalena¹; Stojak, Marta¹; Kij, Agnieszka¹; Banasik, Tomasz¹; Bar, Anna¹; Pacia, Marta, Z¹; Wojnar-Lason, Kamila¹; Mohaissen, Tasnim¹; Chorazy, Natalia¹; Marczyk, Brygida¹; Czyzynska-Cichon, Izabela¹; Chlopicki, Stefan¹

1. Jagiellonian Centre for Experimental Therapeutics (JCET), Krakow, Poland

- ATGL-dependent lipid droplets hydrolysis maintains homeostasis in eicosanoids production
- ATGL-dependent lipolysis is vasoprotective
- ATGL-dependent lipolysis offset possible detrimental effect of lipids overload

1126 Developing a zebrafish gill model of mammalian lung endothelium

Park, Jong, S¹; Castranova, Daniel, A¹; Martinez-Aceves, Celia¹; Margolin, Gennady¹; Dye, Louis¹; Paulissen, Scott¹; Galanternik, Marina, V¹; Goldstein, Allison¹; Kenton, Madeleine¹; Pham, Van, N¹; Weinstein, Brant, M¹

1. NICHD/National Institutes of Health, Bethesda, Maryland, USA

- Developing zebrafish gill as a model to study mammalian lung endothelium.
- scRNAseq reveals unique endothelial cell populations in the gill.
- Confocal and TEM imaging reveals complex vascular anatomy and development in the gills.

1127 Chronic anemia is associated with systemic endothelial dysfunction

Chennupati, Ramesh¹; Solga, Isabella¹; Wischmann, Patricia¹; Dahlmann, Paul¹; Celik, Feyza, G¹; Gerdes, Norbert¹; Kelm, Malte¹; Jung, Christian¹

1. Universitätsklinikum Düsseldorf, Düsseldorf, Germany

- Anemia-associated systemic endothelial dysfunction
- Anemia effects on endothelial nitric oxide synthase
- Anemia effects on endothelial inflammation

1128 Mapping sphingosine 1-phosphate receptor-1 S1PR1 activity and ligand dependence in the blood vascular network

Del Gaudio, Ilaria¹; Nitzsche, Anja¹; Camerer, Eric¹

1. Université Paris Cité, Inserm, Paris Cardiovascular Research Center PARCC, Paris, France

- S1PR1 signaling is mainly restricted to arterial endothelial cells in the blood vasculature
- S1PR1 regulates blood flow and vascular integrity primarily in response to circulating S1P
- Endothelial S1PR1 senses pathophysiological fluctuations in plasma S1P levels

1129 Regulation of endocytic trafficking and VEGFR2 receptor availability by a component of the microtubule motor dynein.

Johnson, Dymonn¹; Yano, Joseph²; Davis, Andrew²; Pham, Van, N²; Melani, Mariana²; Weinstein, Brant, M²; Stratman, Amber¹

1. Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA

2. National Institutes of Health, Bethesda, Maryland, USA

- Dync1li1 regulates VEGFR2 trafficking and angiogenesis.
- Dync1li1 deficiency leads to increased recycling of VEGFR2-contained endosomes back to the membrane.
- Dync1li1 deficiency leads to decrease in Rab7a mediated degradation, causing excess angiogenesis.

POSTERS: IMAGING AND COMPUTATIONAL APPROACHES

1130 Machine learning and high-fidelity computational modeling of microvascular network hemodynamics

Bagchi, Prosenjit¹; Ebrahimi, Saman¹

1. Rutgers University, Piscataway, New Jersey, USA

- microcirculation, microvascular networks, capillary blood flow, red blood cells
- computational modeling; biotransport; hemodynamics;
- machine learning; high-performance computing

1131 Microarchitectural Changes of Cardiovascular Calcification in Response to In Vivo Interventions Using Deep-Learning Segmentation and Computed Tomography Radiomics

Patel, Nikhil, R¹; Setya, Kulveer¹; Pradhan, Stuti¹; Lu, Mimi¹; Demer, Linda¹; Tintut, Yin¹

1. UCLA, Los Angeles, USA

- Deep learning segmentation and CT radiomics allow assessment of aortic calcifications in mice.
- By radiomic analysis, age or Western diet can each alter aortic calcification morphology in mice.
- Statins & exercise associate with greater calcium content but less new deposits in the mouse aorta.

1132 Modeling multimodality human coronary microvascular imaging data with a modified ZKM model.

Metzler, Scott¹; Wayne, Nicole¹; Johnson, Lindsay¹; Moore, Stephen¹; Guerraty, Marie¹

1. University of Pennsylvania, Philadelphia, Pennsylvania, USA

- Coronary Microvascular Disease is under-diagnosed and understudied.
- We extend the ZKM model of coronary blood flow to represent the full range of coronary physiology.
- The modified ZKM model supports a novel relationship between cardiac imaging modalities.

POSTERS: OTHER VASCULAR BIOLOGY

1133 ZEB1 interacts with the AP1 transcription factor complex in endothelial cells

Ahmed, Nada, S¹; Bates, David, O¹; Benest, Andrew, V¹

1. Biodiscovery Institute, School of Medicine, University of Nottingham, Nottingham, United Kingdom of Great Britain and Northern Ireland

- ZEB1 regulate AP1 and Hippo pathway which are involved in regulating lymphatic growth
- ZEB1 interactome with AP1 and interacting partners might be of relevance in lymphatic remodelling
- ZEB1 is downregulated in mitotic endothelial cells which might be linked their phenotypic changes

1134 Role of plasmacytoid dendritic cells in type 2 diabetes-induced macro- and microvascular dysfunction

Alluri, Kiran¹; Srinivas, Balaji¹; Bourdi, Aya¹; O'Regan, Jacob¹; Belmadani, Souad¹; Matrougui, Khalid¹

1. EVMS, Norfolk, USA

- Mechanism of vascular dysfunction in type 2 diabetes
- Immune plasmacytoid dendritic cells dysregulation in type 2 diabetes
- Depletion of plasmacytoid dendritic cells improves vascular function in type 2 diabetes

1135 Ephrin-B2/EphB4 signaling mechanism controlling artery formation

Stewen, Jonas¹; Adams, Ralf, H¹; Pitulescu, Mara, E¹

1. Max Planck Institute for Molecular Biomedicine, Muenster, Germany

- Arteriovenous specification is regulated by ephrin-B2/EphB4 signaling
- Ephrin-B2 and EphB4 regulate sprouting angiogenesis
- Ephrin-B2 and EphB4 are involved in a feedback loop network regulating Notch signaling

1136 Study on in vivo Function of Protein A for Bone Marrow Regeneration by Blood Stem Cells Using Liver-Specific Hormone A Deficient mice

Choi, Jaewoo¹; Kwon, Sang-Mo¹

1. School of Medicine, Pusan National University, Yangsan, Korea (Republic of)

- Liver-derived Protein A deficiency delays bone marrow regeneration and reconstitution in vivo.
- Liver-derived Protein A was shown to regulate BM adipogenesis after chemotherapy.
- Liver-derived Protein A could act as a blood stem cell growth factor in the BM niche.

1137 Altered human artery responsiveness to the sigma receptor agonist PRE-084 with alcohol use.

McQueen, Jenna, F¹; Bloom, Charissa, A¹; Zimmermann Rollin, Isabela¹; Iyer, Vishnu, V¹; Breslin, Jerome, W¹

1. University of South Florida Health Morsani College of Medicine, Tampa, Florida, USA

- Sigma receptor-1 activation attenuates alpha-adrenergic-mediated arterial smooth muscle contraction.
- Chronic, heavy alcohol use impairs sigma receptor-1 attenuation of arterial contraction.
- Sigma receptor-1 may play a role in alcohol-induced hypertension.

1138 Adaptation of peristaltic pumps for laminar flow experiments

Abello, Javier¹; Raghavan, Shreya²; Yien, Yvette, Y³; Stratman, Amber, N¹

1. Washington University in St. Louis School of Medicine, St. Louis, Missouri, USA

2. Department of Biomedical Engineering, Texas A&M University, College Station, Texas, USA

3. University of Pittsburgh, Pittsburgh, Pennsylvania, USA

- We are presenting a new modification to peristaltic pumps to produce laminar flow
- In vitro studies of the effect of flow types on endothelial cells
- Mechanical forces involved in remodeling vascular architecture and function

1139 Resident T-cells in the eye: regulators of neovascularisation in a model of wet age-related macular degeneration

Beattie, Lynette¹; Fletcher, Erica¹; Brandli, Alice¹

1. University of Melbourne, Melbourne, Victoria, Australia

- In a model of wet AMD, gamma-delta T-cells a tissue-resident immune cells increase in the choroid
- In a model of wet AMD, removing gamma-delta T-cells caused greater leakage and larger lesions
- Gamma-delta T-cells are important in wound healing as their presence reduces neovascularization

SATURDAY, OCTOBER 15 – 12:00PM TO 2:00PM – WEST HALL

POSTERS: OCULAR AND CNS VASCULAR DISEASE

2001 The role of extracellular RNA for microglia activation following subarachnoid hemorrhage

Tielking, Katharina¹; Nitzsche, Anja¹; Schoknecht, Felix¹; Kida, Laura¹; Preissner, Klaus, T²; Xu, Ran¹; Vajkoczy, Peter¹

1. Department of Neurosurgery, Charité Universitätsmedizin Berlin, Berlin, Germany

2. Department of Biochemistry, Justus-Liebig-University Gießen, Gießen, Germany

- Microglia activation contributes to secondary brain injury after subarachnoid hemorrhage (SAH).
- Treatment with RNase A before and during SAH reduced microglia activation.
- Inhibition of exRNA by RNase A may serve as a treatment strategy to address secondary brain injury.

2002 Reduced myofibroblast expansion in the fibrotic scar enhances recovery after ischemic stroke

Zeitelhofer, Manuel¹; Stefanitsch, Christina¹; Protzmann, Jil¹; Torrente, Daniel²; Adzemovic, Milena, Z¹; Lewandowski, Sebastian, A¹; Muhl, Lars¹; Eriksson, Ulf¹; Nilsson, Ingrid¹; Su, Enming, J²; Lawrence, Daniel, A²; Fredriksson, Linda¹

1. Karolinska Institutet, Stockholm, Sweden

2. University of Michigan Medical School, Ann Arbor, Michigan, USA

- Stroke-induced cerebrovascular changes orchestrates transdifferentiation of myofibroblasts
- Targeting myofibroblast expansion may provide a novel approach in ischemic stroke management
- Myofibroblasts transdifferentiate from activated PDGFR-alpha positive perivascular cells

2003 PECAM-1 Inhibition Significantly Modulates Neutrophil Extravasation into the Subcortex in Ischemic Stroke

Arias, Erika¹; Nadkarni, Neil¹; Fang, Raymond¹; Haynes, Maureen¹; Zhang, Hao¹; Muller, William¹; Batra, Ayush¹; Sullivan, David¹

1. Northwestern, Chicago, USA

- Neutrophils infiltrate the cortex at early time points post ischemia/prefusion in stroke.
- Neutrophils infiltrate the subcortex at later time points post ischemia/prefusion in stroke.
- PECAM blockade changes leukocyte distribution, with more at the cortex at early and late timepoints.

2004 Impaired neurovascular remodeling mediated by Apelin signaling and Cdc42 activity in endothelial Rbpj deficient brain arteriovenous malformation

Adhichary, Subhodip¹; Fanelli, Kayleigh¹; Nakisli, Sera¹; Ward, Brittney¹; Pearce, Isaac¹; Nielsen, Corinne¹

1. Ohio University, Athens, Ohio, USA

- Endothelial Rbpj maintains brain EC shape, polarity, focal adhesion properties, & directed movement
- Endothelial Rbpj regulates small GTPase activity via Apelin signaling
- Features of Rbpj bAVM can be pharmacologically prevented, despite an underlying genetic mutation

2005 A forward genetic screen identifies novel cerebral pericyte and angiogenesis mutants in zebrafish.

Baltaci, Oguzhan, F¹; Paterson, Scott¹; Dudczig, Stefanie¹; Sokolov, Veronica, U²; Rajesth, Drishti²; Bladen, Cerys¹; Dominado, Nicole²; Cox, Andrew¹; Smith, Kelly²; Hogan, Ben¹

1. Peter MacCallum Cancer Centre, Melbourne, Australia

2. University of Melbourne, Melbourne, Australia

- Key regulators of pericyte and cerebral vasculature development
- Identifying unique zebrafish mutants with altered cerebral vasculature and/or pericyte development
- Whole genome sequence mapping pipeline to allow for rapid gene mapping and mutation detection

2006 Overexpression of endothelial Pannexin1 impairs post-ischemic stroke cerebral blood flow recovery.

Mauro, Amanda, K¹; Tomas Gracia, Maria¹; Duffy, Colleen, K¹; Shahab, Guleer²; Medina, Chris²; Ravichandran, Kodi, S³; Isakson, Brant, E²; Good, Miranda, E¹

1. Tufts Medical Center, Boston, Massachusetts, USA

2. University of Virginia, Charlottesville, Virginia, USA

3. Washington University School of Medicine, St. Louis, Missouri, USA

- We hypothesize that endothelial Pannexin1 overexpression is detrimental to ischemic stroke severity.
- Recovery of cerebral blood flow post-stroke was impaired with endothelial Pannexin1 overexpression.

- Endothelial Pannexin1 content may regulate cerebral myogenic tone and post-stroke reperfusion.

2007 A role for heme in retinal vascular development and disease.

Goncalves, Andreia²; Santander, Nicolas³; Mukherjee, Dibyanti¹; Arnold, Thomas, D¹; Antonetti, David²

1. UCSF, San Francisco, California, USA

2. University of Michigan, Ann Arbor, Michigan, USA

3. Pontificia Universidad Catolica de Chile, Santiago, Chile

- Heme regulates developmental retinal angiogenesis.
- Flvcr2, a heme importer, controls heme endothelial heme levels and retinal angiogenesis.
- Norrin/b-catenin promotes the expression of Flvcr2.

2008 LRG1 disturbs retinal pericytes and delays maturation of the developing vasculature

Greenwood, John¹; Hoeh, Alexandra, E¹; Mueller, Sophie¹; Chang, Jiu-Hsien¹; Turowski, Patric¹; Moss, Stephen, E¹

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

- LRG1 is induced in many diseases which exhibit abnormal vessels or disturbed vessel function
- LRG1 impairs normal angiogenesis partly through affecting pericyte/endothelial cell interactions
- LRG1 is angiopathic and may be an effective therapeutic target

2009 Recapitulating the Arteriovenous Malformations of Hereditary Hemorrhagic Telangiectasia in a microfluidic model

Matsumoto, Satomi¹; Fang, Jennifer, S¹; Chen, Yu-Hsi¹; Lee, Abraham, P¹; Hughes, Christopher, C¹;

1. University of California, Irvine, Irvine, California, USA

- More than 60% of HHT-induced vascular malformation in liver occurs in vessels composed of LSECs.
- Malformations form as a result of Alk1 loss in ECs and LSECs in vitro.
- The model will allow for testing of drugs that may reverse AVMs

2010 ZEB1 is involved in the maintenance of endothelial quiescence.

Green, Kathryn, R¹; Horder, Joseph, L¹; Beazley-Long, Nicholas¹; Lynch, Amy, P¹; Allen, Claire, L¹; Bhalla, Sohni Ria¹; Wahid, Mussarat¹; Bates, David, O¹; Benest, Andrew, V¹

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

- Loss of endothelial Zeb1 results in increased neovascularization and vascular leakage
- Loss of endothelial Zeb1 causes ischemia independent vascular remodeling in skeletal muscle
- Zeb1 knockdown reduces the expression of inflammation associated genes

2011 Fibroblasts repair blood-brain barrier damage and hemorrhagic brain injury partially via TIMP2

Xu, Lingling²; Yao, Yao¹

1. University of South Florida, Tampa, Florida, USA

2. University of South Florida, Athens, FL, USA

- Fibroblasts migrate to capillaries and repair BBB damage after intracerebral hemorrhage
- Fibroblasts repair BBB damage via the paracellular mechanism in a TIMP2-dependent manner
- TIMP2 is able to attenuate BBB damage and hemorrhagic brain injury in fibroblast-ablated mice

2011 Fibroblasts repair blood-brain barrier damage and hemorrhagic brain injury partially via TIMP2

Xu, Lingling²; Yao, Yao¹

1. University of South Florida, Tampa, Florida, USA

2. University of South Florida, Athens, FL, USA

- Fibroblasts migrate to capillaries and repair BBB damage after intracerebral hemorrhage
- Fibroblasts repair BBB damage via the paracellular mechanism in a TIMP2-dependent manner

- TIMP2 is able to attenuate BBB damage and hemorrhagic brain injury in fibroblast-ablated mice

2012 Amyloid beta peptides (A β) from Alzheimer's disease neuronal secretome induce endothelial activation in a human cerebral microvessel model.

Shin, Yu Jung¹; Evitts, Kira¹; Jin, Solhee¹; Howard, Caitlin¹; Sharp-Milgrom, Margaret¹; Young, Jessica, E¹; Zheng, Ying¹

1. University of Washington, Seattle, Washington, USA

- AD neuronal secretomes cause transcriptomic and phenotypic upregulation of adhesion molecules in ECs
- Perfusion of AD neuronal secretomes in microvessels cause fast EC activation and VWF fiber formation
- Inhibiting A β secretion in AD neurons with a BACE1 inhibitor or APPKO media attenuated EC activation

2013 miR-125a establishes the circle of Willis arterial network function

Xia, Ivan, F¹; Cheng, Siyuan¹; Baldissera, Gabriel¹; Nicoli, Stefania¹

1. Yale School of Medicine, new haven, USA

- The circle of Willis variations are found in ~40% of humans and observed in brain vascular diseases.
- miR-125a is a novel regulator of the circle of Willis (CW) development and homeostasis.
- PGC1a targeted by miR-125a fine-tunes mitochondrial metabolism for angiogenesis and CW variation.

POSTERS: TRANSLATIONAL VASCULAR BIOLOGY

2014 Deficiency in Lpcat3 reduces plasma membrane fluidity and increases inflammatory phenotype in endothelial cells

Hong, Soon-Gook¹; Ashby, Julianne¹; Chattopadhyay, Eesha¹; Kennelly, John, P²; Tontonoz, Peter²; Mack, Julia, J¹

1. Department of Medicine, Division of Cardiology, UCLA, Los Angeles, California, USA

- Loss of Lpcat3 reduces plasma membrane fluidity in human aortic endothelial cells.
- Loss of Lpcat3 elevates endothelial cell activation in human aortic endothelial cells.
- Endothelial-specific Lpcat3 deletion leads to endothelial cell activation in mouse aorta.

2015 Targeting long non-coding RNA NUDT6 enhances smooth muscle cell survival and limits vascular disease progression

Winter, Hanna¹; Winski, Greg²; Busch, Albert³; Chernogubova, Ekaterina²; Fasolo, Francesca¹; Wu, Zhiyuan¹; Bäcklund, Alexandra²; Khomtchouk, Bohdan, B⁴; Van Booven, Derek, J⁵; Sachs, Nadja¹; Eckstein, Hans-Henning¹ Wittig, Ilka⁶; Boon, Reinier, A⁷; Jin, Hong²; Maegdefessel, Lars¹

1. Dept. for Vascular Surgery, University Hospital Rechts der Isar, Munich, Germany

2. Department of Medicine, Karolinska Institutet, Stockholm, Sweden

3. University Hospital Carl Gustav Carus, Dresden, Germany

4. Department of Medicine, University of Chicago, Chicago, USA

5. Miller School of Medicine, University of Miami, Miami, USA

6. Inst. of Cardiovascular Physiology, Goethe University, Frankfurt am Main, Germany

7. Inst. of Cardiovascular Regeneration, Goethe University, Frankfurt am Main, Germany

- This is the first attempt to investigate a role for the lncRNA NUDT6 in two vascular diseases
- Therapeutic targeting of NUDT6 can serve as a novel treatment strategy by using local delivery
- Patient-isolated vascular smooth muscle cells enabled translational anti-NUDT6 utilization in vitro

2016 Angiogenesis is required for fibrosis in the pericardial cavity

Sakaue, Tomohisa¹; Namiguchi, Kenji¹; Okazaki, Mikio²; Kanno, Kaho¹; Shikata, Fumiaki¹; Kurata, Mie¹; Ota, Noritaka¹; Kubota, Yoshiaki³; Kurobe, Hirotsugu¹; Nishimura, Takashi¹; Masumoto, Junya¹; Higashiyama, Shigeki¹; Izutani, Hironori¹

1. Ehime University, Toon, Japan

2. Okayama University, Okayama, Japan

3. Keio University, Shinjuku, Japan

- We successfully enabled visualisation of the temporal adhesion process in the pericardial cavity.
- Unique angiogenic process during pericardial adhesion was found.
- Abrogation of angiogenic signaling significantly suppressed the pericardial adhesion.

2017 Endothelial restoration of CAD GWAS gene PLPP3 by nanomedicine suppresses mechano-sensitive YAP/TAZ activity and reduces atherosclerosis in vivo

Zhu, Jiayu¹; Fang, Yun¹

1. University of Chicago, Chicago, Illinois, USA

- Unidirectional flow up-regulates endothelial PLPP3 to inactivate YAP/TAZ
- Endothelial restoration of PLPP3, a CAD GWAS gene, lessens disturbed flow-induced atherosclerosis
- Precision nanomedicine targeting inflamed endothelium effectively treats vascular complications

2018 Shedding light on the role of endothelial-derived extracellular vesicles in the pathogenesis of cancer therapy-related cardiac dysfunction

Ching, Crizza¹; Gustafson, Dakota¹; Zhao, Yimu¹; Radisic, Milica¹; Thavendiranathan, Paaladinesh²; Fish, Jason¹

1. University of Toronto, Toronto, Ontario, Canada

2. University Health Network, Toronto, Ontario, Canada

- Assessing the effect of chemotherapy on endothelial function and phenotype
- Role of endothelial-derived extracellular vesicles in intercellular communication
- Importance of endothelial cell-cardiomyocyte crosstalk in cancer therapy related-cardiac dysfunction

POSTERS: AVMS AND SOMATIC VASCULAR MALFORMATIONS

2019 Altered ribosome biogenesis in kras-driven brain arteriovenous malformation

Khosraviani, Negar¹; Wu, Ruilin¹; Boudreau, Emilie¹; Wythe, Joshua, D²; Fish, Jason, E¹

1. University Health Network, Toronto, Ontario, Canada

2. Baylor College of Medicine, Houston, Texas, USA

- Upregulation of ribosome biogenesis and RNA processing genes in KRAS-G12V endothelial cells
- Increased transcriptional and translational activity in KRAS-G12V endothelial cells
- Increased rRNA synthesis in KRAS-G12V endothelial cells

2020 Mutant KRAS signaling in endothelial cells enhances glycolysis

Wu, Ruilin¹; Khosraviani, Negar¹; Boudreau, Emilie¹; Wythe, Joshua, D²; Fish, Jason, E¹

1. University Health Network, Toronto, Ontario, Canada

2. Baylor College of Medicine, Houston, Texas, USA

- Endothelial changes in brain arteriovenous malformations
- Metabolic reprogramming downstream of mutant KRAS signaling in endothelial cells
- Molecular mechanism underlying the development of brain arteriovenous malformations

2021 EPHB4 and RASA1 act together to restrict Ras-MAPK activation in endothelial cells necessary for normal blood vascular development

Chen, Di¹; Hughes, Elizabeth, D¹; Saunders, Thomas, L¹; Wu, Jianping²; Hernandez Vasquez, Magda³; Makinen, Taija³; King, Philip, D¹

1. University of Michigan Medical School, Ann Arbor, Michigan, USA

2. Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada

3. Uppsala University, Uppsala, Sweden

- EPHB4 and RASA1 act together to inhibit Ras activation in EC to allow export of collagen IV
- MAPK inhibitors and drugs that promote collagen folding rescue EPHB4 or RASA1 loss-induced EC death
- Studies inform upon the pathogenesis of CM-AVM and VGAM and means of treatment

2022 Endoglin cell-autonomously restricts venous endothelial cell size to prevent arteriovenous malformations during zebrafish embryonic development

Diwan, Zeenat¹; Vincent Paul, Elvin Leonard¹; Siekmann, Arndt, F¹

1. University of Pennsylvania, Philadelphia, Pennsylvania, USA

- Endothelial cell size controls vessel diameters.
- Blood flow is required for arterial cell growth.
- Endoglin regulates venous endothelial cell size.

