

ORAL PRESENTATIONS

Springer Junior Investigator Award Babak Razani, Washington University in St. Louis

Dissecting the impact of dietary protein on macrophage mTOR signaling and atherosclerosis

- Mechanism of high protein diet-induced atherosclerosis
- Functional impact of amino acids on macrophage mTORC1 signaling
- Disrupted mitophagy in macrophages and activation of the inflammasome and apoptotic cell death

Vascular Matrix Biology and Bioengineering Workshop

Vascular Tissue Engineering

M001

A completely biological “Off-the-Shelf” arteriovenous graft that reanimates

Tranquillo, Robert; Syedan, Zeeshan; Graham, Melanie; Dunn, Ty; O'Brien, Timothy; Johnson, Sandra; Schumacher, Robert
University of Minnesota, Minneapolis, MN

- acellular and completely biological tissue-engineered arteriovenous graft
- 6-month baboon study
- graft recellularization and endothelialization

M002

Combinatorial extracellular matrix micro-environments induce endothelial differentiation of human pluripotent stem cells

Huang, Ngan; Hou, Luqia; Kim, Joseph; Wanjare, Maureen; Collier, John; Natu, Vanita
Stanford University, Stanford, CA

- Combinatorial ECMs better mimic native endothelial ECM environment
- Combinatorial ECMs induced endothelial differentiation
- integrin $\beta 3$ modulated endothelial differentiation

Mechanotransduction

M003

Disturbed flow reprograms endothelial cell metabolism

Fang, Yun
University of Chicago, Chicago, IL

- Disturbed flow induces glycolysis and reduces mitochondrial respiratory capacity in endothelium
- Disturbed flow stabilizes hypoxia inducible factor-1a (HIF-1a) to reprogram endothelial metabolism
- VCAM1-targeted nanoparticles effectively treat atherosclerosis in Apoe⁻ mice

M004

PECAM-1 mediates shear stress induced endothelial prostacyclin and nitric oxide production by distinct mechanisms

Tarbell, John; Bartosch, Anne Marie W.; Russell-Puleri, Sparkle
The City College of New York, New York, NY

- We show that anti-atherogenic molecules PGI₂ and NO follow distinct mechanotransduction mechanisms
- The mechanosensor for NO is heparan sulfate proteoglycan (HSPG) glypican-1 interacting with PECAM-1
- Conversely PECAM-1 is the mechanosensor for PGI₂ production without the involvement HSPGs

Vascular Mechanics

M005

The proteoglycanome of the aortic wall: Pathogenic role of aggrecan and versican accumulation in thoracic aortic aneurysm and dissection

Koch, Christopher¹; Cikach, Frank S.¹; Mead, Timothy J.¹; Willard, Belinda¹; Galatioto, Josephine²; Emerton, Kelly B.¹; Eagleton, Matthew J.¹; Blackstone, Eugene H.¹; Ramirez, Francesco³; Roselli, Eric E.¹; Apte, Suneel S.¹
1. Cleveland Clinic Lerner Research Institute, Cleveland, OH
2. Icahn School of Medicine at Mount Sinai, New York, NY
3. Mount Sinai School of Medicine, New York, NY

- Aggrecan and versican accumulate in human thoracic aortic aneurysm and dissection (TAAD)
- A Marfan syndrome mouse model has increased aggrecan production and decreased ADAMTS-mediated proteolysis
- Aggrecan and versican are identified as potential TAAD biomarkers

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M006

The role of thrombospondin-1 in ascending aortic aneurysms in fibulin-4 mutant mice

Yanagisawa, Hiromi; Yamashiro, Yoshito; Shin, Seung Jae; Thang, Bui Q.

University of Tsukuba, Tsukuba, Japan

- Thrombospondin-1 is a mechanosensitive molecule involved in matrix-cell interactions
- Thrombospondin-1 is highly upregulated in the aneurysmal wall of fibulin-4 mutant mice
- Deletion of thrombospondin-1 prevents upregulation of Ssh1 and coffin activation and rescues aneurysms

M007

Post-transcriptional regulation of biomechanical genes limit contractile forces to preserve tissue stiffness homeostasis

Moro, Albertomaria¹; Discroll, Tristan¹; Baeyens, Nicolas²; Jouy, Charlene²; Donghoon, Lee¹; Gu, Mengting¹; Zhang, Jing¹; Gerstein, Mark¹; Schwartz, Martin A.¹; Nicoli, Stefania¹

1. Yale University, New Haven, CT

2. University of Manchester, Manchester, United Kingdom

- High throughput sequencing of miR-mRNA-AGO2 complexes in endothelial cells identify cytoskeletal
- AGO2 deletion induced hyper-adhesive, hyper-contractile phenotype in HUVEC and HDF in 2D/3D cultures
- mechanical miRs-mRNAs network is an essential component of stiffness-dependent regulatory machinery