2023 EC expression of activated k-Ras leads to capillary deficiency due to excessive lumen formation, reduced pericyte recruitment, and an increased susceptibility to MMP-1-dependent vascular regression

Sun, Zheyang¹; Lin, Prisca, K²; Davis, George, E²

1. University of South Florida, Lutz, China

2. University of South Florida, Tampa, USA

- K-RasV12 ECs show marked increases in intracellular vacuoles formation, fusion, and lumen expansion
- K-RasV12 ECs show a strong reduction in pericyte recruitment and basement membrane deposition
- K-RasV12 ECs strongly induce and activate MMP-1, causing vessel regress and pathologic hemorrhage

2024 Molecular mechanisms of ACVRL1 function in endothelial cells.

Park, Hyojin¹; Furtado, Jessica¹; Poulet, Mathilde¹; Eichmann, Anne¹

1. Yale School of Medicine, New Haven, Connecticut, USA

- ALK1 deletion in capillary and venous endothelium was sufficient to induce AVMs.
- ALK1 regulates VEGFR2-integrin-PI3K signaling and downstream YAP/TAZ nuclear translocation
- single-cell RNA sequencing using EC specific ALK1 mutants.

POSTERS: BIOENGINEERING

2025 Effects of Mechanical Stiffness and Stress Relaxation on Endothelial Cell Function

Shayan, Mahdis¹; Huang, Michelle¹; Navarro, Renato¹; Heilshorn, Sarah¹; Huang, Ngan, F¹

1. Stanford University, Stanford, California, USA

- ELP is an engineered protein hydrogel with controllable stiffness and stress relaxation
- Slow relaxing hydrogels promote greater cell numbers at intermediate timepoints
- In 3D hydrogels, slow relaxing hydrogels induce tube-like formation at low stiffness

2026 The vascularized Islet-VMO platform provides a unique ex vivo tool for studying insulin secretion and the role of leukocyte trafficking in type 1 diabetes pathogenesis.

O'Donnell, Benjamin, T¹; Bender, Richard, H¹; Tahmouresie, Sima¹; Hughes, Christopher, C¹

1. University of California Irvine, Irvine, California, USA

- Leukocyte trafficking in Type 1 Diabetes is poorly understood due to the lack of in vitro models.
- We have developed a VMO-I that incorporates pseudoislets and is responsive to glucose stimulation.
- Upon perfusion through the VMO-I, activated PBMCs demonstrated increased islet co-localization.

2028 Combining kinase polypharmacology and 3D brain microvessel model to identify kinase targets that regulate endothelial barrier properties in trauma-induced cerebral vascular injuries.

Shin, Yu Jung¹; Wei, Ling²; Jin, Solhee¹; Evitts, Kira, M¹; Dong, Jing-fei³; Kaushansky, Alexis²; Zheng, Ying¹

1. University of Washington, Seattle, Washington, USA

2. Seattle Children's, Seattle, USA

3. Bloodworks Northwest Research Institute, Seattle, USA

- Modeling vascular injury in TBI patients via perfusion of patient-derived sera in 3D microvessels.
- Use of kinase regression model for identification of kinase targets that stabilize brain EC barrier.
- Utilizing 3D microvessels to obtain a functional permeability parameter in kinase regression model.

POSTERS: MYELOID CELLS, VASCULATURE, AND CANCER PROGRESSION

2029 Vasculogenic mimicry structures by melanoma cancer cells support the recruitment of monocytes

Tab, Lih, Y¹; Cockshell, Michaelia, P¹; Moore, Eli¹; Myo Min, Kay, K¹; Ortiz, Michael¹; Brown, Michael, P²; Ebert, Lisa, M²; Bonder, Claudine, S¹

1. Centre for Cancer Biology, University of South Australia & SA Pathology, Adelaide, South Australia, Australia

2. Centre for Cancer Biology & Royal Adelaide Hospital, Adelaide, South Australia, Australia

- Vasculogenic mimicry (VM) by human melanoma cells promotes cancer progression.
- VM-competent cancer cells express adhesion molecules and chemokines to recruit monocytes.
- Leukocyte entry into solid tumors is facilitated by EC-lined and VM formed tumor vasculature.

2030 Endothelial cell-specific transcription factor ERG promotes tumor vascular normalization and anti-cancer drug efficacy

Kamei, Shunsuke¹; Arata, Kanako¹; Miyamura, Yuri¹; Araki, Kimi²; Kubota, Yoshiaki³; Minami, Takashi¹

1. Division of Molecular and Vascular Biology, IRDA, Kumamoto University, Kumamoto, Japan

2. Division of Developmental Genetics, IRDA, Kumamoto University, Kumamoto, Kumamoto, Japan

3. Department of Anatomy, Keio University School of Medicine, Tokyo, Japan

- EC dysfunction caused by ERG reduction in the tumor microenvironment
- EC-specific ERG induction via conditional Tg may lead to tumor EC normalization
- ERG-mediated normalized vessels may increase the anti-cancer drug efficacies

2031 Vascular leakage is associated with reduced claudin-5 vessel coverage, immunosuppression and reduced patient survival in non-small cell lung cancer.

Nwadozi, Emmanuel¹; Strell, Carina¹; Nordling, Sofia¹; Backman, Max¹; Botling, Johan¹; Brunnström, Hans²; Micke, Patrick¹; Claesson-Welsh, Lena¹

1. Uppsala University, Uppsala, Sweden

2. Lund University, Lund, Sweden

- Prognostic implications for vascular leakage in Human Cancer
- Molecular regulation of vascular leakage in Human Cancer
- Influence of vascular leakage on the tumor immune contexture

POSTERS: ATHEROSCLEROSIS

2033 Respiratory complex I in vascular smooth muscle cells is dispensable for artery formation during embryogenesis but required for neointima formation upon arterial injury in adulthood.

Riascos-Bernal, Dario F¹; Sibinga, Nicholas, E¹; Maira, Alishba¹

1. Albert Einstein College of Medicine, Bronx, NY, USA

- Vascular Diseases
- Vascular Biology
- Translation Research

2034 Withdrawn

2035 E-cigarette-induced HDAC9 activation is linked to atherosclerosis by promoting endothelial-to-mesenchymal transition

Liu, Chen-wei¹; Le, Hoai Huong, T¹; Denaro III, Philip¹; Attaluri, Anika²; Ma, Xiaokuang¹; Qiu, Shenfeng¹; Ong, Sang-Ging³; Lee, Won Hee¹

1. Basic Medical Sciences, University of Arizona College of Medicine, Phoenix, Arizona, USA

2. Biomedical Engineering, Arizona State University, Tempe, Arizona, AZ, USA

3. Division of Cardiology, Department of Medicine, University of Illinois, Chicago, Illinois, USA

- Electronic cigarette (E-cig)-induced EndMT is mediated by HDAC9 and leads to vascular pathology.
- HDAC9 inhibition prevented EndMT in ECs following e-cig exposure.
- E-cig aerosols exacerbate atherosclerosis and induced EndMT in ApoE^{-/-} mice.

2036 Transcriptomic and proteomic profiling of progression and regression phases of diabetes-associated atherosclerosis in mice

Chen, Jingshu¹; Jamajjar, Anurag¹; Sausen, Grasiela¹; Randhawa, Vinay¹; Feinberg, Mark¹

1. Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

- Diabetes mellitus contributes to accelerated atherosclerosis and cardiovascular mortality.
- A high fat and high sucrose diet was used to establish a novel diabetic atherosclerosis mouse model.
- Transcriptome and proteome were performed to understand progression and regression phases.

2037 Macrophage Rac1-NF-κB-IL-1β Atherosclerotic Signaling Axis Upstream of ACE2 Expression and SARS-CoV-2 Virulence

Lee, Cadence¹; Carley, Rachel¹; Berus, Joshua¹; Mantsounga, Chris¹; Sharma, Sheila¹; Neverson, Jade¹; Amelotte, Elizabeth¹; Pierce, Julia¹; Butler, Celia¹; Choudhary, Gaurav¹; Morrison, Alan, R¹

1. Brown University, Ocean State Research Institute, Providence, Rhode Island, USA

- The Rac1-NF-κB-IL-1β signaling axis may impact worsened COVID-19 outcomes in the context of CAD.
- Rac1 activation and enhanced systemic IL-1β expression increase ACE2 expression.
- Rac1 is a co-factor for NF-κB transcriptional activity for both IL-1β and ACE2.

2038 Endothelial cell lineage tracing approach revealed new sex differences in atherosclerosis

Cherepanova, Olga, A¹; Shin, Junchul¹; Adognravi, Olga, S¹

1. Cleveland Clinic, Cleveland, Ohio, USA

- Sex plays an important role in atherosclerosis progression.
- Female has higher lipid burden in aortas.
- Endothelial mitochondrial function is different in Females and Males.

2039 Integration of advanced imaging and multiOMICs to elucidate pro-atherogenic effects of endothelial-to-immune cell-like transition (EndICLT)

Baek, Kyung In¹; Chang, Alex¹; Wang, Brendt¹; Tamargo, Ian, A¹; Kang, Dong-won¹; Kumar, Sandeep¹; Jo, Hanjoong¹

1. Emory University, Atlanta, Georgia, USA

- Disturbed blood flow-mediated Endothelial-to-immune cell like-transition.
- Light-sheet fluorescence microscopy and post processing for volumetric detection of atherosclerosis.
- multiOMIC underlying atherosclerosis.

2040 Spatially Resolved Metabolites in Stable and Vulnerable Human Atherosclerotic Plaques Identified by Mass Spectrometry Imaging

Seeley, Erin²; Liu, Zhipeng³; Yuan, Shuai⁴; Stroope, Chad¹; Cockerham, Elizabeth¹; Rashdan, Nabil¹;

Finney, Alexandra¹; Kumar, Dhananjay¹; Das, Sandeep¹; Razani, Babak⁵; Liu, Wanqing⁶; Traylor, James¹; Rom, Oren¹; Patillo, Christopher¹; Yurdagul, Arif¹

1. LSU Health Shreveport, Shreveport, Louisiana, USA
2. University of Texas at Austin, Austin, Louisiana, USA
3. Purdue University, West Lafayette, USA
4. University of Pittsburgh, Pittsburgh, USA
5. Washington University in St. Louis, St. Louis, USA
6. Wayne State University, Detroit, USA

- We performed mass spectrometry imaging of stable and vulnerable human atherosclerotic plaques.
- We identified over 850 metabolite-related peaks and annotated 170 of these using MSI.
- Fatty acid-conjugated amino acids and tryptophan metabolites, among others, were revealed.

2041 Partial myeloid inhibition of key glycolytic enzyme PFKFB3 increases hepatic steatosis and inflammation, but does not affect atherosclerosis

Tillie, Renée¹; de Bruijn, Jenny¹; Dobbie, Ross²; Perales-Patón, Javier³; van Kuijk, Kim¹; Gijbels, Marion¹; Temmerman, Lieve¹; Ghosheh, Yana⁴; Goossens, Gijss⁵; Carmeliet, Peter⁶; Ley, Klaus⁴; Henderson, Neil²; Saez-Rodriguez, Julio³; Wouters, Kristiaan⁵; Sluimer, Judith¹

1. Maastricht University Medical Center, Maastricht, Netherlands
2. University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland
3. Heidelberg University, Heidelberg, Germany
4. La Jolla Institute for Immunology, San Diego, USA
5. Maastricht University, Maastricht, Netherlands
6. KU Leuven, Leuven, Belgium

- Myeloid PFKFB3 inhibition does not affect atherosclerosis
- Myeloid PFKFB3 inhibition does induce an immuno-metabolic phenotype in mouse liver
- This hepatic phenotype is characterized by steatosis, inflammation, and myeloid cell proliferation

2042 Tenascin-X mediates flow-induced suppression of EndMT and atherosclerosis

Liang, Guozheng¹; Offermanns, Stefan¹; Wang, Shengpeng²; Shao, Jingchen¹; Jin, Young-June¹

1. Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany
2. Xi'an Jiaotong University, Xi'an, Shanxi, China

- Laminar flow induces expression of TN-X in endothelial cells through KLF4.
- EC-Tnxb-KO mice results in EndMT, endothelial inflammation, and increased atherosclerosis.
- Anti-TGF- β or endothelial loss of the TGF- β receptors normalized the phenotypes in EC-Tnxb-KO mice.

2043 PCSK9 directly activates inflammation, leading to the activation of cytokines in monocytes and the progression of atherosclerosis independently of LDL-receptor

Jang, Hyun-Duk¹; Shin, Da-Som¹; Kim, Soung-Chan¹; Fukai, Mina¹; No, Gyurae¹; Park, Hyun-woo¹; Kim, Hyo-Soo¹

1. Seoul National University Hospital, Seoul, 서울, Korea (Republic of)

- PCSK9 binding to CAP1 induces inflammation directly or independently of LDLR.
- The pivotal role of PCSK9 in inducing inflammation and atherosclerosis independently of LDLR.
- CAP1 deficient mice were protective from PCSK9-induced atherosclerosis.

2044 ACTA2 pathogenic variant increases atherosclerosis in mice by HSF1-driven cholesterol biosynthesis and augmented smooth muscle cell phenotypic modulation

Chattopadhyay, Abhijan¹; Kaw, Kaveeta¹; Guan, Pujun¹; Chen, Jiyuan¹; Majumder, Suravi¹; Duan, Xueyan¹; Ma, Shuangtao¹; Zhang, Chen²; Kwartler, Callie, S¹; Milewicz, Dianna, M¹

1. The University of Texas Health Science Center at Houston, Houston, Texas, USA
2. Baylor College of Medicine, Houston, Texas, USA

- Alpha smooth muscle actin (α -SMA) R149C variant increases atherosclerotic plaque burden in mice.

- R149C α -SMA activates HSF1, which increases HMG-CoA reductase activity and cholesterol biosynthesis.
- HMG-CoA reductase inhibitors reduce plaques in α -SMA R149C mice despite normal serum lipid levels.

2045 Coronary artery disease: lipogenic enzyme ATP citrate lyase (ACLY) as a novel potential therapeutic target

Grobs, Yann¹; Lemay, Sarah-Éve¹; Romanet, Charlotte¹; Breuils-Bonnet, Sandra¹; Bourgeois, Alice¹; Martineau, Sandra¹; Salem, Mabrouka¹; Voisine, Pierre¹; Potus, François¹; Provencher, Steeve¹; Boucherat, Oliver¹; Bonnet, Sebastien¹

1. *Université Laval, Québec, CA-QC, Canada*

- Lipogenic ATP citrate lyase enzyme: role and implication in the development of vascular remodeling
- ACLY inhibition as a novel potential therapeutic target to treat coronary artery disease.
- ACLY regulates epigenetic and metabolism dysregulation in coronary artery disease

2046 Endothelial RNA-binding Protein Elavl1 (HuR) Regulates Post-Transcriptional Regulation of Genes Involved in Immune Responses to Increase CD8 T cells in the Atherosclerotic Intima.

Nicholas, Sarah-Anne, E¹; Hensel, Jessica¹; Xu, Maria, M¹; Kimble, Amy, L¹; Menoret, Antoine¹; Jellison, Evan, R¹; Reese, Bo²; Zhou, Beiyan¹; Rodriguez-Oquendo, Annabelle¹; Vella, Anthony, T¹; Murphy, Patrick, A¹

1. *University of Connecticut Health Medical School, Farmington, Connecticut, USA*

2. *University of Connecticut, Storrs, Connecticut, USA*

- Splice factor Elavl1 regulates alternative splicing and translation of immune related transcripts
- Deletion of endothelial Elavl1 decreases plaque CD8 T cells in two mouse models of atherosclerosis
- Deletion of endothelial Elavl1 increases translation of C1q, a negative regulator of CD8 T cells

2047 Smooth muscle cell-specific transcriptome profiling of mouse atherosclerosis uncovers SMC-derived microenvironmental factor in atherosclerotic plaques

Ravindran, Aarthi¹

1. *University of Eastern Finland, Kuopio, Finland*

- Developed transgenic mouse model, that expresses EGFP-tagged RPL10a under SMC specific α SMA promoter
- SMC-specific transcriptome from any tissue using Translating Ribosome Affinity Purification (TRAP-Seq)
- Resulted in high enrichment of SMC-specific genes in pulldown fraction, in a cost effective way.

2049 Dietary Rhamnan Sulfate Reduces Vascular Inflammation and Atherosclerotic Plaque Formation

Patil, Nikita¹; Gómez-Hernández, Almudena²; Zhang, Fuming³; Cancel, Limary⁴; Feng, Xu¹; Xia, Ke³; Yan, Lufeng³; Takematsu, Eri¹; Yang, Emily¹; Johnson, Collin¹; Le, Victoria¹; Fischer, Megan¹; Gonzalez-Rodriguez, Agueda⁵; Garcia-Monzon, Carmelo⁵; Tunnell, James¹; Tarbell, John⁴; Linhardt, Robert³; Baker, Aaron¹

1. *University of Texas at Austin, Austin, Texas, USA*

2. *Complutense University of Madrid, Madrid, Spain*

3. *Rensselaer Polytechnic Institute, Troy, New York, USA*

4. *City College of New York, New York, New York, USA*

5. *Instituto de Investigación Sanitaria Hospital Universitario de La Princesa, Madrid, Spain*

- Rhamnan sulfate enhances endothelial barrier function and reduces inflammation.
- Rhamnan sulfate reduces atherosclerosis in ApoE^{-/-} mice, with stronger effects in female mice.
- Rhamnan sulfate reduces non-alcoholic fatty liver disease in female mice on a high fat diet.

2050 Novel new mouse models to assess the normal and pathological functions of smooth muscle cells and endothelial cells simultaneously in both sexes.

Deaton, Rebecca, A¹; Bulut, Gamze, B²; Serbulea, Vlad¹; Salamon, Anita¹; Shankman, Laura, S¹; Nguyen, Ahn, T³; Owens, Gary, K¹

1. University of Virginia, Charlottesville, VA, USA
2. Virginia Commonwealth University, Richmond, Virginia, USA
3. Duke University, Durham, North Carolina, USA

- The autosomal Myh11creERT2-RAD mouse allows SMC lineage tracing and gene KO in male and female mice
- The dual SMC-EC lineage tracing mouse allows simultaneous tracking of SMC and EC in the vasculature
- These novel mouse models address limitations of current SMC and EC lineage tracing and gene KO mice

2051 Network preservation analysis reveals dysregulated metabolic pathways in human vascular smooth muscle cell phenotypic switching.

Perry, Noah¹; Albarracin, Diana¹; Aherrahrou, Redouane¹; Civelek, Mete¹

1. University of Virginia, Charlottesville, Virginia, USA

- Metabolic pathways are rewired as smooth muscle cells transition from quiescent to proliferative.
- Nitrogen metabolism in smooth muscle cells may contribute to atherosclerosis pathogenesis.
- Systems biology methods identify phenotypic specific physiological and pathological processes.

2052 Age of the bone marrow dictates clonality of smooth muscle-derived cells in the atherosclerotic plaque

Kabir, Inamul¹; Zhang, Xinbo¹; Dave, Jui¹; Chakraborty, Raja¹; Qu, Rihao¹; Chandran, Rachana^{1,2}; Ntokou, Aglaia¹; Gallardo-Vara, Eunata¹; Aryal, Binod¹; Rottlan, Noemi¹; Garcia-Milian, Rolando¹; Hwa, John¹; Kluger, Yuval¹; Martin, Kathleen¹; Fernandez-Hernando, Carlos¹; Greif, Daniel¹

1. Yale University, New Haven, Connecticut, USA
2. University of California, Los Angeles, Los Angeles, California, USA

- Aged bone marrow induces smooth muscle cell polyclonality in atherosclerosis and worsens disease
- Aged monocytes downregulate TET2, silencing integrin $\beta 3$ expression and thus enhancing TNF α signaling
- TNF α signals via TNFR1 to recruit and induce polyclonal expansion of SMC progenitors in the plaque

POSTERS: VASCULAR CELL DIFFERENTIATION AND PLASTICITY

2053 Generation of contractile smooth muscle cells from human pluripotent stem cells

Kim, Kyung Hee¹; Jeong, Woo¹; Johnson, Brandon¹; Khan, Rafey¹; Lee, Jun-Hyeok¹; Min, Jaecheol¹; Yoon, Young-sup¹

1. Emory University School of Medicine, Atlanta, Georgia, USA

- Contractile smooth muscle cell differentiation from hPSC for revascularization.
- Smooth muscle cells derived from hPSCs for cell therapy.
- Enrichment of contractile SMCs by FACS-sorting with CDH2.

2054 Exercise training remodels capillary endothelial cell transcriptome in the heart and skeletal muscle

Tolvanen, Erik²; Männistö, Aino³; Amudhala Hemanthakumar, Karthik³; Lackman, Madeleine⁴; Karaman, Sinem⁴; Kivelä, Riikka¹

1. Faculty of Sport and Health Sciences, University of Jyväskylä / WRI / STEMM, Jyväskylä, Finland
2. STEMM Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland
3. Wihuri Research Institute and STEMM Research Program, Helsinki, Finland
4. IndiviDrug Research Program, Faculty of Medicine, University of Helsinki, Helsinki, Finland

- Exercise remodelled capillary EC transcriptome but had little effect on arterial and venous ECs
- Circadian rhythm genes were induced and immunity and senescence genes repressed by exercise
- Heart and skeletal muscle capillary ECs exhibit highly similar responses to exercise training

2055 Dissecting Vascular Reperfusion and Remodeling After Injury in Zebrafish

Greenspan, Leah¹; Castranova, Daniel¹; Pham, Van¹; Weinstein, Brant¹

1. National Institutes of Health, Bethesda, USA

- Reperfusion of blood vessels after injury is vital for proper tissue repair.
- Zebrafish allow us to compare vessel regrowth in live larvae and adult fish.
- Many vessels reconnect and relumenize normally after injury but some change identity.

2056 Role of the pharyngeal endodermal source of VEGF A in establishing the connectivity of the heart with the systemic circulation

Zhao, Huaning¹; Astrof, Sophie¹

1. Rutgers University, Newark, New Jersey, USA

- Pharyngeal VEGFA regulates PAA connectivity with the dorsal aorta during early embryogenesis.
- Alterations in VEGFA lead to the defective arterial-venous specification of the PAA endothelium.
- Signaling among germ layers in the pharynx regulates the formation of the systemic circulation

2057 Dissecting collateral coronary artery formation through multimodal comparative analysis in guinea pig

Fan, Xiaochen¹; Nguyen, Tri¹; Wang, Austin¹; Rios Coronado, Pamela, E¹; Engreitz, Jesse¹; Red-Horse, Kristy¹

1. Stanford University, Stanford, CA, USA

- Comparative multiome sequencing and imaging of cardiac tissue from high-altitude species.
- leveraging novel deep learning model to annotate conserved and divergent CRE in cardiac cell types.
- First in vivo Perturb-seq in mouse endothelial cells to delineate gene function

2058 Cellular mechanisms of coronary artery postnatal expansion

Rios Coronado, Pamela, E¹; Sy-Quia, Ana Natalia, L¹; Fan, Xioachen¹; Gonzalez, Karen, M¹; Red Horse, Kristy¹

1. Stanford University, Department of Biology, San Francisco, California, USA

- Vascular Cell Differentiation and Plasticity
- Angiogenesis and Vascular Remodeling
- Vascular Differentiation

2059 Mouse Placenta Proteome Dynamics Support the Critical Significance of Timing in Placenta Research

Kashpur, Olga¹; Mei, Ariel¹; Kuraoka, Shiori²; Higashi, Hideyuki²; Aikawa, Elena²; Singh, Sasha, A²;

Wallingford, Mary, C¹

1. Tufts Medical Center, Boston, Massachusetts, USA

2. Brigham and Women's Hospital, Boston, Massachusetts, USA

- This study aimed to define developmental stage-specific placental protein networks in mouse.
- Temporal abundance patterns were used for cellular compartment mapping and functional analyses.
- Protein interactomes are defined for chorioallantoic fusion, developmental phases, and tissue aging.

2060 Ensembles of endothelial and mural cells promote angiogenesis in prenatal human brain.

Crouch, Elizabeth, E¹; Bhaduri, Aparna²; Andrews, Madeline³; Cebrian-Silla, Arantxa¹; Diafos, Loukas¹; Ochoa Birrueta, Janeth¹; Wedderburn-Pugh, Kaylee¹; Valenzuela, Edward, J¹; Bennett, Neal, K¹; Eze, Ugomma, C¹;

Sandoval-Espinosa, Carmen¹; Chen, Jiapei¹; Mora, Cristina, N¹; Ross, Jayden, M¹; Howard, Clare, E¹; Haeussler, Maximilian⁴; Paredes, Mercedes, F¹; Nakamura, Ken⁵; Verdugo, Jose Manuel⁶; Alvarez-Buylla, Arturo¹; Kriegstein, Arnold, R¹; Huang, Eric, J¹

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

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

3. Arizona State University, Tempe, USA

4. University of California, Santa Cruz, Santa Cruz, USA

5. Gladstone Institute, San Francisco, California, USA

6. University of Valencia, Valencia, Spain

- Endothelial and mural cell subtypes exist in the human brain as early as the second trimester.
- The ventricular zone is an active angiogenic zone in the developing human brain.
- Collagen, Laminin, and Midkine are dominant signaling pathways in prenatal brain vascular cells.

2061 Histone Deacetylase 6 inhibition induces DNA damage accumulation in aortic smooth muscle cells

Solanki, Reesha¹; Johnson, Robert, T¹; Warren, Derek, T¹

1. University of East Anglia, Norwich, United Kingdom of Great Britain and Northern Ireland

- Microtubules play a role in protecting against DNA damage accumulation in VSMCs
- Deacetylation of microtubules leads to a greater actomyosin force mechanically squashing the nucleus
- Microtubules are destabilised when cells are treated with Tubastatin

2062 Metabolic driver of iPSC differentiation into lymphatic endothelial cells

Jeong, Donghyun, P¹; Saha, Sanjoy¹; Hanjaya-Putra, Donny¹

1. University of Notre Dame, Notre Dame, Indiana, USA

- Fatty acid oxidation driving iPSC differentiation into LEC
- Embryoid body differentiation of iPSC
- Vascularized organoid containing lymphatic endothelial cells

2063 SH2 domain protein E (SHE) and ABL signaling regulate vascular lumen size during normal and pathological tubulogenesis

Schumacher, Jennifer, A²; Wright, Zoe, A²; Rufin Florat, Diandra¹; Anand, Surendra, K¹; Dasyani, Manish¹; Klimkaite, Laurita²; Koller, Gretchen, M¹; Aguera, Kalia, N¹; Schrenk, Sandra²; Bischoff, Lindsay²; Boscolo, Elisa²; Davis, George, E¹; Sumanas, Saulius¹

1. University of South Florida, Tampa, Florida, USA

2. Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

- Src homology 2 domain containing E (She) zebrafish mutants show enlarged dorsal aorta
- She functions as an effector of Abl kinase signaling
- SHE regulates lumen size in human endothelial cells and in venous malformation cell culture model

2064 Generic attributes in adult endothelial cell are choreographed through Erg/Fli1, while c-Maf maintains organotypic properties.

Gomez Salinero, Jesus, M¹; Itkin, Tomer¹; Izzo, Franco¹; Birdsey, Graeme²; Randi, Anna²; Rafii, Shahin¹

1. Weill Cornell Medicine, New York, New York, USA

2. Imperial College London, London, United Kingdom of Great Britain and Northern Ireland

- Adult Endothelial cell identity is maintained by expression of Erg and Fli1 transcription factors.
- During fetal and postnatal development endothelial cells adapt and acquire organotypic attributes.
- The transcription factor c-Maf choreographs liver sinusoidal differentiation.

POSTERS: ANGIOGENESIS

2065 Temporally and regionally distinct morphogenetic processes govern zebrafish tail fin blood vessel network expansion

Leonard, Elvin, V¹; Hasan, Sana, S²; Siekmann, Arndt, F¹

1. Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania, USA

2. German Cancer Research Center, Heidelberg, Germany

- Successive waves of angiogenic sprouting establish the caudal fin vascular network
- Blunt ended interlaced plexus are formed in the proximal regions of the caudal fin
- Inter ray connections are established through intussusceptive angiogenesis

2067 Tumorigenic changes of mast cells in mice lung carcinoma

Yamazaki, Arisa¹; Itoh, Fumiko²; Kobayashi, Koji¹; Yamamoto, Teruko¹; Nagata, Nanae¹; Nakamura, Tatsuro¹; Murata, Takahisa¹

1. The University of Tokyo, Tokyo, Japan

2. Tokyo University of Pharmacy and Life Science, Tokyo, Japan

- Immature mast cells infiltrate the peripheral area of growing tumor.
- Mast cells express CXCR4 in response to TGF- β stimulation in the tumor microenvironment.
- Pro-tumorigenic mast cells stimulate angiogenesis and macrophage infiltration in tumor.

2068 Defining the conserved function of chloride intracellular channels (CLICs) in Rho/Rac signaling

Jesse, Jordan¹; Escudero, Julianna²; Mao, De Yu¹; Arena, Anthony¹; Kitajewski, Jan¹; Shaye, Daniel¹

1. University of Illinois at Chicago, Chicago, USA

2. Washington University in St. Louis, Saint Louis, USA

- C. elegans EXC-4, and vertebrate CLICs are conserved players in Rho/Rac signaling.
- Determinants for CLIC function and specificity in Rho/Rac signaling reside in their C-termini.
- Combined approaches in C. elegans and HUVEC will define conserved CLIC functions

2069 UNC5B is a novel target of Notch signaling and a potential effector for endothelial cell migration and junctional integrity

Youn, Seock-Won¹; Raza, Qanber¹; Swaminathan, Bhairavi¹; Gupta, Ahana¹; Du, Jing¹; Naiche, L. A.¹; Eichmann, Anne²; Kitajewski, Jan¹

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

2. Yale University School of Medicine, New Haven, Connecticut, USA

- UNC5B is a novel Notch target gene.
- UNC5B EC knockout increases retina angiogenesis.
- UNC5B regulates endothelial migration, proliferation, and cell-cell junction.

POSTERS: ANGIOGENESIS AND VASCULAR REMODELING

2070 Aspartate metabolism in endothelial cells activates the mTORC1 pathway to initiate translation during angiogenesis

Oberkersch, Roxana¹; Rampazzo, Alessandra¹; Biffo, Stefano²; Tardito, Saverio³; Liddonici, Jacopo¹; Santoro, Massimo¹;

1. University of Padua, Padua, Italy

2. University of Milan, Milan, Italy

3. Beatson Institute, Glasgow, United Kingdom of Great Britain and Northern Ireland

- Transaminases couple glutaminolysis-derived glutamate to aspartate synthesis in EC
- mTORC1 activation is driven by glutamate and aspartate metabolism in EC
- mTORC1-activation leads to control of endothelial growth factor receptor translation

2071 Key role of endothelial cell Jcad in exercise induced vascular remodelling.

Draycott, Sally¹; Shimell, Katherine, E¹; Drydale, Edward²; Channon, Keith, M¹; Douglas, Gillian¹

1. BHF Centre of Research Excellence, University of Oxford, Oxford, United Kingdom of Great Britain and Northern Ireland

2. Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, United Kingdom of Great Britain and Northern Ireland

- Jcad, a novel GWAS gene associated with CAD, has a known role in pathological vascular remodelling
- Exercise is thought to mediate CAD risk through beneficial vascular remodelling
- We have shown that Jcad plays a role in exercise capacity and exercise induced vascular remodelling.

2072 Macrophage IL-1 β -VEGF-A Signaling Axis Drives Angiogenesis During Wound Healing

Sharma, Sheila¹; Mantsounga, Chris¹; Lee, Cadence¹; Neverson, Jade¹; Pierce, Julia¹; Amelotte, Elizabeth¹; Carley, Rachel¹; Butler, Celia¹; Choudhary, Gaurav²; Morrison, Alan, R²

1. Brown University/Ocean State Research Institute, Providence, Rhode Island, USA

2. Alpert Medical School/Brown University/Ocean State Research Institute, Providence, Rhode Island, USA

- Early infiltrating inflammatory macrophages may prime angiogenesis-dependent healing.
- We hypothesize that macrophage IL-1 β -deletion disrupts pro-angiogenic VEGF-A expression.
- Rescue of macrophage VEGF-A expression may require targeting downstream effectors of the IL-1 β axis.

2073 Notch signaling regulation of smooth muscle derived vascular endothelial growth factor

Merkulov, Sergei¹; Basu, Sanchita¹; Proweller, Aaron¹

1. Case Western Reserve University, Cleveland, Ohio, USA

- Hypoxia induces VEGF production in vascular smooth muscle cells
- Notch1 enhances Hif1a binding to the VEGF promoter in vascular smooth muscle cells
- Hypoxia induced Notch signals regulate Hif1a mediated VEGF expression in vascular smooth muscle

2074 Glutamatergic Neuronal Activity Regulates Retinal Angiogenesis and Blood-Retinal Barrier Maturation via Müller Cell-Dependent Norrin/ β -Catenin Signaling.

Biswas, Saptarshi¹; Shahriar, Sanjid¹; Bachay, Galina²; Arvanitis, Panos¹; Brunken, William, J²; Menon, Vilas¹; Agalliu, Dritan¹

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

2. SUNY Upstate Medical University, Syracuse, New York, USA

- Glutamatergic neuronal activity promotes retinal angiogenesis
- Glutamatergic neuronal activity promotes paracellular blood-retinal barrier maturation
- Glutamatergic neuronal activity regulates Norrin expression in Müller cells

2075 The vascular gene Apold1 regulates pathological angiogenesis in ischemia and cancer

Ardicoglu, Raphaela¹; Fan, Zheng¹; von Ziegler, Lukas²; Bohacek, Johannes²; De Bock, Katrien¹

1. Laboratory of Exercise and Health, ETH Zürich, Schwerzenbach, Switzerland

2. Laboratory of Molecular and Behavioral Neuroscience, ETH Zürich, Zürich, Switzerland

- Apold1 regulates pathological angiogenesis without affecting physiological angiogenesis
- Apold1 deletion leads to an endothelial proliferation deficit in vivo and in vitro
- Mice lacking Apold1 develop smaller tumors and exhibit an altered tumor vascularization

2076 CD44 and Coronary Microvascular Rarefaction in HFpEF

Fopiano, Katie Anne¹; Tian, Yanna¹; Buncha, Vadym¹; Lang, Liwei¹; Bagi, Zsolt¹

1. Medical College of Georgia, Augusta University, Augusta, Georgia, USA

- Coronary microvascular rarefaction underlies the development of HFpEF.
- Decreased angiogenesis in coronary vessels in HFpEF.
- CD44 variants could play a role in changed angiogenesis in HFpEF.

2077 Single cell and bulk RNA sequencing of invading endothelial cells reveals that angiogenic sprout initiation is driven by rapid AP-1 induction of partial EndMT

Abbey, Colette¹; Coffell, Ashley¹; Duran, Camille¹; Roy, Sukanya¹; Chakraborty, Sanjukta¹; Wells, Gregg, B¹; Bayless, Kayla¹

1. Texas A&M School of Medicine, Bryan, Texas, USA

- This study contains a comprehensive transcriptomic analysis focused on endothelial sprout initiation
- We found 16 candidate genes were upregulated rapidly with the onset of endothelial sprouting
- These data show sprout initiation is associated with EndMT and driven by AP-1 transcription factors

2078 The RNA-decay protein ZFP36 regulates Jagged1 in endothelial cells

Sunshine, Hannah¹; Symons, Chloe²; Cicchetto, Andrew³; Christofk, Heather³; Vallim, Thomas³; Iruela-Arispe, Luisa²

1. UCLA and Northwestern University, Chicago, USA

2. Northwestern University, Chicago, USA

3. UCLA, Los Angeles, USA

- VEGF induces temporary robust upregulation of ZFP36 in endothelial cells
- ZFP36 targets Jagged1 mRNA and endothelial ZFP36 knockout increases Jagged1 expression
- ZFP36 knockout in mice delays retinal angiogenesis

2079 An injury-responsive endothelial mmp14b enhancer promotes heart regeneration in zebrafish.

Zlatanova, Ivana¹

1. UCSF, San Francisco, California, USA

- Mammals' ability to regenerate damaged cardiac muscle following injury.
- Endothelial cells in response to injury.
- ATAC-seq on regenerating hearts to identify active endothelial enhancers during regeneration.

2080 Specialized endothelial tip cells guide neuroretina vascularization and blood-retina-barrier formation

Zarkada, Georgia²; Howard, Joel³; Xiao, Xue¹; Park, Hyojin²; Bizou, Mathilde¹; Leclerc, Severine³; Kunzel, Steffen²; Boisseau, Blanche³; Li, Jinyu²; Cagnone, Gael³; Joyal, Jean Sebastien¹; Andelfinger, Gregor¹; Eichmann, Anne²; Dubrac, Alexandre¹

1. Université de Montréal, Montréal, Canada

2. Yale University School of Medicine, New Haven, Connecticut, USA

3. Centre de Recherche, CHU St. Justine, Montréal, Canada

- scRNA-seq identifies two distinct tip cell populations guiding retina vascularization
- D-tip cells diving into the neuroretina have a distinct molecular signature
- Non-canonical TGF- β signaling is essential for D-tip cell specification

2081 Mitochondrial dysfunction as a primary trigger of impaired angiogenesis and vascular remodeling in pulmonary arterial hypertension

Rafikov, Ruslan¹; Niihori, Maki¹; James, Joel¹; McClain, Nolan¹; Rafikova, Olga¹

1. University Of Arizona, Tucson, Arizona, USA

- Mitochondrial dysfunction impairs normal angiogenesis in the lungs.
- Altered angiogenesis induces pulmonary micro-environmental hypoxia and vascular remodeling.
- Restoration of mitochondrial function is sufficient to prevent initiation of pulmonary hypertension

2082 Short-chain fatty acid butyrate is a metabolic and bioenergetic regulator of pulmonary artery vasa vasorum endothelial cells

Fini, Mehdi¹; Paucek, Petr¹; D'Alessandro, Angelo¹; Haines, Julie¹; Weston, Philip¹; Stenmark, Kurt, R¹;

Gerasimovskaya, Evgenia¹

1. University of Colorado Denver, Aurora, Colorado, USA

- Endothelial metabolic activity is essential for vascular growth
- Butyrate is utilized in oxidative phosphorylation, glycolysis, and the fatty acid synthesis pathways
- Butyrate may have therapeutic relevance for vascular stabilization therapies in CVDs

2083 The kinase PIG-1/MELK is a novel cytoskeletal regulator functioning in *C. elegans* tubulogenesis and in vertebrate angiogenesis.

Socovich, Alexandra¹; Francis, Caitlin²; Kushner, Erich²; Shaye, Daniel¹

1. University of Illinois at Chicago - Dept. of Physiology and Biophysics, Chicago, Illinois, USA

2. University of Denver - Dept. of Biological Sciences, Denver, Colorado, USA

- *C. elegans* RNAi screen identifies the kinase PIG-1 as new cytoskeletal regulator in tubulogenesis
- MELK is expressed in HUVEC and required for 2D migration and 3D sprouting angiogenesis in culture
- Zebrafish Melk is required for developmental angiogenesis

2084 CLIC4 regulates endothelial barrier control by mediating PAR1 signaling via RhoA

Kleinjan, Matthew, L¹; Naiche, L. A.¹; Mao, De Yu Brian¹; Joshi, Jagdish, C¹; Metha, Dolly¹; Kitajewski, Jan, K¹

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

- Specific CLIC proteins differentially mediate endothelial GPCR signal transduction
- CLIC4, but not CLIC1, is required for thrombin signaling via PAR1 in vitro and in vivo
- CLIC4 mediates endothelial barrier response to thrombin signaling via RhoA activation

2085 Endothelial-specific Piezo1 is involved in the regulation of the uterine vascular plasticity?

Chilton, Susannah¹; Glessner-Fischer, Annie¹; Harraz, Osama¹; Ko, Nga Ling¹

1. University of Vermont, Burlington, Vermont, USA

- Prepregnancy physiologic predisposition is critical for the development of preeclampsia.
- EC-Piezo1 knockout attenuated uterine vascular plasticity in non-pregnant mice.
- EC-Piezo1 channels contribute to a normal uteroplacental blood flow and a healthy pregnancy.

2086 Multi-scale Computational Modeling of Microvascular Remodeling in Idiopathic Pulmonary Fibrosis

Leonard-Duke, Julie¹; Peirce, Shayn, M¹

1. University of Virginia, Charlottesville, Virginia, USA

- Multi-scale computational modeling of endothelial cell - pericyte interactions in fibrotic disease.
- Microvascular remodeling in idiopathic pulmonary fibrosis.
- Inhibiting angiogenic mediators to restore microvascular stability in idiopathic pulmonary fibrosis

2087 Endothelial-derived sphingolipids are required for vascular development and systemic lipid homeostasis

Kuo, Andrew¹; Checa, Antonio²; Niaudet, Collin¹; Jung, Bongnam¹; Fu, Zhongjie³; Wheelock, Craig, E²; Singh, Sasha, A⁴; Aikawa, Masanori⁴; Smith, Lois, E³; Proia, Richard, L⁵; Hla, Timothy¹

1. Vascular Biology Program, Boston Children's Hospital, Boston, Massachusetts, USA

2. Unit of Integrative Metabolomics, Karolinska Institute, Stockholm, Sweden

3. Department of Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, USA

4. Brigham and Women's Hospital, Boston, USA

5. National Institutes of Health, Bethesda, Maryland, USA

- De novo synthesis of sphingolipids (SL) in the endothelium impacts retinal vascular development.
- SL produced from the de novo pathway are needed for efficient VEGF signaling in EC.
- EC provide SL through the de novo synthesis pathway for SL homeostasis in circulation and organs.

2088 Inhibition of TRPM5 leads to developmental and functional cardiovascular abnormalities

Goeckel, Megan¹; Stratman, Amber¹

1. *Washington University in St. Louis School of Medicine, St. Louis, USA*

- TRPM5 is a blood-flow dependent ion channel.
- Inhibited TRPM5 leads to disruptions of ISV and caudal plexus development.
- TRPM5 inhibition reduces p-Erk activity resulting in less motile endothelial cells.

POSTERS: NEW THERAPEUTICS

2089 Withdrawn

2090 Lesion-specific suppression of YAP by targeted nanodrug ameliorates inflammation and atherosclerosis development

Huang, Hui-Chun¹; Wang, Ting-Yun¹; Rousseau, Joshua¹; Wang, Kuei-Chun¹

1. *Arizona State University, Tempe, Arizona, USA*

- Suppression of YAP decreases proatherogenic phenotypes in vascular cells and macrophages.
- Nanoparticles cloaked by monocyte membrane retain critical features of circulating monocytes.
- Targeted delivery of therapeutic agents is more effective, safer than systemic administration.

2091 Understanding the role of exercise in cardiac angiogenesis and protection from ischemia

Kocijan, Tea¹; Masschelein, Evi¹; De Bock, Katrien¹

1. *ETH Zürich, Zürich, Switzerland*

- Pathways regulating physiological cardiac vessel formation are not sufficiently explored.
- Exercise is a physiological stimulus that causes an increase in cardiac vessel density.
- Mediators of exercise-induced cardiac vessel formation could serve as novel pro-angiogenic therapy.