Extracellular Matrix and Disease

M008

Mutations in collagen COL22A1 cause intracranial aneurysms

Sumanas, Saulius¹; Ton, Quynh V.¹; Leino, Daniel¹; Farlow, Janice²; Foroud, Tatiana M.²; Broderick, Joseph³

1. Cincinnati Children's Hospital, Cincinnati, OH

2. Indiana University, Indianapolis, IN

3. University of Cincinnati, Cincinnati, OH

- Whole exome sequencing identified mutations in COL22A1 associated with intracranial aneurysms
- Zebrafish COL22A1 mutants have defects in vascular integrity and develop hemorrhages
- Human mutant variants perturb COL22A1 function in zebrafish embryos

M009

Plasma fibronectin acts as a safeguard in the vasculature and supports synergistic and differential roles with cellular fibronectin in vascular matrix integrity

Kumra, Heena¹; Sabatier, Laetitia¹; Mosher, Deane F.²; Sakai, Takao³; Chambon, Pierre⁴; Reinhardt, Dieter P.¹

1. McGill University, Montreal, PQ, Canada

2. University of Wisconsin, Madison, WI

3. University of Liverpool, Liverpool, United Kingdom

4. Institut de Génétique et de Biologie Moléculaire et Cellulaire, Strasbourg, France

- Deletion of cellular fibronectin leads to minor effects as the plasma fibronectin is present in vessel wall
- Deletion of plasma fibronectin do not have any obvious effects because cellular fibronectin is present
- Deletion of both cellular and plasma fibronectin leads to lethality of the mice

Vascular Calcification

M010

DDR1 acts as a mechanotransducer to promote vascular calcification

Ngai, David; Bendeck, Michelle P.

University of Toronto, Toronto, ON, Canada

- Discoidin Domain Receptor-1
- Mechanotransduction
- Vascular Calcification

M011

Calcified vessels act as an important acute depot for oral phosphate in an experimental model of chronic kidney disease

Turner, Mandy; Jeronimo, Paul S.; Ward, Emilie C.; Laverty, Kimberly J.; Holden, Rachel M.; Adams, Michael A.

Queen's University, Kingston, ON, Canada

- The acute deposition of an oral load of phosphate is modified by vascular calcification
- Calcified arteries act as one of the most important depot for de novo phosphate per mg of tissue
- The deposition is equivalent or higher to that found in bone per mg of tissue

Visit the Exhibits

Vascular Imaging

M012

Vessel remodeling during allantois development: Establishing embryo-placenta blood circulation

Le, Henry

Baylor College of Medicine, Houston, TX

- Umbilical vessels
- vascular development imaging
- embryos development

M013

Imaging of atherosclerotic plaques using a novel SPECT radiotracer targeting LFA1

Meester, Eric¹; Krenning, Boudewijn¹; de Blois, Erik¹; Norenberg, Jeffrey²; de Jong, Marion¹; Bernsen, Monique¹; van der Heiden, Kim¹

1. Erasmus Medical Center Rotterdam, Rotterdam, Netherlands

2. University of New Mexico, Albuquerque, NM

- Novel SPECT Radiotracer (DANBIRT) for atherosclerosis imaging targets LFA1 on inflammatory cells
- Successful in imaging mouse plaque as confirmed by *in/ex vivo* SPECT, autoradiography and histology
- Preliminary data demonstrate feasibility of DANBIRT imaging to detect human atherosclerosis

Engineering Angiogenesis

M014

Engineering Ubx-based materials for scaffold neovascularization

Howell, David; Mendes, Gabriella; Bondos, Sarah; Bayless, Kayla

Texas A&M Health Science Center, College Station, TX

- VEGF-Ubx materials instigate and guide neovascularization *ex vivo* and *in vivo*
- To enhance Ubx materials we have incorporated FGF and SDF and VEGF alone and in combination
- Ubx-based materials will be useful for promoting vascularization of biocompatible 3D scaffolds

M015

Enhanced therapeutic angiogenesis of mesenchymal stem cells through combined mechanotransduction and pharmacological conditioning

Lee, Jason; Henderson, Kayla; Maceda, Pablo; Armenta-Ochoa, Miguel; Yoon, Eun; Samarnah, Lara; Veith, Austin; Wong, Mitchell; Dunn, Andrew; Baker, Aaron

University of Texas at Austin, Austin, TX

- Novel system that induces dynamic physiological strain waveforms was used on mesenchymal stem cells
- Combination of mechanical strain and pharmacological drugs were used to enhance angiogenesis
- Obtained endothelial and pericyte like markers in mesenchymal stem cells through the conditioning

M016

Lymphatic to blood vessel transition in adult microvascular networks

Murfee, Walter Lee^{1,2}; Azimi, Mohammad S.¹; Motherwell, Jessica¹; Hodges, Nicholas A.¹

1. Tulane University, New Orleans, LA

2. University of Florida, Gainesville, FL

- Lymphatic vessels transition into blood vessels during network growth in a novel tissue culture model
- Loss of lymphatic endothelial cell identity is supported by discontinuous lymphatic marker labeling
- Our results offer a new paradigm for investigating cell dynamics during microvascular network growth