2092 Targeting the gap junction protein connexin 43 disrupts neointimal formation in human vascular tissues

Sedovy, Meghan, ^{W1}; King, D. Ryan²; King, D. Ryan²; Eaton, Xinyan¹; Joshi, Ramya, C¹; Malek, Arya¹; Baillie, George, S³; Baker, Joseph, W⁴; Joseph, Mark⁴; Smyth, James, W¹; Isakson, Brant, E⁵; Johnstone, Scott, R¹

1. *Fralin Biomedical Research Institute at Virginia Tech Carilion, Roanoke, Virginia, USA*

2. *Dorothy M. Davis Heart and Lung Institute, The Ohio State University, Columbus, Ohio, USA*

3. *Institute of Cardiovascular & Medical Sciences, University of Glasgow, Glasgow, United Kingdom of Great Britain and Northern Ireland*

4. *Virginia Tech Carilion School of Medicine, Department of Surgery, Roanoke, Virginia, USA*

5. *Robert M. Berne Cardiovascular Research Center, University of Virginia, Charlottesville, Virginia, USA*

- Cx43-cyclin E interactions control neointima formation in human blood vessels
- Identifying the interacting domain for Cx43 and cyclin E allows for disruptor peptide design
- Cx43 disruptor peptides can limit neointima formation in ex vivo human saphenous veins

2093 Recombinant Design of a Soluble Angiopoietin-1 Analog

Liu, Pan¹; Jin, Jing¹

1. *Northwestern University, Chicago, Illinois, USA*

- Native Angiopoietin has affinities to cells and matrices, making it unsuitable for injection.
- We replaced the "sticky" coiled-coil domain with a short tag that naturally forms a rigid heptamer.
- Chimeric HeptaAng1 fusion is more soluble and potent than native Angiopoietin-1 in i.v. injection.

2094 A natural supplement formula reduces anti-oxidative stress and enhances osteochondrogenic differentiation potential in mesenchymal stem cells

Shin, Joonhong¹; Hur, Jin¹; Lee, Hyesook¹; Han, Junghwa¹; Kang, Yunjeong¹; Jeong, Roogam¹; Yoon, Aeseon¹; An, Kangbin¹; Shin, Hyecheon¹; Oh, Jeongseon¹

1. *Pusan National University School of Medicine, Yangsan, Korea (Republic of)*

- NS-J inhibit adipogenesis of mesenchymal stem cells

- NS-J protected MSCs from oxidative stress.
- The chondrogenic effects of NS-J could reduce the pain and symptoms of osteoarthritis.

2095 Restoration of endothelial KLF2 via the targeted delivery of mRNA for the treatment of ARDS

Zhou, Zhengjie¹; Huang, Ru-Ting¹; Meliton, Angelo¹; Asby, Nick¹; Budina, Erica¹; Alpar, Aaron¹; Wu, David¹; Huang, Jun¹; Hubbell, Jeffrey¹; Mutlu, Gökhan, M¹; Tirrell, Matthew, V¹; Fang, Yun¹

1. *The University of Chicago, Chicago, Illinois, USA*

- Reduction of KLF2 in inflamed endothelium leads to ARDS induced by SARS-CoV-2 and influenza viruses.
- We engineered a rationally designed nanoparticle to effectively deliver KLF2 mRNA to inflamed EC.
- KLF2 mRNA encapsulated, VCAM1-targeting nanoparticle significantly lessens ARDS in vivo

2096 Drugging the undrugged: Targeting an endothelial-specific transcription factor with small compounds in rare diseases and vascular neoplasms.

Francois, Mathias¹

1. *The University of Sydney, Sydney, Australia*

- Unlocking the untapped potential of drugging the transcription process in endothelial cells.
- Molecular strategy for drug discovery that specifically targets developmental transcription factors
- New mode of action of the mainstay treatment in infantile hemangioma and drug repurposing

2097 Magacizumab is a novel antibody against LRG1 with diverse vascular-normalizing therapeutic applications

Moss, Stephen, E¹; Kallenberg, David¹; Blackburn, Jack¹; Greenwood, John¹

1. *UCL Institute of Ophthalmology, London, United Kingdom of Great Britain and Northern Ireland*

- LRG1 is a novel driver of pathological angiogenesis
- Blocking LRG1 inhibits pathological angiogenesis in a wide range of disease models
- We have developed a fully humanized blocking antibody against LRG1 that is ready for clinical trials

2098 Study of the impact of the inward rectifier potassium channel blocker Tertiapin-Q and a novel Peptibody on vascular and intestinal smooth muscle function

Zimmermann Rollin, Isabela¹; McQueen, Jenna, F¹; Iyer, Vishnu, V¹; Noujaim, Sami, F¹; Breslin, Jerome, W¹

1. *University of South Florida, Tampa, Florida, USA*

- The impact of Tertiapin Q and a novel targeting peptibody on human arteries was investigated.
- Tertiapin Q differentially impacts arterial versus gastrointestinal smooth muscle.
- The impact of Tertiapin Q on gastrointestinal smooth muscle is age and sex dependent.

POSTERS: 3D MODELS

2099 Engineering of capillary networks in soft hydrogels utilized for 3D bioprinting

Jaros, Josef¹; Acimovic, Ivana²; Chochola, Vaclav²; Hampl, Ales¹

1. *ICRC/FNUSA St. Anne's University Hospital, Brno, Czechia*

2. *Masaryk University, Brno, Czechia*

- Formation of capillary network in soft hydrogels is non-trivial.
- Incorporation of specific stromal cells induce specific response of ECs in hydrogels.
- Certain growth factors and medium supplements support or inhibit EC network formation in our system.

2100 Marked enhancement of human capillary tube network assembly and maturation in 3D collagen matrices by thrombin addition and upregulated expression of pericyte-derived TIMP-3

Castano, Maria, A¹; Yrigoin, Ksenia, M¹; Davis, George, E¹

1. *Molecular Pharmacology and Physiology, Morsani College of Medicine, USF, Tampa, Florida, USA*

- Pericyte derived TIMP-3 and thrombin enhance human capillary assembly and maturation
- Enhanced human capillary networks with increased basement assembly
- Understanding normal capillary assembly to create capillary networks for bioengineering

2101 Development of a Port Wine Birthmark Microphysiological System

Van Trigt, William¹; Ewald, Makena¹; Hatch, Chris¹; Chen, Joy¹; Kelly, Kristen¹; Hughes, Christopher¹

1. *UC Irvine, Irvine, California, USA*

- Endothelial cells with GNAQ activating mutations form dilated, dysfunctional capillaries called PWB.
- Previous cell culture models of port wine birthmark unsuccessfully capture disease biology.
- Our MPS model of PWB shows hallmarks of the disease and can be used to screen therapeutics.

2102 Development of a perfusable Vascularized Micro Brain for the study of glioblastoma and its stem-cell niche.

Ewald, Makena, L¹; Phan, Duc TT¹; Hatch, Christopher, J¹; Hughes, Christopher CW¹

1. *University of California, Irvine, Irvine, California, USA*

- Current models fail to recapitulate the complexity of the human GBM tumor and its BBB vessel niche.
- The human-derived Vascularized Micro Brain captures BBB functions and mirrors in vivo expression.
- The VMB can be applied to evaluate novel therapeutics and interrogate GBM disease biology.

2103 Creation of disease-inspired engineered aortic valve models to study sexual dimorphic features of CAVD progression

Figueroa, Lysmarie¹; Pollard, Noah¹; Masters, Kristyn¹

1. *University of Wisconsin Madison, Madison, Wisconsin, USA*

- Tissue-engineered models of valvular disease provide a controlled platform to study sex dimorphism.
- Fibrillar collagen influences fibrotic responses in valvular interstitial cells.
- Female valve cells may be more sensitive to pathological changes in the ECM.

POSTERS: INFLAMMATION

2104 Inhibition of NLRP3 inflammasome protects against cardiac senescence by regulating mitochondrial biogenesis

Song, Min-Young¹; Cho, Haneul¹; Lee, Sora¹; Lee, Kyung Hye²; Kim, Weon¹

1. *Kyung Hee University, Seoul, Seoul, Korea (Republic of)*

2. *Cha University, Pocheon, Korea (Republic of)*

- Proteomics discovered NNT, a key protein regulating the NLRP3 inflammasome
- NNT depletion facilitates the activation of the NLRP3 inflammasome
- NNT prevents and reverses aging-associated inflammation

2105 Observation of single platelet recruitment during dermal immune complex-mediated inflammation with real-time confocal microscopy and correlative electron microscopy

Stegmeyer, Rebekka, J¹; Currie, Silke, M¹; Mildner, Karina²; Breitsprecher, Leonhard³; Zeuschner, Dagmar²; Psathaki, Olympia Ekaterini³; Schäfer, Kerstin¹; Wilkens, Markus¹; Volkery, Stefan⁴; Nieswandt, Bernhard⁵; Vestweber, Dietmar¹

1. *Max Planck Institute for Molecular Biomedicine, Münster, Germany*

2. *Electron Microscopy Unit, Max Planck Institute for Molecular Biomedicine, Münster, Germany*

3. *Center of Cellular Nanoanalytics (CellNanOs), University of Osnabrück, Osnabrück, Germany*

4. *BioOptic Service, Max Planck Institute for Molecular Biomedicine, Münster, Germany*

- Excessive sequential diapedesis causes thrombocytopenic hemorrhage in the dermal murine vasculature.
- Bleedings are prevented by single platelet binding to the vessel via ITAM receptors GPVI and CLEC-2.
- Recruited platelets safeguard vascular integrity by plugging preferential neutrophil exit sites.

2107 Withdrawn

2108 Trained immunity in human pulmonary microvascular endothelial cells.

Markowska, Zaneta¹; Stojak, Marta²; Mezyk-Kopec, Renata³; Chlopicki, Stefan²

1. University of Virginia, 1340 Jefferson Park Ave, Charlottesville, USA, Charlottesville, Virginia, USA

2. Jagiellonian University, Michala Bobrzynskiego 14, 30-348 Krakow, Poland, Krakow, Lesser Poland, Poland

3. Jagiellonian University, Gronostajowa 7, 30-387 Krakow, Poland, Krakow, Lesser Poland, Poland

- The phenomenon of trained immunity is detectable in human lung microvascular endothelial cells.
- Trained immunity contributes to an overactive inflammatory response in the human endothelium.
- Trained immunity may play a potential role in acute or chronic inflammatory lung diseases.

POSTERS: PERMEABILITY

2109 CD93 stabilizes endothelial junctions and preserves vascular integrity

Lugano, Roberta¹; Vemuri, Kalyani¹; Claesson-Welsh, Lena¹; Dimberg, Anna¹

1. Department of Immunology, Genetics and Pathology. Uppsala University, Uppsala, Sweden

- CD93 interacts with VE-cadherin and regulates its phosphorylation and internalization
- CD93 regulates endothelial junction stability through the Rho/Rho kinase-dependent pathway
- Loss of CD93 leads to defective endothelial junctions and increased blood-brain barrier permeability

2110 Target promiscuity of BRAF inhibitors compromises endothelial function and signaling

Bromberger, Sophie¹; Larsen, Martin, R²; Schossleitner, Klaudia¹

1. Medical University of Vienna, Vienna, Austria

2. University of Southern Denmark, Odense, Denmark

- BRAF inhibitors can disrupt vascular endothelial barriers
- BRAF inhibitors modify endothelial signaling
- Targeted therapies against BRAF have unique off-targets in endothelial cells

2111 Short-chain fatty acid butyrate promotes vasa vasorum endothelial cell barrier protection: potential role of epigenetic and signaling mechanisms

Verin, Alexander²; Simon, Liselle²; Cherian-Shaw, Mary²; Strassheim, Derek¹; Karoor, Vijaya¹; Hu, Cheng-Jun¹; Stenmark, Kurt, R¹; Gerasimovskaya, Evgenia¹

1. University of Colorado, Aurora, Colorado, USA

2. Augusta University, Augusta, Georgia, USA

- Butyrate significantly enhances vasa vasorum endothelial cells (VVEC) barrier
- Our data suggest a potential epigenetic mechanisms of BT-mediated VVEC barrier protection
- Our data suggest a role of Gi proteins in BT-mediated signaling

2112 Differential Impact of S1P on hCMEC/D3 and HUVEC Monolayer Barrier Function

Iyer, Vishnu, V¹; Zimmermann Rollin, Isabela¹; McQueen, Jenna, F¹; Breslin, Jerome, W¹

1. University of South Florida, Tampa, Florida, USA

- S1P enhances barrier function in HUVEC, but disrupts barrier function of hCMEC/D3 monolayers.
- Thrombin disrupts barrier function of both HUVEC and hCMEC/D3 monolayers.
- S1P-induced disruption of hCMEC/D3 monolayers appears to involve PI3K/Akt signaling.

POSTERS: DISEASES OF THE AORTA

2113 Mitochondrial Damage with mtDNA Leak Activates Cytosolic DNA-Sensor cGAS Which Contributes to Smooth Muscle Cells Senescence and Death, Leading to Aortic Aneurysm and Dissection Formation

Chakraborty, Abhijit¹; Wei, Leu¹; Li, Yanming¹; Zhang, Chen¹; Li, Yang¹; Rebello, Kimberly, R¹; Zhang, Lin¹; Coselli, Joseph, S¹; LeMaire, Scott, A¹; Shen, Ying, H¹

1. Baylor College of Medicine, Houston, Texas, USA

- Mitochondrial damage induces mtDNA leak which activates the cGAS-STING pathway.
- cGAS-STING induces SMC senescence and death, leading to aortic aneurysm, dissection, and rupture.
- lncRNA induces SMC senescence-associated secretory phenotype upon cGAS-STING activation in SMC.

2114 Distinct Roles of PDGF-BB and TGF- β 1 on Smooth Muscle Cell Mitochondrial Homeostasis in Ascending Thoracic Aortic Aneurysms

Cha, Hanjaaram¹; Martinez, Ryan, N¹; Liu, Kristen¹; Lee, Susanna¹; Flaherty, Colin¹; Kerolos, Mariam, B¹; Billaud, Marie¹

1. Brigham and Women's Hospital, Boston, Massachusetts, USA

- Human aneurysmal SMCs had higher levels of α SMA vs. non-aneurysmal SMCs, yet contraction was reduced
- Aneurysmal SMCs were more glycolytic vs. non-aneurysmal SMC; mitochondrial respiration was similar
- TGF- β 1 and PDGF-BB have distinct effect on aneurysmal SMCs depending on the etiology of the disease

2115 Zebrafish chd7 mutants show concomitant craniofacial and cardiovascular defects

Sun, Yuhua¹; Wong, David¹; Tian, Zhiyu²; Bai, Haipeng³; Crump, Gage²; Bajpai, Ruchi²; Lien, Ching-Ling¹

1. Children Hospital of Los Angeles/ University of Southern California, Los Angeles, California, USA

2. University of Southern California, Los Angeles, California, USA

3. Peking University, Beijing, Beijing, China

- Using zebrafish to generate a disease model for CHARGE syndrome
- The chd7 mutant fish have a weak CHARGE-like craniofacial phenotype.
- The chd7 mutants have defects in the ventral aorta and aortic arch arteries.

2116 Development of a 3D Cellularized Construct to Study the Effects of Cyclic Strain on Vascular Smooth Muscle Behavior in Marfan Syndrome

Hall, Franklyn, D¹; Boheler, Kenneth¹; Gerecht, Sharon¹

1. Department of Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, USA

- MFS-hiPSC can be fully differentiated into contractile vascular smooth muscle cells
- MFS-vSMCs replicate several behavioral aspects of aortic-vSMCs in MFS, validating their use in vitro
- MFS-vSMC cell sheets attach to fibrin-based grafts and retain contractile marker expression

2117 Fibrillin-1 deletion in endothelial cells replicates early events promoting arterial disease in Marfan syndrome

Cantalupo, Anna¹; Asano, Keiichi¹; Dikalov, Sergey²; Halabi, Carmen³; Mecham, Robert³; Di Lorenzo, Annarita⁴; Iyengar, Ravi¹; Ramirez, Francesco¹

1. Icahn School of Medicine at Mount Sinai, New York, NY, USA

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

3. Washington University, St Louis, Missouri, USA

4. Weill Cornell Medicine, New York, New York, USA

- Endothelial fibrillin-1 has a key role in preserving aortic integrity
- Endothelial fibrillin-1 is required to maintain proper EC-SMC communication in the aorta
- Altered endothelial-derived signaling triggers aneurysm disease in Marfan syndrome

2118 Partial EndMT mediated by HIF-induced CD45 in neointima formation

Yamashiro, Yoshito¹

1. National Cerebral and Cardiovascular Center Research Institute, Suita, Osaka, Japan

- The origin of neointima cells and their relevance to vascular wall remodeling
- HIF-induced CD45 expression is required for the retention of an EC fate and cell-cell junctions
- Partial EndMT promoted an integrin α 11-SHARPIN complex, thereby destabilizing cell-cell junctions

2119 Sustained Activation of Endothelial YAP1 Causes Epithelioid Hemangioendothelioma

Jung, Roy¹; Janardhan, Harish, P¹; Dresser, Karen¹; Cotton, Jennifer, L¹; Hutchinson, Lloyd¹; Mao, Junhao¹; Trivedi, Chinmay, M¹

1. UMass Chan Medical School, Worcester, Massachusetts, USA

- Sustained activation of endothelial YAP1 causes intravascular epithelioid hemangioendothelioma
- Animal model of human intravascular and cardiac epithelioid hemangioendothelioma
- Intravascular EHE in the aorta and the pulmonary artery leads to severe deep vessel occlusion

2120 Zinc-Finger Protein 148(ZFP148) Attenuates Vascular Smooth Muscle Cell Phenotypic Cell Transitions during Chronic Aortic Aneurysm Formation and Rupture

Salmon, Morgan¹; Spinosa, Michael²; Scott, Erik³; Montgomery, William³; Ailawadi, Gorav¹

1. University of Michigan, Ann Arbor, Michigan, USA

2. Virginia Tech, Roanoke, Virginia, USA

3. University of Virginia, Charlottesville, Virginia, USA

- Vascular Diseases
- arterial diseases
- abdominal aortic aneurysm and rupture

2121 GLP-1 receptor agonist Semaglutide inhibits aortic rupture in the Angiotensin II mouse model

Balboa Ramilo, Amanda¹; Mani, Kevin¹; Wanhainen, Anders¹; Lindeman, Jan, H²; Friederich-Persson, Malou¹; Wågsäter, Dick¹

1. Uppsala University, Uppsala, Sweden

2. Leiden University Medical Center, Leiden, Netherlands

- Prophylactic treatment (from day one of disease induction) reduces death caused by aortic rupture
- Rescue treatment (from day 7 after disease induction) does not prevent death or aneurysm development
- Semaglutide acts during the initial phase of disease development preventing death by aortic rupture

2122 Defective vascular cells phenotype can lead to endothelial dysfunction in Marfan syndrome in model derived from iPSCs

Nolasco, Patricia¹; Laurindo, Francisco Rafael, M²; Pereira, Lygia, V¹

1. USP, São Paulo, Sao Paulo, Brazil

2. InCor-HC-FMUSP, SAO PAULO, Sao Paulo, Brazil

- Endothelial phenotype is important to understand the relationship between distinct genotypes in MFS
- Endothelial dysfunction is a mechanism in which may be associated with aneurysms development in MFS
- hiPSC is an important tool to investigate vascular disease development, including Marfan syndrome

2123 Multi-transcriptomic profiling reveals novel molecular mediators during abdominal aortic aneurysm expansion.

Sachs, Nadja¹; Wu, Zhiyuan²; Li, Zhaolong²; Pauli, Jessica²; Winski, Greg³; Paloschi, Valentina²; Dueck, Anne⁴; Engelhardt, Stefan⁴; Busch, Albert⁵; Eckstein, Hans-Henning¹; Maegdefessel, Lars²

1. Vascular und Endovascular Surgery, Klinikum rechts der Isar, TUM, Munich, Germany

2. Molecular Vascular Medicine, Klinikum rechts der Isar, TUM, Munich, Germany

3. Molecular Vascular Medicine, Karolinska Institute, Stockholm, Sweden

4. Institute of Pharmacology and Toxicology, TUM, Munich, Germany

- Utilize multi-transcriptomic profiling for discovery of AAA disease regulators.
- Identify lncRNAs as potential disease modulators during AAA development.
- Assess whether changes in human disease are reflected in preclinical AAA animal models.

2124 The potential protective role of FBN1 deficiency-induced miR146b-5p in aneurysm progression through inhibiting the expression of MMP16, TRAF6 and IRAK1.

Hemani, Darshi, V¹; Wu, Shichao¹; Xie, Daniel¹; Pham, Lucynda¹; Ju, DongHong¹; Xie, Youming¹; Li, Li¹

1. Wayne State University, Detroit, Michigan, USA

- Generated a new mouse model with Q2469X nonsense mutation in fibrillin-1 causing thoracic aneurysm.
- miR146b-5p level was elevated in both thoracic and abdominal aortic aneurysms in the mouse model.
- miR146b-5p has a potential protective role by downregulating targets like TRAF6, IRAK1 and MMP16.

2125 Compensatory aortic remodeling in Marfan syndrome protects against sexually dimorphic rupture during a BAPN challenge

Weiss, Dar¹; Rego, Bruno¹; Cavinato, Cristina¹; Li, David¹; Kawamura, Yuki¹; Emuna, Nir¹; Humphrey, Jay¹

1. Yale university, New Haven, Connecticut, USA

- Vascular disease
- Marfan Syndrome
- Role of collagen

SUNDAY, OCTOBER 16 – 12:00PM TO 2:00PM – WEST HALL

POSTERS: TUMOR BIOLOGY

3001 Multi-organ systems map of vascular reprogramming during cancer-cachexia

Preuss, Stephanie, F¹; Kamiyama, Miki²; Singhal, Mahak²; Augustin, Hellmut, G¹

1. European Center for Angioscience (ECAS), Medical Faculty Mannheim, Mannheim, Baden-Württemberg, Germany

2. AngioRhythms, European Center for Angioscience, Medical Faculty Mannheim, Mannheim, Germany

- Cancer cachexia initiates systemic endothelial cell reprogramming
- Surgical tumor resection mitigates the cachectic phenotype and vascular reprogramming
- IL6-JAK-STAT3 signaling is upregulated across different vascular beds during cachexia progression

3002 PTPN11 mosaicism causes a spectrum of pigmentary and vascular neurocutaneous disorders and predisposes to melanoma

Polubothu, Satyamaanasa¹; Bender, Nicole²; Muthiah, Siobhan³; Zecchin, Davide⁴; Demetriou, Charalambos¹;

Barberan Martin, Sara⁴; Malhotra, Sony⁵; Travnickova, Jana⁶; Zeng, Zhiqiang⁶; Böhm, Markus⁷; Barbarot, Sebastien⁸;

Cottrell, Catherine⁹; Davies, Olivia²; Baselga, Eulalia¹⁰; Burrows, Nigel, P¹¹; Carmignac, Virginie¹²;

Diaz, Joey¹³; Fink, Christine¹⁴; Haenssle, Holger¹⁴; Happle, Rudolf¹⁵; Harland, Mark¹³; Majerowski, Jacqueline²;

Vabres, Pierre¹⁶; Vincent, Marie⁸; Newton-Bishop, Julia, A¹³; Bishop, D. Tim¹³; Siegel, Dawn²; Patton, E. Elizabeth⁶;

Topf, Maya⁵; Rajan, Neil³; Drolet, Beth²; Kinsler, Veronica, A⁴

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

2. Department of Dermatology, Medical College of Wisconsin, Wisconsin, USA

3. Institute of Genetic Medicine, Newcastle University, Newcastle, United Kingdom of Great Britain and Northern Ireland
4. Francis Crick Institute, London, United Kingdom of Great Britain and Northern Ireland
5. Biological Sciences, Birkbeck, University of London, London, United Kingdom of Great Britain and Northern Ireland
6. MRC Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland
7. Department of Dermatology, University of Münster, Münster, Germany
8. Department of Dermatology, CHU Nantes, Nantes, France
9. Institute for Genomic Medicine, Nationwide Children's Hospital, Columbus, Ohio USA
10. Department of Dermatology, SJD Barcelona Children's Hospital, Barcelona, Spain
11. Department of Dermatology, Addenbrooke's Hospital, Cambridge, MA, USA
12. Génétique des Anomalies du Développement, Université de Bourgogne, Dijon, France
13. Leeds Institute of Cancer and Pathology, Leeds, United Kingdom of Great Britain and Northern Ireland
14. Department of Dermatology, University of Heidelberg, Heidelberg, Germany
15. Department of Dermatology, Medical Center, University of Freiburg, Freiburg, Germany
16. Department of Dermatology, CHU Dijon, Dijon, France
 - Phakomatosis pigmentovascularis is a vascular and pigmentary multisystem disease
 - Clonal mosaic variants in gene PTPN11 cause both the vascular and pigmentary features
 - This may give important insights into early embryological origins of endothelial cells & melanocytes

3003 Long pentraxin 3 (PTX3) as a regulator of lymphangiogenesis and lymphogenous dissemination in melanoma

Turati, Marta¹; Giacomini, Arianna¹; Rezzola, Sara¹; Maccarinelli, Federica¹; Gazzaroli, Giorgia¹; Valentino, Sonia²; Bottazzi, Barbara²; Presta, Marco¹; Ronca, Roberto¹

1. University of Brescia, Brescia, Italy
2. IRCCS Humanitas Research Hospital, Milan, Italy
 - Long pentraxin 3 traps FGF during lymphangiogenesis
 - Long pentraxin 3 reduces lymphangiogenesis in vitro and in vivo
 - Reduced lymphangiogenesis by PTX3 impairs lymphatic dissemination of melanoma

3004 Radiotherapy induced lymphatic dysfunction in lymphangiogenic tumors

Mukherjee, Anish¹; MacDonald, Margo¹; Ang, Phillip¹; Baginski, Ariana¹; Swartz, Melody, A¹

1. University of Chicago, Chicago, Illinois, USA
 - Lymphangiogenic tumors respond better to radiotherapy and immunotherapy.
 - Lymphatic vessels in the tumor periphery have increased clots in irradiated lymphangiogenic tumors.
 - Tumor draining lymph nodes of irradiated lymphangiogenic tumors have increased fibrin clots.

POSTERS: VASCULATURE IN HEALTH AND DISEASE

3005 Lyso-globotriaosylsphingosine induces endothelial dysfunction via autophagy-dependent regulation of necroptosis

Hwang, Ae Rang¹; Hong, Changui¹; Lee, Haegyul¹; Lee, Suyeon¹; Woo, Chang-Hoon¹

1. Department of Pharmacology, College of Medicine, Yeungnam University, Daegu, Korea (Republic of)
 - Fabry disease is an X-linked lysosomal storage disorder caused by diminished activities of α -gal A.
 - Necrosis and inflammatory activation of the innate immune system are general responses in FD.
 - Necroptosis is a type of programmed cell death with unique features with apoptosis and necrosis.

3006 Interplay of cell types in hypoxia driven microvascular remodeling

Juusola, Greta¹; Wirth, Galina¹; Mäkinen, Kimmo¹; Hakoviirta, Harri²; Ylä-Herttua, Seppo³; Korpisalo, Petra¹

1. Heart Center, Kuopio University Hospital, Kuopio, Finland
2. Department of Vascular Surgery, Turku University Hospital, Turku, Finland
3. Dept. Mol Med, A.I. Virtanen Institute, University of Eastern Finland, Kuopio, Finland

- Different cell types may play a role in modulating hypoxic microvascular changes.
- Gene expression analyses of RNA sequencing data from chronically ischemic human muscles.
- Fibro-adipogenic progenitors, pericytes, fibroblasts and macrophages show regulatory potential.

3007 Withdrawn

3008 Functional and metabolic characterization of human endothelial progenitor cell response to physoxia and hypoxia

Bertelli, Pietro Maria¹; Guduric-Fuchs, Jasenka¹; Pathak, Varun¹; Pedrini, Edoardo¹; Hughes, David¹; Branco, Cristina¹; Medina, Reinhold J.¹; Stitt, Alan W.¹

1. Queen's University Belfast, WWIEM, Belfast, United Kingdom of Great Britain and Northern Ireland

- Physoxia "priming" shifts endothelial progenitor glycolytic profile, enhancing their functionality
- Hypoxia upregulates glycolysis-related genes
- Metabolic modulation in endothelial progenitor cells improves vascular regeneration in ischemia

3009 Withdrawn

3011 Notch signaling regulates pericyte coverage and vessel morphogenesis in the germinal matrix, a critical region for brain hemorrhage in preterm infants.

Nadeem, Taliha¹; Bommareddy, Apoorva¹; Naiche, L A¹; Kitajewski, Jan, K¹; Cuervo, Henar¹

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

- Notch signaling is active in pericytes during stages of early embryonic brain angiogenesis.
- Reduced Notch signaling leads to pericyte loss and vessel dilation in the brain germinal matrix.
- Loss of Notch signaling in pericytes may lead to germinal matrix hemorrhage in preterm infants.

3012 A humanised neutralising antibody to VEGF-A165b induces collateral formation in obese and diabetic models of peripheral arterial disease

Amartey, Jason, O¹; Agrawal, Jyoti¹; Wahid, Mussarat¹; Bhalla, Sohni Ria¹; Gao, Yizhuo¹; Bates, David, O¹

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

- Humanised Antibodies to VEGF165b improve collateralisation in models of diabetes and obesity
- Humanised antibody dose-dependently reduced the binding affinity of rhVEGF-A165b to VEGFR2.
- Antibody may have therapeutic potential for patients with CAD by enhancing the collateral formation

3013 Defective autophagy impairs endothelial cells' function and barrier integrity.

Mameli, Eleonora¹; Szymkowiak, Stefan²; McColl, Barry²; Santi, Spartaco³; Caporali, Andrea¹

1. University/BHF Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland

2. UK Dementia Research Institute, University of Edinburgh, Edinburgh, United Kingdom of Great Britain and Northern Ireland

3. CNR Institute of Molecular Genetics "Luigi Luca Cavalli-Sforza", Bologna, Italy

- Impairment of autophagy is involved in Endothelial Dysfunction and vascular diseases.
- Trichoplein controls autophagosome formation, linking autophagy with ECs function and inflammation.
- Knock-down of TCHP causes impaired barrier function in heart, skeletal muscles and brain vessels.

POSTERS: EPIGENETIC REGULATION

3014 Endothelial Dnmt3a controls placenta vascularization and function to support fetal growth

Gehrs, Stephanie¹; Jakab, Moritz¹; Gu, Zuguang²; Gutjahr, Ewgenija³; Weichenhan, Dieter⁴; Mogler, Carolin⁵; Schlesner, Matthias⁶; Plass, Christoph⁴; Augustin, Hellmut¹; Schlereth, Katharina¹

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

2. *Molecular Precision Oncology Program, National Center for Tumor Diseases, Heidelberg, Germany*
3. *Institute of Pathology, University Clinic Heidelberg, Heidelberg, Germany*
4. *Division of Cancer Epigenomics, German Cancer Research Center, Heidelberg, Germany*
5. *Institute of Pathology, Technical University of Munich, Munich, Germany*
6. *Biomedical Informatics, University of Augsburg, Augsburg, Germany*

- Reduced DNMT3A expression in human placenta EC is associated with preeclampsia.
- In mouse, loss of Dnmt3a results in late IUGR and reduced placenta vascularization.
- Loss of DNA methylation reduces the angiogenic capacity of EC.

3015 Loss of heterochromatin primes osteogenic phenotype conversion in vascular smooth muscle cells

Wu, Meng-Ying¹; Ho, Chin Yee¹; Ahmad, Sadia¹; Shanahan, Catherine¹

1. *King's college London, London, United Kingdom of Great Britain and Northern Ireland*

- Cell type switching driven by transcriptomic changes acquired in response to epigenetic modulation
- Global reduction of the heterochromatin marks occurred prior to the onset of calcification
- Inhibiting histone modifiers induced pre-senescence and accelerated mineral deposition

3016 Endothelial Chromatin Remodeling Enzymes BRG1 and CHD4 Promote Lung Development by Transcriptionally Regulating Extracellular Matrix Production

Wu, Meng Ling¹; Griffin, Courtney, T¹

1. *Oklahoma Medical Research Foundation, Oklahoma, Oklahoma, USA*

- Deleting both Brg1 and Chd4 in ECs causes developmental lung defects with impaired ECM deposition.
- Endothelial-derived TGFb1 signaling is downregulated in double-knockout lungs.
- Endothelial BRG1 and CHD4 directly regulate ECM component transcripts independent of TGFb1.

3017 Inhibition of the Histone Methyltransferase EZH2 Induces Vascular Stiffness with Increased MMP2 and Elastin Fiber Degradation

Ibarrola, Jaime¹; El Kabbout, Reem²; Breuils Bonnet, Sandra²; Xiang, Rachel¹; Martineau, Sandra²; Lu, Qing¹; Bourgeois, Alice²; Jaffe, Iris, Z¹; Provencher, Steeve²; Boucherat, Olivier²; Bonnet, Sébastien²; Potus, Francois²

1. *Tufts Medical Center, Boston, Massachusetts, USA*

2. *CRIUCPQ, Quebec, Canada*

- Mineralocorticoid receptor drives aging-associated vascular stiffness by suppressing EZH2.
- GSK126 induces vascular stiffness via increased MMP2 activity to promote elastin degradation.
- EZH2 inhibitors developed to treat in cancer could negatively impact the vasculature.

3018 Loss of lncRNA SAS causes cell cycle defect and hypertrophy in vascular smooth muscle cells

Espinosa-Diez, Cristina¹; Wei, Jianxin¹; Liu, Mingjun¹; Ahmed, Ibrahim¹; An, Wenxi¹; Straub, Adam¹

Gomez, Delphine¹;

1. *University of Pittsburgh, Pittsburgh, Pennsylvania, USA*

- SAS (SMC-Angiotensin-II-Sensitive) long non-coding RNA is highly expressed in the vasculature.
- Downregulation of SAS is observed in hypertensive mice and smooth muscle cells treated with Ang-II.
- Loss of SAS induces SMC hypertrophy, polyploidy and senescence by defective cell cycle completion.

3019 microRNA-223 Limits Hemogenic Endothelial Cell Specification and Myelopoiesis.

Wu, Yinyu¹; Paila, Umadevi¹; Genet, Gael¹; Hirschi, Karen, K¹

1. *University of Virginia, Charlottesville, Virginia, USA*

- miR-223 inhibits mouse hematopoiesis from early embryonic stages to adulthood.

- miR-223 negatively regulates retinoic acid signaling in mouse embryonic hematopoiesis.
- Embryonic hemogenic EC defects in miR-223KO can lead to adult myeloid-differentiation disorder.

POSTERS: CARDIOVASCULAR REGENERATIVE MEDICINE

3020 CD39 (NTPDase1) prevents development of pulmonary arterial hypertension in a mouse model when targeted to up-regulated pulmonary endothelial VCAM-1

Willcox, Abbey¹; Wang, Xiaowei²; Calvello, Ilaria¹; Bongcaron, Viktoria²; Selan, Carly¹; Lee, Natasha¹; Walsh, Aidan²; Song, Yuyang²; Peter, Karlheinz²; Sashindranath, Maithilji¹; Nandurkar, Harshal¹

1. Australian Centre for Blood Diseases, Monash University, Melbourne, Australia

2. Baker Heart & Diabetes Institute, Melbourne, Victoria, Australia

- CD39 maintains the endogenous antithrombotic profile of the endothelium - it is disrupted in PAH
- Endothelial dysfunction occurs in mice within 72 hours of MCTP injection, they go on to develop PAH
- Anti-VCAM-CD39, a novel therapeutic, ameliorates the development of pulmonary hypertension in mice

3021 Enhancing endothelial cell engraftment via transplantation of exogenous mitochondria

Lin, Rwei-Zeng¹; Hong, Xuechong¹; Luo, Allen, C¹; Neumeyer, Joseph¹; Melero-Martin, Juan¹

1. Boston Children's Hospital, Boston, USA

- Abrogating mitochondrial transfer from MSCs to ECs drastically impairs EC engraftment
- Transplanting mitochondria into ECs enhances their ability to engraft without a secondary cell type
- Transplanting mitochondria into ECs renders transient cytoprotection via mitophagy

3022 Withdrawn

3023 Heterogeneous pdgfrb+ cells regulate coronary vessel development and revascularization during heart regeneration

Kapuria, Subir¹; Lien, Ching-Ling¹

1. Children's Hospital Los Angeles, Los Angeles, California, USA

- Zebrafish coronary artery mural cells express cxcl12b, beside pdgfrb and are smooth muscle cells.
- Zebrafish coronary artery mural cells remain associated with the vessels in pdgfrb mutants.
- Pdgfrb+ cells express pro-regenerative genes in the injured zebrafish heart.

3024 A cross-species approach using an in vivo evaluation platform in mice demonstrates that sequence variation in the human RABEP2 gene modulates ischemic stroke outcomes

Lee, Han Kyu¹; Marchuk, Douglas, A¹

1. Duke University School of Medicine, Durham, North Carolina, USA

- In vivo evaluation platform using adeno-associated virus gene replacement
- Cross-species complementation
- Human RABEP2 sequence variation plays any role in ischemic stroke outcomes

3025 New Treatment for Heart Failure: Unleashing the Power of Lymphangiogenesis with Rejuvenated Fibroblasts

Iwamiya, Takahiro¹; Matsuoka, Yuimi¹; Segard, Bertrand, D¹; Matsuyama, Makoto¹; Ikeda, Ayana¹; Obara, Mari¹; Machino, Takeshi²; Sato, Akira³; Murakoshi, Nobuyuki²

1. Research & Development Department, Metcela Inc., Kawasaki, Kanagawa, Japan

2. Department of Cardiology, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

3. Department of Cardiology, University of Yamanashi, Yamanashi, Japan

- Human fetal cardiac fibroblasts are capable of lymphangiogenesis, but adults are not.
- NF-kB converts adult cardiac fibroblasts into fetal-like fibroblasts inducing lymphangiogenesis.

- Injection of fetal-like adult cardiac fibroblasts improves cardiac function in rats and pigs post-MI

3026 Protective Effect of Drug G on Anticancer Drugs-induced Cardiovascular disease in Human Cardiac Progenitor Cells

Lee, Eunji¹; Kwon, Sang-mo¹

1. School of Medicine, Pusan National University, Yangsan, Korea, Korea (Republic of)

- ACDs are induced apoptosis by generation reactive oxygen species in hCPCs.
- Drug G increased the function in damaged hCPC by ACDs, including migration, tube-formation.
- Drug G prevented by regulating of pERK signaling in ACDs-induced CVD.

POSTERS: SIGNALING IN VASCULAR DISEASE

3027 Deficiency of PROX1 causing myxomatous valve degeneration

Ho, YenChun¹; Geng, Xin¹; King, Jang¹; Varshney, Rohan¹; Surbrahmanian, Sandeep, M¹; Subramani, Kumar¹; Alvandi, Zahra²; Chen, Lijuan¹; Azartash-Namin, Zheila, J¹; Matsuzaki, Fumio³; Aikawa, Elena⁴; Olson, Lorin¹; Ahamed, Jasimuddin¹; Bischoff, Joyce⁵; Srinivasan, Sathish¹

1. Cardiovascular Biology Program, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA

2. Department of Surgery, Harvard Medical School, Boston, Massachusetts, USA

3. RIKEN Center for Developmental Biology, Wako, Saitama, Japan

4. Cardiovascular Division Brigham and Women's Hospital Harvard Medical School, Boston, MA, USA

5. Department of Surgery, Harvard Medical School, Boston, Massachusetts, USA

- PROX1 is expressed in a subset of VECs that are located on the fibrosa side of cardiac valves
- Mice lacking PROX1 in VECs develops myxomatous aortic and mitral valves in an age-dependent manner.
- Hyperactivation of PDGF-B signaling in valve interstitial cells in mice results in myxomatous valves

3028 Ginsenoside Rh1 alleviates LPS-induced endothelial cell dysfunction in human umbilical vein endothelial cells through suppressing TLR2/4-mediated NF- κ B/STAT3 signaling pathway and ER stress

Jin, Yujin¹; Nguyen, Le Lam Thuy¹; Myung, Chang-Seon¹; Heo, Kyung-Sun¹

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

- Rh1 attenuates LPS-induced EC inflammation by suppressing phosphorylation of ERK1/ and STAT3
- Rh1 interrupts LPS binding to TLR2 and TLR4 to activate LPS-induced EC dysfunction
- Rh1 stabilized EC homeostasis by suppressing the LPS-induced ER stress

3029 Key role of Kruppel-like factor 4 activation on vascular smooth muscle cell dysfunction via regulating mitochondrial fission

Huynh, Diem Thi Ngoc¹; Jin, Yujin¹; Tangchang, Warisraporn¹; Son, Hwa-Young¹; Heo, Kyung-Sun¹

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

- Ang II-induced VSMC proliferation and migration through KLF4 activation.
- KLF4 activation induces mitochondrial fission.
- Rh1 inhibits VSMC dysfunction by suppressing ROS-mediated ERK1/2 and KLF4 signaling pathway

3030 Vascular endothelial growth factor signaling in the white adipose tissue regulates hepatic steatosis and development of diabetic fatty liver disease and hepatocellular carcinoma

Falkevall, Annelie¹; Folestad, Erika¹; Mehlem, Annika¹; Chenfei Ning, Frank¹; Palombo, Isolde¹; Wright, Samuel, D²; Scotney, Pierre³; Nash, Andrew³; Eriksson, Ulf¹

1. Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden

2. CSL Behring, King of Prussia, PA, USA

3. CSL Innovation Pty Ltd, Parkville, Victoria, Austria

- In T2DM different vascular diseases lead to tissue lipotoxicity, e.g diabetic fatty liver disease
- Inhibition of VEGF-B signaling ameliorated NAFLD and NASH-mediated HCC in diabetic mice

- The beneficial effect was due to targeting of the VEGF-B signaling pathway and lipolysis in the WAT

3031 Inhibition of VEGF-B signalling prevents development of non-alcoholic fatty liver disease by targeting lipolysis in the white adipose tissue

Folestad, Erika¹; Falkevall, Annelie¹; Mehlem, Annika¹; Ning, Frank Chenfei¹; Osorio, Oscar²; de Hollanda, Anna²; Wrigh, Samuel, D³; Scotney, Pierre⁴; Nash, Andrew⁴; Eriksson, Ulf¹

1. Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden

2. Centro de Investigación Biomédica (CIBERDEM), Madrid, Spain

3. CSL Behring, King of Prussia, Philadelphia, USA

4. CSL Innovation Pty Ltd, Melbourne, Australia

- Targeting development of non-alcoholic fatty liver disease
- Vascular Endothelial Growth Factor B controlling tissue lipid accumulation
- Tight control of lipolysis in the WAT

3032 ENPP1-Fc inhibits proliferation of pathological synthetic phenotype vascular smooth muscle cells (VSMCs) in the presence of ATP: the role of ecto-5'-nucleotidase CD73.

Tchernychev, Boris¹; Chu, Di¹; Sullivan, Caitlin¹; O'Brien, Kevin¹; Ortiz, Daniel¹; Cheng, Zhiliang¹; Sabbagh, Yves¹

1. Inozyme Pharma, Boston, Massachusetts, USA

- ENPP1-Fc inhibits proliferation of synthetic vascular smooth muscle cells in the presence of ATP
- Anti-proliferative effect of ENPP1-Fc/ATP co-treatment requires enzymatic activity of CD73
- Generated by vascular smooth muscle cells adenosine activates cAMP-PKA signaling pathway

3033 Protein kinase N1 and N2 differentially mediate flow pattern-dependent endothelial function

Jin, Young-June¹; Chennupati, Ramesh¹; Liang, Guozheng¹; Wang, ShengPeng¹; Iring, Andrés¹; Graumann, Johannes¹; Wettschureck, Nina¹; Offermanns, Stefan¹

1. Max-Planck Institute, Bad Nauheim, Germany

- PKN2 regulates laminar flow-induced eNOS phosphorylation.
- PKN1 regulates disturbed flow-induced inflammatory gene expression
- PKN1 and PKN2 regulates endothelial function.

3034 Endothelial senescence mediates hypoxia-induced vascular remodeling in the lung through TWIST1 signaling.

Kyi, Priscilla¹; Hunyenyiwa, Tendai¹; Matus, Kienna¹; Mammoto, Tadanori¹; Mammoto, Akiko¹

1. Medical College of Wisconsin, Wauwatosa, Wisconsin, USA

- Cellular senescence is stimulated in the pulmonary hypertension patient lungs.
- Endothelial senescence mediates hypoxia-induced vascular remodeling in the lung through TWIST1.
- Senescence mediates the effect of exosomes on smooth muscle cell behaviors under hypoxia.

3035 SHetA2 Interference with p66Shc signaling prevents renal vascular dysfunction in rat model of hypertension-induced nephropathy

Miller, Bradley, S¹; Imig, John, D¹; Schupbach, Perrin¹; Woo, Sukyung²; Benbrook, Doris, M³; Sorokin, Andrey¹

1. Medical College of Wisconsin, Milwaukee, Wisconsin, USA

2. University at Buffalo, Buffalo, New York, USA

3. The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA

- Adaptor protein p66Shc is implicated in the loss of microvascular reactivity in hypertensive rats.
- Small molecule SHetA2 (modulator of p66Shc signaling) restores renal microvascular reactivity.
- Chronic administration of SHetA2 mitigated renal damage in hypertensive rats.

3036 SNRK regulates TGFβ levels in atria to prevent cardiac fibrosis

Thirugnanam, Karthikeyan¹; Rizvi, Farhan²; Jahangir, Arshad²; Shabnam, Fathima³; Palecek, Sean³; Sekine, Hidekazu⁴; Bai, Xiaowen¹; Ramchandran, Ramani¹

1. Medical College of Wisconsin, Milwaukee, WisconsinWI, USA

2. Aurora Healthcare, Milwaukee, Wisconsin, USA

3. University of Wisconsin-Madison, Madison, Wisconsin, USA

4. Tokyo Womens Medical University, Shinjuku City, Japan

- Heart failure
- Atrial fibrosis
- Cardiomyocytes

3037 Endothelial Cell-Specific Deletion of MiR-409-3p Promotes Angiogenesis After Myocardial Infarction

Fritsche, Colette, M¹; Bestepe, Furkan²; Ghosh, Ruma²; Zhu, Megan²; Niosi, Carolyn²; Becker-Greene, Dakota³; Lakhotiya, Kartik²; Martin, Gregory²; Feinberg, Mark, W²; Blanton, Robert, M²; Icli, Basak⁴

1. Tufts Medical School, Boston, USA

2. Tufts Medical Center, Boston, Massachusetts, USA

3. Brigham and Women's Hospital, Boston, USA

4. Tufts Medical School/Molecular Cardiology Research Institute, Boston, USA

- Reduction in capillary density post myocardial infarction negatively impacts the heart function.
- MicroRNAs are small non-coding RNAs and important regulators of angiogenesis.
- Identification of microRNAs to restore impaired angiogenesis may provide new targets for therapy.

3038 Alk1 deficiency elicits AVMs with venous but not arterial identity from capillaries

Yuan, Sai¹; Li, Shang¹; Lee, Eric¹; Huang, Jacky¹; Liu, Cynthia¹; Bollen, Andrew¹; Wang, Rong¹

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

- AVMs elicited by Alk1 deletion originated from capillary-like vessels by two-photon live imaging.
- Slco1c1-CreERT2-mediated Alk1 deletion induced AVMs in mice at the postnatal developmental stage.
- AVMs elicited by Alk1 deletion exhibited venous, but not arterial molecular identity.

3039 Krüppel-Like Factor-4 in the maintenance of Endothelial Cell Quiescence

Mastej, Victoria¹; Axen, Cassondra¹; Wary, Anita¹; Minshall, Richard, D¹; Wary, Kishore¹

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

- Mature endothelial cells (ECs) are metabolically active, but live in a quiescent state.
- In quiescent ECs, Krüppel-like factors (KLFs) -2 and -4 are highly expressed.
- The role of KLF4 as it relates to EC quiescence is not clearly understood.

3040 Inflammation upregulates Signal Transducer and Activator of Transcription 5A (STAT5) and Telomerase Reverse Transcriptase (TERT) in Aortic Valve Cells

Cuevas, Rolando, A¹; Chu, Claire, C¹; Wong, Ryan¹; Crane, Alex¹; Sembrat, John¹; Sultan, Ibrahim¹; St Hilaire, Cynthia¹

1. University of Pittsburgh, Pittsburgh, USA

- The osteogenic transition of a healthy aortic valve cell into a calcific state remains ill-defined.
- Osteogenic reprogramming requires a delicate cross-talk between transcription factors and co-factors
- Inflammation is an important driver of calcific aortic valve disease.

3041 Defining a Factor-induced signaling signature for EC tubulogenesis, sprouting behavior, and pericyte recruitment using ECs expressing oncogenic activating mutations

Lin, Prisca, K¹; Sun, Zheyang¹; Kemp, Scott, S¹; Davis, George, E¹

1. University of South Florida, Tampa, Florida, USA

- The three capillary formation steps are EC sprouting, tubulogenesis, and pericyte recruitment

- k-Ras, Akt1, and Mek1 are lumen signals; Jak2, Stat3, Mek1, PIK3CA, and Rheb are sprouting signals
- EC signals affect not only EC morphology but also pericyte recruitment

POSTERS: METABOLISM

3042 Long Non-Coding RNA LEENE Promotes Angiogenesis and Ischemic Recovery

Tang, Xiaofang¹; Luo, Yingjun¹; Yuan, Dongqiang¹; Calandrelli, Riccardo²; Malhi, Naseeb¹; Sriram, Kiran¹; Miao, Yifei¹; Lou, Chih-Hong³; Tsark, Walter³; Tapia, Alonso⁴; Chen, Aleysha, T¹; Zhang, Guangyu¹; Roeth, Daniel⁵; Markus Kalkum, Markus⁵; Wang, Zhao¹; Chien, Shu²; Natarajan, Rama¹; Cooke, John P.⁶; Zhong, Sheng²; Chen, Zhen¹

1. Beckman institute, Duarte, California, USA
 2. Department of Bioengineering, La Jolla, California, USA
 3. Gene Editing and Viral Vector Core, Duarte, California, California, USA
 4. Irell and Manella Graduate School of Biological Sciences, Duarte, California, California, USA
 5. Department of Immunology, Duarte, California, California
 6. Department of Cardiovascular Sciences, Houston, Texas, USA
- lincRNA
 - peripheral arterial disease (PAD)
 - lncRNA in ECs function associated with PAD

3043 Elucidating the spatial transcriptome of Type 2 diabetic mesenteric arteries

Malhi, Naseeb¹; Luo, Yingjun¹; Tang, Xiaofang¹; Chen, Zhen¹

1. City of Hope, Duarte, California, USA
- scRNA sequencing reveals transcriptomic changes in multiple cell types in human mesenteric artery.
 - These transcriptomic changes can be anchored spatially using commercially available platforms.
 - Cellular composition changes with diabetic pathogenesis.

3044 Vascular Regulation by Super Enhancer-Derived LINC00607

Yuan, Dongqiang¹; Sriram, Kiran¹; Luo, Yingjun¹; Malhi, Naseeb¹; Chen, Zhen¹

1. City of Hope Comprehensive Cancer Center, Duarte, California, USA
- the transcriptomes regulated by LINC00607 in ECs and vascular smooth muscle cells (VSMCs).
 - LINC00607 is a vascular-enriched lncRNA expressed in ECs and VSMCs and is upregulated in diabetes
 - LINC00607 act as an integral regulator in the dysfunctional ECs

3045 Endothelial Regulation of Pancreatic Islet: Role of Endothelial AGO1 in β -Cell Function

Tapia, Alonso, A¹

1. City of Hope Irell and Manella Graduate School of Biological Sciences, Duarte, California, USA
- Islet EC-AGO1 plays a role in affecting islet related phenotypes during beta cell damage.
 - Endothelial AGO1 suppression promotes beta cell function in vitro and ex vivo.
 - Transcriptomic analysis of EC-AGO1-KO islets reveals EC and beta cell crosstalk.

3046 Adaptations of liver sinusoidal endothelial cells in obesity

Aizaim, Ibrahim¹; Skov, Frederik¹; Wu, Qi¹; Høst Dørflinger, Gry²; Fenton, Rob¹; Jessen, Niels³; Bjerre, Mette²; Kalucka, Joanna¹

1. Department of Biomedicine, Aarhus University, Aarhus, Denmark
 2. Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
 3. Steno Diabetes Center Aarhus, Aarhus University Hospital, Aarhus, Denmark
- LSECs exhibit a pro-inflammatory phenotype and altered bioenergetics in a murine model of NAFLD
 - LSECs expression of junctional proteins is disrupted in a murine model of NAFLD

- In mice with NAFLD, LSECs display enhanced fatty acid metabolism and oxidative phosphorylation

3047 Effects of obesity on angiogenesis and regenerative lung growth.

Hunyenyiwa, Tendai¹; Kyi, Priscilla¹; Matus, Kienna¹; Mammoto, Tadanori¹; Mammoto, Akiko¹

1. *Medical College of Wisconsin, Milwaukee, Wisconsin, USA*

- Angiogenesis is inhibited in a condition.
- Vascular and alveolar regeneration after pneumonectomy is inhibited in the obese mouse lungs.
- Obesity inhibits regenerative lung growth through adiponectin-VEGF signaling.

3048 Hyperglycemia-induced adaptation is associated with a metabolic shift, which is required for protection from the deleterious effects of high glucose

Serikbaeva, Anara¹; Lietuvninkas, Lina¹; Kazlauskas, Andrius¹

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

- Prolonged hyperglycemia induces adaptation in endothelial cells
- Glycolysis is associated with hyperglycemia-induced mitochondria adaptation
- Metabolic shift in endothelial cells protects against high glucose-driven damage

3049 Microvessel metabolic preferences regulate cerebral blood vessel tone

Noterman-Soulinthavong, Maria, F¹; Harraz, Osama, F¹; Nelson, Mark, T¹

1. *University of Vermont, Burlington, VT, USA*

- Myogenic tone is influenced by vascular cell fuel sources.
- A mouse model of human small vessel disease has deficits in glycolysis.
- Endothelial cell Kir2.1 electrical activity may be regulated by glycolysis.

POSTERS: LYMPHATIC BIOLOGY

3050 Defining the Role of Lztr1 in the Murine Lymphatic Endothelium

Largoza, Gabrielle, E¹; Devine, Patrick, W²; Wythe, Joshua, D¹

1. *Baylor College of Medicine, Houston, Texas, USA*

2. *Genomic Medicine Laboratory, University of California, San Francisco, California, USA*

- Non-immune hydrops fetalis is a life-threatening disease identified by pathological fluid overload
- 1/3 of NIHF cases present with mutations in genes encoding proteins present in the RAS-MAPK pathway
- We seek to know how LZTR1 regulates RAS-MAPK signaling to better our understanding of NIHF etiology

3051 A potential role of ZEB1 in ischaemic lymphangiogenesis

Tabrizi, Zarah, B¹; Mok, Heunglam¹; Horder, Joseph, L¹; Green, Kathryn, R¹; Bhalla, Sohni, R¹;

Wahid, Mussarat¹; Beazley-Long, Nicholas¹; Bates, David, O¹; Benest, Andrew, V¹

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

- ZEB1 is dynamically regulated in lymphatic endothelial cells
- Ischaemic hindlimb does not appear to induce lymphangiogenesis
- Loss of ZEB1 promotes lymphatic vessel growth in skeletal muscle

3052 Lymphoangiocrine signals vs. lymphangiogenesis in cardiac repair

Liu, Xiaolei¹; Bhalla, Sohni Ria¹; Ma, Wanshu¹; Oliver, Guillermo¹

1. *Northwestern University, Chicago, Illinois, USA*

- Reln conditional null mice have impaired cardiac function post-MI.
- VEGFC-promoted cardiac lymphangiogenesis in the infarcted heart improves cardiac function after MI.
- We will assess whether Vegfc-improved cardiac function is mainly promoted by lymphatic derived Reln.

3053 Identifying the cytokine drivers of recurrent lymphangiogenesis

Majumder, Ahana¹; Paulson, Jacob¹; Crow, Mason¹; Budden, Zachary¹; Fink, Darci, M¹

1. *South Dakota State University, Brookings, South Dakota, USA*

- Recurrent lymphangiogenesis is not VEGF-C dependent
- FGF-2, PDGF-BB and VEGF-C are sufficient to drive recurrent lymphangiogenesis
- Blocking PDGF-BB and FGF-2 can affect lymphangiogenesis during suture-induced recurrent inflammation

3054 Loss of primary cilia protein IFT20 impairs lymphatic vessel function and disrupts VE-cadherin expression on mature lymphatics

Paulson, Delayna¹; Lehmann, Zachary¹; Majumder, Ahana¹; Knutson, Luke¹; Pazour, Gregory²; Fink, Darci¹

1. *South Dakota State University, Brookings, South Dakota, USA*

2. *University of Massachusetts Medical School, Worcester, Massachusetts, USA*

- lymphatic endothelial primary cilia and IFT20
- inflammation-induced lymphangiogenesis
- flow sensing

3055 Clodronate depletion of macrophages prevents corneal lymph-/hemangiogenesis during both initial and recurrent inflammation and may modulate corneal lymphatic regression

Paulson, Jacob, T¹; Crow, Mason, J¹; Majumder, Ahana¹; Budden, Zachary¹

1. *South Dakota State University, Brookings, South Dakota, USA*

- Clodronate liposomes can successfully deplete macrophages in the cornea
- Depletion of macrophages during initial or recurrent inflammation decreases lymphangiogenesis
- Macrophage involvement in lymphatic vessel regression

3056 Button and Zipper-like Junctions between Lymphatic Endothelial Cells

Baluk, Peter¹; McDonald, Donald, M¹

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

- Lymphatics
- Endothelial cell junctions
- Plasticity

3057 Characterizing the Lymphatic Response to Osmotic Edema in the Zebrafish

Olayinka, Olamide, S¹; Ryu, Hannah¹; Malik, Asrar¹; Jung, Hyun min¹

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

- Developed a reproducible osmotic edema model in the zebrafish
- Characterized the lymphatic response to edema using the osmotic edema model
- Identify novel factors modulating edema-induced lymphangiogenesis in zebrafish

3058 A specific requirement for physical interaction between EPHB4 and RASA1 for the development and function of lymphatic vessel valves

Chen, Di¹; Davis, Michael, J²; King, Philip, D¹

1. *University of Michigan Medical School, Ann Arbor, Michigan, USA*

2. *University of Missouri, Columbia, Missouri, USA*

- EPHB4 and RASA1 act together to restrict Ras-MAPK activation in the blood and lymphatic vasculatures
- EPHB4-RASA1 control of Ras-MAPK activation is essential for vascular development and function
- EPHB4-RASA1 binding is specifically required for lymphatic vessel valve development and function

3059 RICTOR, a key component for mTOR complex 2 (mTORC2) is required for lymphatic valve formation and maintenance

Yang, Ying¹; Banerjee, Richa¹; Knauer, Luz¹

1. *University of South Florida, Tampa, Florida, USA*

- Genetic deletion of Rictor in lymphatic endothelial cells results in loss of valves.
- Rictor regulates flow response in lymphatic endothelial cells through AKT.
- The RICTOR-AKT signaling is essential for lymphatic valve formation.

3060 Piezo1 Activates Lymphatic Sprouting through the Orai1-Controlled Notch Downregulation Mechanism in Response to Fluid Flow

Choi, Dongon¹; Park, Eunkyung¹; Baluk, Peter²; McDonald, Donald²; Huang, Alex³; Wong, Alex⁴;

Hong, Young-Kwon¹

1. *USC, Los Angeles, California, USA*

2. *UCSF, San Francisco, California, USA*

3. *UCSD, San Diego, California, USA*

4. *City of Hope, Duarte, California, USA*

- We identified Piezo1 as the Orai1 upstream mechanosensor in lymphatics in response to fluid flow.
- Piezo1 is required for normal lymphatic development and function.
- Genetic or pharmacological stimulation of Piezo1 resulted in robust lymphatic sprouting.

POSTERS: IMMUNE-VASCULAR CROSSTALK FOR CANCER THERAPY

3061 The role of CD93 in endothelial activation and immune cell infiltration in glioma

de Alves Pereira, Beatriz¹; Vaccaro, Alessandra¹; van de Walle, Tiarne¹; Melssen, Marit, M¹; Hedlund, Marie¹; Barbera, Stefano¹; Lugano, Roberta¹; Dimberg, Anna¹

1. *Department of Immunology, Genetics and Pathology / Uppsala University, Uppsala, Sweden*

- Glioblastoma is a lethal cancer of poorly infiltrated nature, which limits access to new therapies.
- CD93 deficiency has been shown to delay tumor growth and improve survival in murine glioma models.
- CD93 may have a novel role in adhesion molecule expression and immune cell infiltration in glioma.

3062 PHGDH-mediated endothelial metabolism induces aberrant vascularity and drives tumor resistance to immunotherapy

Zhang, Duo¹; Fan, Yi¹

1. *Department of Radiation Oncology, University of Pennsylvania, Philadelphia, Pennsylvania, USA*

- Tumor microenvironmental stress and VEGF induce PHGDH expression in endothelial cells.
- PHGDH-mediated serine metabolism induces vascular aberrancy and tumor resistance to immunotherapy.
- PHGDH inhibition activates anti-tumor T cell immunity and sensitizes tumors to CAR-T cell therapy.

3063 Lymphatic system controls immune cell trafficking during carcinogenesis in a mouse model of breast adenocarcinoma

Nougué, Manon¹; Coulibaly, Ami-Marie¹; Draia-Nicolau, Tangra¹; Pujol, Françoise¹; Karaman, Sinem²;

Morfoisse, Florent¹; Prats, Anne-Catherine¹; Alitalo, Kari²; Garmy-Susini, Barbara¹

1. *I2MC, Toulouse, France*

2. *Wihuri Research Institute and Translational Cancer Medicine Program, Helsinki, Finland*

- Lymphatic system controls immune cell trafficking during carcinogenesis
- Overexpression of VEGF-C in tumor surrounding adipose tissue induces an immune switch
- Lymphatic system regulates differently early and late stages of breast carcinogenesis

3064 Modulation of Nr2f2 reprograms tumor blood endothelium to enhance anti-tumor immunity and immunotherapy

Zhu, Yu¹

1. Stanford University, Palo Alto, California, USA

- Ectopic Nr2f2 expression in tumor endothelial cells (ECs) drives capillary-to-venule reprogramming
- Ectopic Nr2f2 expression in tumor ECs enhances recruitment of anti-tumor T cell recruitment
- EC reprogramming sensitizes adoptive T cell transfer therapy and checkpoint-based immunotherapy

3065 Exploring the Role of Lymphatic Endothelial Cells in T cell Activation and Memory Formation

Swartz, Melody¹; Mateos Salles, Calixto¹

1. U Chicago Pritzker School for Molecular Engineering, Chicago, Illinois, USA

- Memory T cell development in cancer and disease.
- Lymphatic endothelial cell interactions with naive T cells at different cytokine environments.
- Possible activation targets for adoptive T cell therapies and CAR T cells.

3066 Regulation of T cell function by endothelial cells in glioma

Melssen, Marit¹; He, Liqun¹; de Alves Pereira, Beatriz¹; van de Walle, Tiarne¹; Hedlund, Marie¹; Pietilä, Ilkka¹; Betsholtz, Christer¹; Lugano, Roberta¹; Dimberg, Anna¹

1. Uppsala University, Uppsala, Sweden

- Subclustering of glioma-associated endothelial cells by single cell RNA sequencing.
- T cell localization relative to blood vessels with distinct phenotypic characteristics.
- Direct or indirect inhibition of T cell function by endothelial cells.

POSTERS: LEUKOCYTE TRANSENDOTHELIAL MIGRATION

3067 Neutrophils prime the endothelium to promote CD8+ T cell transendothelial migration in a chemokine-dependent manner

Grönloh, Max¹; van Maanen, Tatum¹; Palacios Martínez, Sebastián¹; Kuijpers, Taco²; van Buul, Jaap¹

1. Amsterdam UMC, Amsterdam, Noord-Holland, Netherlands

- Neutrophil transmigration primes the endothelium to promote CD8+ T cell paracellular TEM.
- Neutrophil adhesion results in local CXCL12 production by the endothelium.
- CXCL12 drives CD8+ T cell, but not subsequent CD4+ T cell, monocyte or neutrophil adhesion.

3068 Mechanosensitive ion channel Piezo1 is required for hydrodynamic force-induced monocyte cell spreading on VCAM-1.

Ibrahim, Hisham¹; Hyduk, Sharon, J¹; Cybalsky, Myron, I¹

1. Toronto General Hospital Research Institute, University Health Network, Toronto, Ontario, Canada

- Monocyte spreading on a VCAM-1-coated surface is triggered by an external hydrodynamic force (HF).
- Extracellular ion influx is critical for integrin-mediated monocyte spreading in response to HF.
- Integrin-mediated, HF-induced monocyte spreading requires the mechanosensitive ion channel Piezo1.

3069 α -Catenin undergoes tension-induced conformational changes during transendothelial migration of neutrophils

van der Meer, Werner, J¹; Grönloh, Max¹; van Buul, Jaap¹

1. University of Amsterdam / Sanquin Amsterdam / Amsterdam UMC, Amsterdam, Netherlands

- Neutrophils transendothelial migration induces phosphorylation of non-muscle myosin 2
- Myosin contractility leads to tension on the cadherin-catenin complex

- Tension on the cadherin-catenin complex leads to a conformational change in alfa-catenin.

POSTERS: VASCULATURE IN THE INFLAMMATORY RESPONSE

3070 Protective role of the endothelial pluripotency factor OCT4 in pathological angiogenesis

Shin, Junchul¹; Tkachenko, Svyatoslav²; Cherepanova, Olga, A¹

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

2. Case Western Reserve University, Cleveland, Ohio, USA

- The pluripotency factor OCT4-signaling in endothelial cells is athero-protective.
- Loss of OCT4 results in pathological angiogenesis in atherosclerosis and after vascular injury.
- OCT4-deficient endothelial cells express higher levels of proinflammatory cytokines, including MCP1.

3071 Single cell RNA-seq study reveals LSEC drives liver sinusoid capillarization through Collagen 4 deposition and inflammatory macrophages in fibrotic mouse liver

Cao, Sheng¹

1. Mayo Clinic, Rochester, Minnesota, USA

- Liver endothelial cells
- Single cell RNA-seq
- liver sinusoid capillarization and inflammatory macrophages

3072 Some vasculo-toxic BCR-ABL kinase inhibitors used for CML increase endothelial adhesion molecular expression and vascular leukocyte trafficking

Stepanian, Alec¹; Lu, Qing¹; Travers, Richard, J¹; Jaffe, Iris, Z¹

1. Molecular Cardiology Research Institute, Tufts Medical Center, Boston, Massachusetts, USA

- Some vasculo-toxic chemotherapeutics increase expression of leukocyte adhesion molecules in vitro
- Mass spectrometry can be used to determine accurate chemotherapy dosing in mice
- Some vasculo-toxic CML TKIs increase the number of rolling cells measured by intravital microscopy

3073 Endothelial RIPK3 plays a protective role in intestinal ischemia-reperfusion injury

Johnson, Charmain, F¹; Burge, Kathryn, Y²; Chaaban, Hala²; Griffin, Courtney, T¹

1. Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA

2. University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA

- Endothelial RIPK3 plays a protective role in ischemia-reperfusion injury induced permeability
- Endothelial RIPK3 and adhesion molecule expression
- Endothelial RIPK3 and regulation of serum cytokines

3074 Organotypic regulation of the endothelial transcription factor ERG impacts pulmonary inflammation response

Schafer, Chris, M¹; Martin-Almedina, Silvia²; Kurylowicz, Kataryzna³; Birdsey, Graeme, M⁴; Randi, Anna, M⁴;

Griffin, Courtney, T¹

1. Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA

2. Molecular and Clinical Sciences Institute, St. George's University, London, United Kingdom of Great Britain and Northern Ireland

3. University of Chicago, Chicago, Illinois, USA

4. National Heart and Lung Institute, Imperial College, London, United Kingdom of Great Britain and Northern Ireland

- The transcription factor ERG is downregulated in the lung, but not other organs, during inflammation
- The cytokine TNF α promotes the ubiquitination and degradation of ERG
- ERG downregulation represses Tek/TIE2 expression and destabilizes the pulmonary vasculature

3075 A dual role for Notch signaling in control of segment-specific hemostatic and inflammatory properties of vascular endothelium

Pan, Junliang¹; Bi, Yuhan²; Butcher, Eugene, C²; Xiang, Menglan²; Brulois, Kevin²; Zhu, Yu²; Ocon, Borja²

1. Palo Alto Veterans Institute for Research, Palo Alto, California, USA
2. Stanford University, Palo Alto, California, USA

- scRNA-seq profiling uncovers vascular segment-specific hemostatic and inflammatory properties
- Notch signaling promotes anticoagulant TM and restrains procoagulant & proinflammatory determinants.
- EC-deletion of Rbpj decreases TM expression while increasing procoagulants, and causes thrombosis.

3076 Microfluidic 3D human lymphatic vessel model for analyzing dendritic cell chemotaxis

Jeon, Noo Li¹; Jo, Hyeonsu¹; Lee, Somin¹; Park, Inae²; Doh, Junsang¹

1. Seoul National University, Seoul, Korea (Republic of)
2. Pohang University of Science and Technology, Pohang, Korea (Republic of)

- Recapitulating blind-ended characteristics of an initial lymphatic vessel using a specific method
- Establishing lymphatic vessel and dendritic cell co-culture model using injection-molded chip
- Enable high-throughput analysis of chemotactic migration of dendritic cell during inflammation

3077 Development of a Humanized In Vitro Vascular Model to Study Hypercytokinemia and Endothelial Dysfunction in SARS-CoV-2 Infection

Hatch, Christopher¹; Piombo, Sebastian¹; Fang, Jennifer¹; Gach, Johannes¹; Ewald, Makena¹; Van Trigt, William¹; Coon, Brian²; Forthal, Donald¹; Hughes, Christopher¹

1. UC Irvine, Irvine, California, USA
2. Yale Cardiovascular Research Center, Dept of Medicine, Yale University, New Haven, CT, USA

- Development of a microphysiological system to study SARS-CoV-2 endothelial infectivity
- ACE2 expression is modulated by fluid flow and is required to model SARS-CoV-2 infection
- An increase in Angiotensin II leads to EC dysfunction and an increase in inflammation

3078 Endothelial PARs Control Hepatic Vascular Permeability During APAP Overdose

Rajala, Rahul¹; Griffin, Courtney, T²

1. University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA
2. Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA

- Acetaminophen Overdose Results in Hepatic Sinusoidal Hemorrhage
- Endothelial PARs Regulate Vascular Permeability
- Novel Roles for Endothelial PAR4

3079 Macrophages contribute to vascular maturation and pruning important for tissue normalization during healing of ischemic injuries

Testini, Chiara¹; Herrera-Hidalgo, Carmen¹; Xu, Feifei¹; Parv, Kristel¹; Phillipson, Mia¹

1. Uppsala University, Uppsala, Sweden

- Macrophage depletion impairs vascular maturation and pruning during healing of ischemic injuries.
- Specific sub-cluster of M2 macrophages have distinct roles in vascular normalization post-ischemia.
- Macrophage functions can be utilized to enhance tissue recovery following ischemic injury.

POSTERS: PATHOPHYSIOLOGY OF VASCULAR DISEASE

3080 Vascular Ehlers-Danlos Syndrome cell-derived-matrix elucidates role of COL3A1 mutations in ECM mechanics

Doherty, Elizabeth, L¹; Aw, Wen Yih¹; Warren, Emily, C¹; Krohn, Grace, A¹; Howell, Stefanie²; Diekman, Brian¹; Nia, Hadi, T³; Hickey, Anthony, J²; Polacheck, William, J¹

1. Biomedical Engineering, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
2. Catalyst for Rare Diseases, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

3. *Biomedical Engineering, Boston University, Boston, Massachusetts, USA*

- Collagen III plays a key role in the mechanical properties of ECM.
- ECM derived from cells with COL3A1 mutations is distinct in structure, composition, and mechanics.
- The type of pathogenic variants in COL3A1 contributes to the mechanical properties of the ECM.

3081 NOTCH3 active immunotherapy reduces NOTCH3 deposition in brain capillaries in a CADASIL mouse model

Oliveira, Daniel, V²; Coupland, Kirsten, G¹; Shao, Wenchao³; Jin, Shaobo³; Del Gaudio, Francesca¹ Wang, Sailan¹; Fox MPhil, Rhys¹; Rutten, Julie, W⁴; Sandin, Johan³; Zetterberg, Henrik⁵; Lundkvist, Johan⁶; J. Lesnik Oberstein, Saskia, A⁴; Lendahl, Urban¹; Karlström, Helena³

1. *Dept of Cell and Molecular Biology, Karolinska Institutet, Stockholm, Sweden*
2. *Dept of Cell Biology, Charles University, Prague, Czechia*
3. *Dept of Neurobiology, Care Sciences and Society, Karolinska Institutet, Stockholm, Sweden*
4. *Dept of Clinical Genetics, Leiden University Medical Center, Leiden, Netherlands*
5. *Dept of Psychiatry and Neurochemistry, Sahlgrenska Academy, Gotheburg, Sweden*
6. *Alzecure Pharma, Huddinge, Sweden*

- Active immunization reduces NOTCH3 ECD deposition around brain capillaries in a CADASIL mouse model
- The number of activated microglia is increased in CADASIL-vaccinated mice.
- Targeting NOTCH3 deposits is an efficacious and tolerable therapeutic strategy for CADASIL therapy.

3082 Characterization of an ANGPTL6 variant predisposing to intracranial aneurysm formation

Vion, Anne-Clémence¹; Fréneau, Milène²; Baron-Menguy, Céline²; L'allinec, Vincent²; Mrad, Mary-Adel²; Rio, Marc²; Loirand, Gervaise²

1. *Institut du Thorax - INSERM UMR1087, Nantes, France*
2. *Nantes Université, CHU Nantes, CNRS, INSERM, l'institut du thorax, Nantes, France*

- A rare variant of the ANGPTL6 gene predisposes to intracranial aneurysm
- Mice expressing the ANGPTL6 variant present anomalies of the cerebrale arteries.
- ANGPTL6 participates to smooth muscle cells adhesion and function

3083 Imaging cerebral arteries by transcranial Doppler is a reliable assessment of brain aneurysm in mouse models and reveal a role of platelets in aneurysm formation

Lebas, Héloïse¹; Maupu, Clémence¹; Boutigny, Alexandre¹; Salfati, Jonas¹; Orset, Cyrille²; Porteu, Françoise³; Mazighi, Mikael⁴; Bonnin, Philippe⁵; Boulaftali, Yacine¹

1. *Institut National de la Santé et de la Recherche Médicale, Paris, France*
2. *Institut National de la Santé et de la Recherche Médicale, Caen, France*
3. *INSERM U1170, Cancer Campus Gustave Roussy, Villejuif, France*
4. *Fondation Rothschild, Paris, France*
5. *Hôpital Lariboisière, Paris France*

- Arterial tortuosity observed on Doppler imaging is correlated to the presence of a brain aneurysm
- High tortuosity grade is associated to decreased blood flow velocities and greater artery dilation
- Thrombocytopenic mice display a lower tortuosity grade revealing a deleterious role of platelets

3084 Platelet activation participates to elastin degradation and intracranial aneurysm rupture in mice

Maupu, Clémence¹; Lebas, Héloïse¹; Salfati, Jonas¹; Boutigny, Alexandre¹; Casari, Caterina¹; Fletcher, Craig²; Ware, Jerry³; Loyau, Stéphane¹; Bouton, Marie-Christine¹; Arocas, Véronique¹; Bonnin, Philippe¹; Boulaftali, Yacine¹

1. *Institut National de la Santé et la Recherche Médicale, Paris, France*
2. *Department of Pathology and Laboratory Medicine, Chapel Hill, North Carolina, USA*
3. *University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA*

- Platelets are in a preactivated state and platelet-leukocyte aggregates are found in brain aneurysm

- Platelet adhesion mediated by the GPIIb/3a/ von Willebrand factor axis is beneficial in brain aneurysm
- Platelet CXCL4 play an instrumental role in aneurysm formation and rupture

3085 Analyzing the role of junctional proteins for Schlemm's canal development and function

Mishra, Sarthak¹; Shirakura, Keisuke¹; Ipe, Ute¹; Nottebaum, Astrid¹; Vestweber, Dietmar¹

1. Max Planck Institute for Molecular Biomedicine, Muenster, NRW, Germany

- Role of highly stabilized endothelial junctions on Schlemms canal (SC) structure and function.
- Highly stabilized junctions impaired the development and maintenance of SC .
- Highly stabilized junctional SC phenotype might be associated with an early onset of glaucoma.

3086 Sox17 deficiency promotes pulmonary arterial hypertension via HGF/c-Met signaling

Park, Chan Soon¹; Yang, Hae Young²; Park, HyeonJin²; Lee, Eunhyeong²; Kim, Ju-Hee²; Cho, Ye Seul¹;

Kang, Hyejeong¹; Lee, Seung-Pyo¹; Park, Jun-Bean¹; Kim, Injune²

1. Seoul National University Hospital, Seoul, Korea (Republic of)

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

- Sox17 deficiency and hypoxia jointly induce long-lasting PAH with high penetrance in mice.
- Hepatocyte grow factor (HGF), a ligand of c-Met, was upregulated in Sox17-deficient lung ECs.
- Pharmacologic inhibition of HGF/c-Met signaling attenuated and reversed the features of PAH.

3087 Claudin-17 deficiency in mice results in vascular permeability, fluid-electrolyte imbalance, and oxidative stress leading to lung injury

Adil, Mir, S¹; Parvathagiri, Varun¹; Narayanan, Subhadra, P¹; Somanath Shenoy, Payaningal, R¹

1. University of Georgia, Augusta, Georgia, USA

- Claudin-17 deficiency disrupts endothelia-barrier in vitro and causes vascular permeability in mice
- Lack of claudin-17 results in ion/electrolyte imbalance, ROS generation, and lung injury in mice
- Claudin-17 deficient mice exhibit endothelial dysfunction and inflammation in the lungs

3088 ENDOTHELIAL CELLS AGGRAVATE CALCIPROTEIN PARTICLE-INDUCED VASCULAR SMOOTH MUSCLE CELL CALCIFICATION VIA PARACRINE SIGNALLING

Feenstra, Lian¹; Zeper, Lara²; Chatre, Laurent³; Kuipers, Jeroen¹; Giepmans, Ben¹; Zuidsherwoude, Malou²;

de Baaij, Jeroen²; Hoenderop, Joost²; Krenning, Guido¹; Hillebrands, Jan-Luuk¹

1. University of Groningen, University Medical Center Groningen, Groningen, Netherlands

2. Radboud University Medical Center, Nijmegen, Netherlands

3. CNRS, ISTCT, Normandie University, Caen, France

- CPP-induced EC-conditioned medium enhances VSMC calcification in a paracrine manner
- CPP activate EC and induce VSMC dedifferentiation
- Uptake of CPP by EC is considered a key factor in CPP-induced vascular calcification

3089 The onset of diabetes is associated with protection of retinal vessels from diabetes-related insult-induced death

Li, Yanliang¹; Serikbaeva, Anara¹; Kazlauskas, Andrius¹

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

- In early DM, retinal vessel is resistant to oxidative stress-induced death
- Changes in mitophagy and mitochondrial functionality are required for the acquisition of protection
- There is an endogenous system that protects from DM-induced damage to retinal vessel

3090 The role of KATP channel activation in lymphatic contractile dysfunction associated with metabolic disease

Kim, Hae Jin¹; Davis, Michael, J¹

1. University of Missouri, Columbia, Missouri, USA

- KATP channels in lymphatics are activated by metabolic stress, which inhibits lymphatic pumping.

- Lymphatics from diabetic animals showed contractile dysfunction and were rescued by glibenclamide.
- KATP channels are a therapeutic target to treat lymphedema associated with metabolic disorders.

3091 Inflammatory and immune response of engineered 3D human brain microvessels to plasmodium falciparum binding

Howard, Caitlin¹; Joof, Fatou²; Smith, Joseph²; Zheng, Ying¹

1. *University of Washington, Seattle, WA, USA*

2. *Seattle Childrens' Research Institute, Seattle, WA, USA*

- We used 3D engineered microvessels to study endothelial inflammatory response to parasite binding.
- We showed different stimulatory role for brain endos by thrombin, TNF α , and cytoadherence of IEs.
- IEs binding upregulated endothelial inflammatory pathways, and recruited leukocytes heterogeneously.

3092 Inflammatory potential of aortic valve interstitial cells is regulated by estrogen in a sex-specific manner

Scott, Ashley, J¹; Masters, Kristyn¹

1. *University of Wisconsin, Madison, Wisconsin, USA*

- Sexual dimorphic features in aortic stenosis may be regulated by sex hormones
- Sex hormones can regulate pathological behaviors in aortic valve cells
- Estrogen may protect against valve cell inflammation in females

3093 A new aneurysm rupture mouse model caused by a FBN1Q2467X nonsense mutation associated with Marfan Syndrome: comparing pathobiological processes between Marfan patients and mouse models

Wu, Shichao¹; Zhao, Jiawei¹; Xie, Daniel²; Ponce, Alejandro¹; Ju, Donghong¹; Pham, Lucynda¹; Li, Claire³; Chung, Charles¹; Komnenov, Dragana¹; Rossi, Noreen¹; Hao, Weilong¹; Xie, Youming¹; Li, Li¹

1. *Wayne State University, Detroit, Michigan, USA*

2. *University of Minnesota, Minneapolis/St. Paul, Minnesota, USA*

3. *Cornell University, Ithaca, NY, USA*

- A new aneurysm rupture mouse model caused by a Fbn1Q2467X nonsense mutation in Marfan Syndrome.
- The mouse model develops the thoracic aorta aneurysm processing from early-stage to rupture rapidly.
- The comparison of Fbn1Q2469X/Q2469X mice and the two existing mouse models with those in patients

POSTERS: -OMICS

3094 Tissue vesiculomics identifies conserved and divergent modulators of cardiovascular calcification

Blaser, Mark, C¹; Buffolo, Fabrizio¹; Halu, Arda¹; Turner, Mandy, E¹; Schlotter, Florian¹; Higashi, Hideyuki¹; Kuraoka, Shiori¹; Pham, Tan¹; Vromman, Amelie¹; Camussi, Giovanni²; Robson, Simon³; Body, Simon, C⁴; Kaneko, Tsuyoshi¹; Muehlschlegel, Jochen, D¹; Singh, Sasha, A1; Aikawa, Masanori¹; Aikawa, Elena¹

1. *Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA*

2. *University of Torino, Turin, Italy*

3. *Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA*

4. *Boston University School of Medicine, Boston, Massachusetts, USA*

- Under 50% of patients develop vascular & valvular calcification, implying differential pathogenesis.

- This 1st omics study of human arteries & valves links extracellular vesicles (EVs) to both diseases.
- We reveal novel & divergent tissue-specific roles for EVs in mediating cardiovascular calcification.

3095 Defining the pathogenic mechanisms of calcific aortic valve disease through single-cell RNA-sequencing analysis

Villa-Roel, Nicolas¹; Park, Christian¹; Cornell, Abby²; Cho, Hannah²; Andueza, Aitor¹; Leshnower, Bradley³; Jo, Hanjoong¹

1. Georgia Institute of Technology & Emory University, Atlanta, Georgia, USA
2. Georgia Institute of Technology, Atlanta, Georgia, USA
3. Emory University Hospital, Atlanta, Georgia, USA

- Single-cell RNA-seq of human AVs reveals 27 individual cell clusters with age-dependent proportions
- Side-dependent expression of various transcription factors indicates potential mechanisms for CAVD
- Gene ontology and cell-cell interaction analyses point to new roles for each identified cell cluster

3096 Targeted proteomics of endothelium-related proteins in plasma of young and aging mice in endotoxemia; a role of endothelial Nrf2-dependent pathway.

Suraj-Prażmowska, Joanna¹; Sternak, Magdalena¹; Kurpińska, Anna¹; Bar, Anna¹; Mateuszuk, Łukasz¹; Buczek, Elżbieta¹; Sitek, Barbara¹; Chlopicki, Stefan¹

1. Jagiellonian Centre for Experimental Therapeutics, Jagiellonian University, Krakow, Poland

- LC/MS-MRM method enables to characterize changes in endothelial function in endotoxemia development.
- Multi-marker approach appears to be a useful tool for understanding age-related changes in vessels.
- Endothelial Nrf2-dependent pathway may have an impact on LPS-induced endothelial dysfunction.

3097 Characterization of CD157 positive endothelial cells at the single-cell resolution.

Iba, Tomohiro¹; Naito, Hisamichi¹

1. Kanazawa University School of Medicine, Kanazawa, Ishikawa, Japan

- We identified unique mRNA expressing EC clusters at the single-cell resolution among several organs.
- These EC clusters show the characteristics related to highly proliferative ECs.
- These ECs are distinguished by using IHC techniques in vivo.

3098 Using Phosphoproteomics to Identify Drugs to Mitigate VEGFR Inhibitor-Induced Endothelial Cell Dysfunction and Hypertension

Camarda, Nicholas, D¹; Man, Joshua¹; Lu, Qing¹; Gopal, Srila¹; Baur, Wendy¹; Martin, Greg¹; Litichevskiy, Lev²; Lopez, Katie²; Biwer, Lauren¹; Travers, Richard¹; Stepanian, Alec¹; Ibarrola, Jaime¹; Yang, Vicky³; Jaffe, Jacob, D²; Jaffe, Iris, Z¹

1. Tufts Medical Center, Boston, Massachusetts, USA
2. Broad Institute, Cambridge, Massachusetts, USA
3. Cummings Veterinary Medical Center, Grafton, Massachusetts, USA

- VEGFR inhibitors improve human and canine cancer survival but cause EC dysfunction and HTN.
- Identified a phospho-signature of VEGFRi-induced EC toxicity, alpha1 blockers reverse this best.
- In vitro, the alpha blocker doxazosin prevented sunitinib- and sorafenib-induced EC dysfunction.

3099 scRNA-sequencing of endothelial cells during salivary gland fibrosis and regeneration

Altrieth, Amber¹; Nelson, Deirdre¹; Majka, Gabriella¹; Larsen, Melinda¹

1. University at Albany, Albany, New York, USA

- Changes in gene expression of endothelial cells during ductal ligation induced fibrosis.

- Endothelial cell gene expression following recovery from ductal ligation injury.
- Examining signaling pathways enriched during salivary gland injury and recovery.

3100 Chronic loss of ERG in endothelial cells increases inflammatory response and extracellular matrix reorganization.

Golebiewski, Anna¹; Tran, Binh¹; Tzu-Pin, Shentu²; Whalen, Michael¹; Adelus, Maria¹; Stolze, Joey¹; Fang, Yun²; Romanoski, Casey¹

1. University of Arizona, Tucson, Arizona, USA

2. The University of Chicago, Chicago, Illinois, USA

- ERG KO induces enriched ECM organization, cell junction organization, and cell adhesion.
- ERG-knockout enhances TGF- β signaling in disturbed flow compared to unidirectional flow.
- ERG has an athero-protective role in HAECs by maintaining endothelial homeostasis.

3101 Withdrawn

POSTERS: HETEROGENEITY OF VASCULAR AND IMMUNE CELLS

3102 Molecular atlas of the human brain vasculature across development, adulthood and disease at the single-cell level

Ghobrial, Moheb¹

1. ETH, University Hospital of Zurich, Schwerzenbach, Switzerland

- Constructing a single-cell atlas of the human brain vasculature in development, adulthood & disease.
- Addressing inter-tissue heterogeneity, AV-specification in brain vascular endothelial cells
- Loss of CNS-specificity, upregulation of MHC-II receptors in pathological ECs, key role in the NVU

3103 Multi-omics of circulating monocytes and plasma from SARS-CoV-2 infected individuals unveils mechanisms of immune regulation leading to major cardiovascular events in COVID-19

Matamalas, Joan T.¹; Chelvanambi, Sarvesh¹; Decano, Julius L.¹; Santinelli-Pestana, Diego V.¹; Yanagihara, Yoshihiro¹; Whelan, Mary C.¹; Aikawa, Elena¹; Aikawa, Masanori¹

1. Harvard Medical School, Boston, Massachusetts, USA

- Increased inflammatory response on COVID-19 patients that developed major cardiovascular events
- Heterogeneous immune response on COVID-19 patients who later developed cardiovascular outcomes
- Facilitate the prediction of COVID-19 patients who are at risk for developing cardiovascular events

3104 Ex vivo expansion of regulatory T cell and T helper 2 cells using a hematosphere culture

Shin, Hyecheon¹; Hur, Jin¹; Lee, Hyesook¹; Han, Junghwa¹; Kang, Yunjeong¹; Jeong, Roogam¹; Yoon, Aeseon¹; Shin, Joonhong¹; An, Kangbin¹; Oh, Jeongseon¹

1. Pusan National University School of Medicine, Yangsan, Korea (Republic of)

- T-reg and Th2 cell populations were greatly expanded during hematosphere culture.
- Secretion of Th2-related cytokines such as IL-5, IL-10, and IL-13 also increased.
- Human PBMCs derived blood-born hematosphere culture induces ex vivo expansion of T-reg and Th2.

3105 Tumor-Infiltrating Neutrophils and Non-Classical Monocytes as Potential Therapeutic Targets for HER2negative Gastric Cancer.

Kim, Duk Ki¹; Jeong, Juhee¹; Jung, Keehoon¹; Kong, Seong-Ho²; Park, Geon Woo¹

1. Seoul National University College of Medicine, Seoul, Korea (Republic of)

2. Seoul National University Hospital, Seoul, Korea (Republic of)

- Patients with HER2negative AGC receive limited clinical benefit from this treatment.

- Her2 negativity associates with tumor infiltration of neutrophils and non-classical monocytes.
- Neutrophils in gastric cancer highly express pro-angiogenic molecules.

POSTERS: VASCULAR DISEASES

3106 Blocking the β 1 adrenergic receptor prevents Cerebral Cavemous Malformations

Li, Wenging¹; Muccurdy, Sara¹; Shenkar, Robert²; Awad, Issam²; Ginsberg, Mark¹

1. Department of Medicine, University of California, San Diego, San Diego, California, USA

2. Department of Surgery, University of Chicago, Chicago, IL, USA

- adrb1 null zebrafish were completely protected from the CVP lesion and adult CCM.
- Metoprolol, a selective β 1 receptor antagonist resulted in a reduction in CCM lesion volume.
- Adrb1's essential role in CCM pathogenesis might be mediated by its effects on blood flow.

3107 Targeting DNA hypermethylation as a potential therapeutic strategy in pulmonary arterial hypertension

El Kabbout, Reem¹; Breuils Bonnet, Sandra¹; Martineau, Sandra¹; Bourgeois, Alice¹; Provencher, Steeve¹;

Boucherat, Olivier¹; Bonnet, Sébastien¹; Potus, Francois¹

1. CRIUCPQ, Quebec, Canada

- Increase DNA methylation is associated with pulmonary arterial hypertension
- Targeting DNA methylation could represent an attractive novel therapeutic strategy for PAH
- Epigenetic reprogramming of gene expression might contribute to vascular remodelling diseases

3108 Repurposing Narciclasine as potential therapeutic strategy in pulmonary arterial hypertension : An unbiased transcriptomic study.

Abi Sleimen, Antonella¹; Breuils-Bonnet, Sandra¹; Martineau, Sandra¹; Bourgeois, Alice¹; Boucherat, Olivier¹;

Provencher, Steeve¹; Bonnet, Sébastien¹; Potus, francois¹;

1. CRIUCPQ, Quebec, Canada

- Pharmaco-transcriptomic study identifies narciclasine as a drug candidate in PAH.
- reversing adverse transcriptomic reprogramming might improve adverse vascular remodeling in PAH
- Narciclasine treatment decreases PAH-PASMC pro-survival phenotype and improves oxidative metabolism.

3109 Intussusceptive capillary remodeling increases capillary density during post-ischemic muscle regeneration

Wirth, Galina¹; Korpisalo, Petra¹; Juusola, Greta¹; Laakkonen, Johanna²; Ylä-Herttuala, Seppo²

1. Heart Center, Kuopio University Hospital, Kuopio, Finland

2. University of Eastern Finland, Kuopio, Finland

- It is important to understand the dynamics of post-ischemic capillary responses.
- Acute hindlimb ischemia model used to study capillary dynamics during natural regeneration.
- Capillary enlargement and intussusception involved in the post-ischemic angiogenic response.

3110 Analysis of lung endotheliopathy in lethal mice infected with mouse-adapted SARS-CoV-2

Takeda, Ryo¹; Sawa, Hirofumi¹; Sasaki, Michihito¹; Orba, Yasuko¹; Maishi, Nako¹; Ito, Wataru¹; Teshirogi, Takahito¹;

Kitagawa, Yoshimasa¹; Hida, Yasuhiro²; Hida, Kyoko¹

1. Hokkaido University, Sapporo, Japan

2. Fujita Health University, Toyoake, Japan

- Mouse-adapted SARS-CoV-2 caused aggravation in aged mice
- Endothelial cells were isolated from the lungs of infected aged/young mice and subjected to RNA-seq
- Thrombogenesis-related molecules were up-regulated only in infected aged mice

3111 The ambiguous role of TRPM4 in myocardial infarction

Boukenna, Mey¹; Rougier, Jean-Sebastien¹; Aghagolzadeh, Parisa²; Pradervand, Sylvain³; Hämmerli, Anne-Flore¹; Guichard, Sabrina¹; Pedrazzini, Thierry⁴; Abriel, Hugues¹

1. Institute of Biochemistry and Molecular Medicine, University of Bern, Bern, Switzerland

2. Departement Biomedizin, University of Basel, Basel, Switzerland

3. Centre d'Oncologie de Précision, Département d'Oncologie, CHUV, Lausanne, Lausanne, Switzerland

4. Experimental Cardiology Unit, University of Lausanne, Lausanne, Switzerland

- Upon ischemia, endothelial cells are the first front and trigger a large inflammatory response.
- TRPM4 was shown to be involved in response to infection as well as stroke in endothelial cells.
- Here, we study the role of TRPM4 in endothelial and immune cells in myocardial infarction.

3112 zCldn5 is required for the functional integrity of the blood-neural barrier

Hwang, Su Jung¹; Song, Ye-Seul¹; Choi, Young Bin¹; Lee, Hyo-Jong¹

1. Sungkyunkwan University, Suwon, Gyeonggi-do, Korea (Republic of)

- zCldn5a is expressed in the brain surface, ventricular ependyma, and cerebral microvessels
- zCldn5a silencing induces BBB leakages and downregulates GLUT1 expression
- zCldn5a is required for building the blood-neural barrier during development

3113 The association between impairment of HDL cholesterol efflux capacity and the degree of aortic valvular calcification in patients with severe aortic stenosis

Funamizu, Takehiro¹; Iwata, Hiroshi¹; Moriya, Soshi¹; Koike, Takuma¹; Yasuda, Hidetoshi¹; Chikata, Yuichi¹; Doi, Shinichiro¹; Okazaki, Shinya¹; Daida, Hiroyuki¹; Minamino, Tohru¹

1. Juntendo University / Cardiovascular Biology and Medicine, Tokyo, Japan

- The associations between HDL cholesterol efflux capacity and the aortic valvular calcification
- We quantified three types of HDL-CECs (Global-, ABCA1-, and Non-ABCA1-CEC)
- Sex-specific contribution of reduced HDL-CEC to the pathophysiology in aortic valvular calcification

3114 Targeting Complex Extracranial Arterial Venous Malformation with MEK Inhibitor

Teng, Joyce, M¹; Do, Huy¹

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

- Targeted medical treatment for extracranial AVMs.
- disease modulating medical treatment that can be used alone or with surgical interventions.
- safety of the treatment is being evaluated as well.

3115 Fatty acid-binding proteins promote arterial programming

Liu, Bin¹; Li, Shuai¹; Yi, Dan¹; Pan, Jiakai¹; Li, Rebecca¹; Singh, Indrapal²; Sullivan, Ryan¹;

Kala, Mrinalini¹; Frye, Richard²; Fallon, Michael¹; Dai, Zhiyu¹

1. University of Arizona/Department of Internal Medicine, Phoenix, AZ, USA

2. University of Arizona/Department of Child Health, Phoenix, Arizona, USA

- Both FABP4 and 5 were highly induced in the ECs of EglN1Tie2Cre mice, human IPAH patients
- Deletion of Fabp4 and 5 in EglN1Tie2Cre mice exhibited a reduction of arterial gene programming.
- EglN1Tie2Cre/Fabp45^{-/-} mice were protected from pulmonary hypertension and right heart failure.

3117 Defective Ca²⁺- dependent activation of TRPM4 channels contributes to age-related cerebral small vessel disease in Col4a1 mutant mice

Yamasaki, Evan¹; Thakore, Pratih¹; Ali, Sher¹; Solano, Alfredo, S¹; Labelle-Dumais, Cassandre²; Wang, Xiaowei²; Gao, Xiao²; Chaumeil, Myriam, M²; Gould, Douglas, B²; Earley, Scott¹

1. University of Nevada, Reno School of Medicine, Reno, Nevada, USA

2. University of California, San Francisco School of Medicine, San Francisco, California, USA

- Mutations in collagen IV alpha 1 (COL4A1) cause cerebral small vessel disease (cSVD).
- Col4a1 mutant mice present hallmarks of cSVD associated with loss of myogenic vasoconstriction.
- Loss of myogenic vasoconstriction is due to disrupted SR Ca²⁺ signaling that impairs TRPM4 activity.

3118 PDE5A Inhibition Enhances Vascular Outward Remodeling and Changes Hemodynamic Profiles in Rat Arteriovenous Fistulas

Northrup, Hannah¹; Lee, Timmy²; Shiu, Yan-Ting¹

1. University of Utah, Salt Lake City, Utah, USA

2. University of Alabama at Birmingham, Birmingham, Alabama, USA

- Sildenafil treatment improves arteriovenous fistula remodeling in rats by increasing flow rate.
- The effect size of sildenafil treatment in rat arteriovenous fistula is heterogeneous.
- Sildenafil treatment may be a potential therapeutic for AVF maturation.

3119 Impaired endothelial Pannexin1-purinergic receptor signaling attenuates flow-induced dilation of pulmonary arteries in pulmonary hypertension

Daneva, Zdravka¹; Chen, Yen-Lin¹; Kuppusamy, Maniselvan¹; Sonkusare, Swapnil, K¹

1. University of Virginia, Charlottesville, Virginia, USA

- Endothelial TRPV4 channel activity is reduced in pulmonary arteries from a mouse model of PH.
- Flow/shear stress increase of ATP efflux via endothelial Pannexin1 channels is impaired in PH.
- ATP activation of endothelial TRPV4 channels via P2Y2 receptors activation is impaired in PH.

POSTERS: VASCULAR BEDS AND CELLS

3120 Dissecting vascular endothelial cell heterogeneity in skeletal muscle-specific endothelial cell-muscle stem cell culture models

Laurillard, Emily, J¹; Walter, Lauren, D¹; Cosgrove, Benjamin, D¹

1. Cornell University, Ithaca, New York, USA

- Muscle ECs are transcriptionally heterogeneous and relevant cell culture models are lacking.
- Muscle-specific ECs provided a unique benefit to MuSC self-renewal.
- Transcriptomic comparison of primary isolated ECs and tissue- and non-tissue-specific cultured ECs

3121 RAMP2-AS1 Regulates Endothelial Homeostasis and Aging

Lai, Chih-Hung²; Chen, Aleysha, T¹; Burns, Andrew, B¹; Sriram, Kiran¹; Luo, Yingjun¹; Tang, Xiaofang¹; Branciamore, Sergio¹; O'Meally, Denis³; Chang, Szu-Ling²; Huang, Po-Hsun⁴; Shyy, John⁵; Chien, Shu⁵; Rockne, Russell, C⁶; Bouman Chen, Zhen¹

1. Department of Diabetes Complications and Metabolism, City of Hope, Duarte, California, USA

2. Cardiovascular Center, Taichung Veterans General Hospital, Taichung, Taiwan

3. Center for Gene Therapy, City of Hope, Duarte, California, USA

4. Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan

5. Department of Medicine, University of California, San Diego, La Jolla, California, USA

6. Irell and Manella Graduate School of Biological Sciences, City of Hope, Duarte, California, USA

- PCA of transcriptome changes maps EC aging trajectory associated with pulsatile or oscillatory flow.
- RAMP2-AS1 knockdown suppresses RAMP2 activity, impairs angiogenesis, and promotes endothelial aging.
- Temporal analysis of EC transcriptome under different flow quantifies and uncovers EC aging factors.

3122 Single-Cell RNA-Seq Identifies Dynamic Cardiac Transition Program from Adipose Derived Cells Induced by Leukemia Inhibitory Factor

Zhang, LI¹; Yao, Jiay¹; Ma, Feiyang¹; Cai, XinJiang¹; Qiao, XiaoJing¹; Pellegrini, Matteo²; Yao, Yucheng¹; Boström, Kristina, I¹

1. Division of Cardiology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

2. Department of Molecular, Cell, Biology at UCLA, Los Angeles, California, USA

- stem cells
- Endothelial organ heterogeneity and stem cells
- Cardiovascular regenerative medicine

3123 Protein disulfide isomerase A3-based pharmacology regulates cross-talk between the endothelium and breast cancer cells

Stojak, Marta¹; Suraj-Prazmowska, Joanna¹; Kurpinska, Anna¹; Wojnar-Lason, Kamila¹; Milczarek, Magdalena²; Stachowicz-Suhs, Martyna²; Rossowska, Joanna²; Kalviņš, Ivars³; Wietrzyk, Joanna²; Chlopicki, Stefan¹

1. Jagiellonian Centre for Experimental Therapeutics (JCET), Krakow, Poland

2. Hirszfeld Institute of Immunology and Experimental Therapy, PAN, Wroclaw, Poland

3. Latvian Institute of Organic Synthesis, Riga, Latvia

- The inhibition of PDIA3 modulates breast cancer cell adhesion and transmigration
- The anti-adhesive effect of C-3399 is linked with integrin activation
- The inhibition of extracellular PDIA3 represents an interesting target for anti-metastatic treatment

3124 Akt3 activation by R-Ras stabilizes endothelium via intercellular crosstalk mediated by Jagged1-Notch

Herrera, Jose, L¹; Komatsu, Masanobu¹

1. Johns Hopkins University All Children's Hospital, St Petersburg, Florida, USA

- The endothelial Small GTPase R-Ras is involved in vascular stabilization
- Jagged1-Notch signaling between endothelial cells is important for vascular stabilization
- Akt3 is important to control endothelial cell migration, proliferation, and vessel stabilization.

3125 Detection of the transcription factors (TFs) possibly associating with the maintenance of Vascular Endothelial Stem Cells (V ESCs)

Konishi, Hirotaka¹

1. Research Institute for Microbial Diseases, Osaka University, Suita, Osaka, Japan

- We detected 10 TFs to induce the expression of CD157 which is V ESCs marker.
- 10 TFs overexpressed cells had a high capability of drug efflux which is shared among stem cells.
- Among 10 TFs, 6TFs were associated with drug efflux.

3126 Type VIII Collagen Mediates Dynamic Changes in Endothelial Cell Mechanotype During Inflammatory Endothelial-to-Mesenchymal Transition

Talapaneni, Sriharsha¹; Ly, Chau¹; Wong, Leela¹; Rowat, Amy¹; Demer, Linda, L¹; Tintut, Yin¹; Hsu, Jeffrey, J¹

1. UCLA, Los Angeles, California, USA

- TNF-alpha induces endothelial-to-mesenchymal transition in human aortic endothelial cells
- Endothelial cells undergoing EndMT experience a biphasic response in their cell stiffness
- Type VIII Collagen (COL8A1) may mediate the mechanical response of endothelial cells to TNF-alpha

3127 ERBB2 as a novel candidate gene for congenital heart defects affecting cardiomyocytes and endothelial cells

Ampuja, Minna¹; Selenius, Sabina¹; Paatero, Ilkka²; Ranta, Amanda¹; Chowdhury, Iftekhar³; Villman, Jenna²; Varjosalo, Markku³; Kivelä, Riikka⁴; Helle, Emmi⁵

1. University of Helsinki, Faculty of Medicine, Helsinki, Finland

2. Turku Bioscience Centre, University of Turku and Åbo Akademi University, Turku, Finland

3. Institute of Biotechnology, HiLIFE, University of Helsinki, Helsinki, Finland

4. University of Helsinki, Wihuri Research Institute, University of Jyväskylä, Jyväskylä, Finland

5. University of Helsinki, Pediatric Cardiology New Children's Hospital, Helsinki, Finland

- A potential disease-causing variant in ERBB2 gene found in congenital heart defect patients.
- ERBB2 gene mutation remodels gene expression in cardiomyocytes and endothelial cells.
- Zebrafish embryos expressing the mutant allele have compromised heart function.

3128 TRPM4 channels are required for myogenic tone in retinal arterioles

Alvarado, Michael, G¹; Sanchez Solano, Alfredo¹; Yamasaki, Evan¹; Thakore, Pratish¹; Earley, Scott¹

1. University of Nevada, Reno School of Medicine, RENO, Nevada, USA

- TRPM4 channels are expressed in smooth muscle cells of retinal arterioles.
- Retinal arterioles require TRPM4 channels to generate pressure-induced myogenic tone.
- Retinal arterioles may be used as a surrogate to study cerebral blood vessels.

POSTERS: VASCULATURE IN DISEASE II

3129 TNF α rewires cellular metabolism to support pro-inflammatory gene transcription via histone acetylation in human endothelial cells

*Boutagy, Nabil E. Boutagy^{1,2}; Fowler, Joseph W. Fowler^{1,2}; Grabinska, Kariona A.^{1,2}; Cardone, Rebecca¹; Sun, Qiushi¹; Whalen, Michael B.³; Martin, Kathleen A.^{1,2}; Kibbey, Richard G.¹; Romanoski, Casey E.³; Sessa, William C.^{*1,2}*

1. Yale University School of Medicine, New Haven, Connecticut, USA

2. Vascular Biology and Therapeutics Program, Yale University School of Medicine, New Haven, Connecticut, USA

3. Bioscience Research Laboratories, University of Arizona, College of Medicine, Tucson, Arizona, USA

- TNF α increases glucose oxidation and mitochondrial flux to support pro-inflammatory gene transcription in human endothelial cells.
- TNF α promotes mitochondrial flux of glucose carbon by inducing the degradation of pyruvate dehydrogenase kinase 4 protein (inhibitory of pyruvate dehydrogenase) via an NF κ B mechanism
- Elevated TNF α mediated mitochondrial flux mediates pro-inflammatory gene transcription via histone acetylation

3130 PD-L1-directed PIGF/VEGF blockade synergizes with chemotherapy by targeting CD141+ cancer-associated fibroblasts in pancreatic cancer

Kim, Duk Ki¹; Jeong, Juhee¹; Lee, Dong Sun²; Park, Geon Woo¹; Kim, Ho Min²; Jung, Keehoon¹

1. Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea (Republic of)

2. Center for Biomolecular and Cellular Structure, Institute for Basic Science, Daejeon, Korea (Republic of)

- Pancreatic ductal adenocarcinoma patients have poor prognosis and required new therapeutic approach
- Cancer associated fibroblasts (CAFs) are activated by PIGF to promote tumor fibrosis
- We developed Ate-Grab by fusing the single-chain Fv of atezolizumab to VEGF-Grab to target CAFs

3131 The role of Ackr3a in zebrafish cardiac lymphatic vessel growth

Feng, Xidi¹; Lien, Ching-ling¹; Harrision, Michael²

1. CHLA, Los Angeles, CA, USA

2. Cornell University, Ithaca, New York, USA

- Zebrafish has a post-adult stage cardiac lymphatic vessel development, unlike mammalian
- Ackr3a interacts with Vegfc signaling in regulating cardiac lymphatic growth in zebrafish
- Better inflammation clearance is observed in ackr3a mutant which has extra cardiac lymphatic vessels

3132 Endothelial IRF3-activation links inflammation and phenotypic changes

Wagman, Olivia, L¹; Christensen, Julie, N¹; Müller, Monja¹; Bross, Peter²; Magalhaes Novais, Silvia³; Rohlena, Jakub³; Rohlenova, Katerina³; Frye, Maïke⁴; Fenton, Robert¹; Wu, Qi¹; Paludan, Søren, R¹ Fendt, Sarah, M⁵; Kalucka, Joanna, M¹

1. Department of Biomedicine, Aarhus University, Aarhus, Denmark
2. Research Unit for Molecular Medicine, Aarhus University Hospital, Aarhus, Denmark
3. Institute of Biotechnology of the Czech Academy of Sciences, Vestec, Czechia
4. University Medical Center Hamburg, Hamburg, Germany
5. VIB-KU Leuven Center for Cancer Biology, Leuven, Belgium

- IRF3 activation alters EC phenotype by inducing inflammation and disrupting cell junctions
- The altered phenotype evoked by IRF3 activation is independent of changes in glycolysis and FAO
- Increased oxidative metabolism was seen after IRF3 activation, crucial for an inflammatory response

3133 Novel modes of mouse corneal lymphatic remodeling identified using intravital microscopy.

Collazo, Heather¹; Harms, Rebecca¹; Fink, Darci¹

1. South Dakota State University, Brookings, South Dakota, USA

- Lymphatics
- Intravital microscopy
- Inflammation and wound healing

3134 The adherence of monocytes to the endothelium is enhanced by SARS-CoV-2 accessory protein ORF7a.

Hallwood, James, H¹; Bates, David, O¹

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

- The accessory protein ORF7a facilitates leukocyte interactions via Mac-1 and LFA-1 binding.
- Monocyte adherence to endothelial cells increased three-fold after exposure to ORF7a concentrations.
- Results indicate ORF7a's role in facilitating the binding of monocytes to endothelial cells.

3135 Investigating the role of blood vessels and VEGF splicing axis in inflammatory arthritis in mice

Sohail, Roheena¹; Beazley-Long, Nicholas¹; Bates, David, O¹; Donaldson, Lucy, F¹

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

- Endothelial cell disruption involves in the control of transcription in synoviocytes.
- Cartilage damage in VEGFR2ECKO is associated with complete loss of vessels in subchondral bone
- Superficial subchondral bone vessels are important in maintaining cartilage integrity in IA.

3136 Uncovering capillary endothelial cells injury-repair response across lung injury models

Kong, Celine Shuet Lin¹; Chen, Jichao²

1. University of Texas MD Anderson Cancer Center UTHHealth Houston GSBS, Houston, Texas, USA
2. MD Anderson Cancer Center, Houston, TX USA

- Understanding endothelial cell heterogeneity across lung injury models
- Understanding similarities & differences in lung endothelial cell injury-repair across injury models
- Understanding lung endothelial cell regeneration across injury models

3137 Intrahepatic transcriptomic differences in patients with Fontan-associated liver disease

Wu, Xiujü¹; Bravo Jaimes, Katia¹; Reardon, Leigh¹; Lluri, Gentian¹; Naini, Bitia¹; Venick, Robert¹; Böstrom, Kristina¹; Aboulhosn, Jamil¹; Kaldas, Fady¹

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

- Assess intrahepatic transcriptomics among Fontan patients with advanced vs early fibrosis.
- Over 900 genes in advanced fibrosis were up-regulated compared to early fibrosis.
- The up-regulated genes were enriched in the pathways of inflammation, congestion, and angiogenesis.

3138 GSK3 inhibition and vascular calcification

Wu, Xiuju¹; Qiao, Xiaojing¹; Zhang, Li¹; Cai, Xinjiang¹; Bostrom, Kristina, I¹

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

- Inducing osteoblastic-endothelial transdifferentiation
- High throughput screening for the compounds
- Identification the role of GSK3beta in vascular calcification

3139 Novel melatonin derivative inhibits hypoxia-induced angiogenesis via downregulation of HIF-1 α pathway

Hwang, Su Jung¹; Song, Ye-Seul¹; Choi, Young Bin¹; Lee, Hyo-Jong¹

1. Sungkyunkwan University, Suwon, Gyeonggi-do, Korea (Republic of)

- Among melatonin derivatives, N-MEB showed high HIF-1 α targeting activity without toxicity
- N-MEB inhibits HIF-1 α protein stability and AKT phosphorylation
- N-MEB suppresses angiogenesis in vivo and in vitro

3140 miR-125a-5p as a novel regulator of Ninjurin1 in vascular remodeling

Hwang, Su Jung¹; Song, Ye-Seul¹; Choi, Young Bin¹; Lee, Hyo-Jong¹

1. Sungkyunkwan University, Suwon, Gyeonggi-do, Korea (Republic of)

- Five miRNAs targeting Ninj1 were selected using algorithm and comparison of expression patterns.
- miR-125a-5p suppressed cell adhesion and expression of pro-inflammatory factors mediated by Ninj1.
- miR-125a-5p inhibited the recruitment of macrophages in inflamed retina and diabetic retinopathy.