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Developmental Vascular Biology and Genetics Workshop

Vascular Progenitors

D001

A glycolytic switch is required for transdifferentiation to endothelial lineage

Lai, Li; Reineke, Erin; Hamilton, Dale; Cooke, John P.
Houston Methodist Research Institute, Houston, TX

- Transdifferentiation from fibroblast to endothelial cells requires glycolytic switch
- Glycolytic manipulators could regulate transdifferentiation *in vitro* and *in vivo*
- Poly I:C initiates the metabolic shift

D002

microRNA-223 limits hematopoietic stem cell production from endothelium during development

Kasper, Dionna; He, Zhiheng; Mandl, Hanna; Moro, Albertomaria; Hirschi, Karen; Nicoli, Stefania
Yale University Cardiovascular Research Center, New Haven, CT

- Hematopoietic stem/progenitor cells (HSPCs) arise by budding from hemogenic endothelium in development
- Zebrafish miR-223 mutant embryos have an increased number of budding HSPCs
- miR-223-dependent inhibition of HSPC production is conserved during mammalian embryogenesis

Vascular Cell Biology

D003

EndophilinA2 mediated endocytosis: A new internalization pathway for VEGFR2 regulating endothelial cell migration

Genet, Gael; Boye, Kevin; Ola, Roxana; Zhang, Feng; Dubrac, Alexandre; Benedetti, Lorena; De Camilli, Pietro; Eichmann, Anne

Yale School of Medicine, New Haven, CT

- Regulation of VEGFR2 signaling by endocytosis
- High resolution microscopy
- Developmental and pathological angiogenesis

D004

Excessive plasmin activity promotes endothelial Ripk3 transcription and murine embryonic vascular rupture

Colijn, Sarah; Ingram, Kyle; Menendez, Matthew; Muthukumar, Vijay; Silasi-Mansat, Robert; Lupu, Florea; Griffin, Courtney T.

Oklahoma Medical Research Foundation, Oklahoma City, OK

- Embryos with excessive plasmin activation have elevated RIPK3 in endothelial cells at midgestation

- Genetically reducing either plasmin activation or Ripk3 rescues embryos from lethal vascular rupture
- Plasmin works through PAR4 to upregulate Ripk3 transcription in cultured endothelial cells

Vascular Signaling

D005

Endothelial Notch signaling limits angiogenesis via control of artery formation

Siekman, Arndt¹; Hasan, Sana S.¹; Tsaryk, Roman¹; Lange, Martin¹; Wisniewski, Laura¹; Moore, John C.²; Lawson, Nathan D.²; Wojciechowska, Karolina³; Schnittler, Hans⁴

1. Max Planck Institute for Molecular Biomedicine, Muenster, Germany
2. University of Massachusetts Medical Sch, Worcester, MA
3. University of Warsaw, Warsaw, Poland
4. WWU Muenster, Muenster, Germany

- Artery formation
- Notch Signaling
- Control of gene expression

D006

ALK2 mediates venous specific pro-angiogenic function of BMP signaling in mammalian vessels

Jin, Suk-Won

Gwangju Institute of Science and Technology, Republic of Korea

- BMP signaling modulates vascular morphogenesis in a venous specific manner in mammals
- ALK2 but not ALK3 mediates venous specific angiogenic response toward BMP signaling in mammalian ECs
- ALK2 activates COUP-TFII, which in turn, facilitates cell proliferation in venous ECs

D007

A novel Smad4 model of Hereditary Hemorrhagic Telangiectasia (HHT) links angiopoietin/Tek signaling to the formation of arteriovenous malformations

Meadows, Stryder¹; Crist, Angela M.¹; Garai, Jone²; Baddoo, Melody³; Zabaleta, Jovanny²

1. Tulane University, New Orleans, LA
2. Louisiana State University Health Sciences Center, New Orleans, LA
3. Tulane Cancer Center, New Orleans, LA

- Generation of a novel Smad4 mouse model of HHT that exhibits AVMs similar to patients
- Identification of 150+ potential TGF β downstream effectors/therapeutic targets of HHT
- Defective Angiopoietin/Tek signaling is associated with AVM formation

Transcriptional Control/ Gene Regulation

D008

Transcriptional regulation of the SMC-selective, blood pressure-associated Rho-specific GTPase, GRAF3

Mangum, Kevin; Taylor, Joan M.; Mack, Christopher P. University of North Carolina, Chapel Hill, NC

- smooth muscle cell-selective transcription mechanisms
- genetic control of hypertension
- Notch signaling

D009

The ETS factor ERG controls an endothelial-specific transcriptional regulatory program associated with super-enhancers

Birdsey, Graeme¹; Yang, Youwen¹; Kalna, Viktoria¹; Hannah, Rebecca²; Shah, Aarti V.¹; Osuna Almagro, Lourdes¹; Boyle, Joseph J.¹; Leiper, James M.³; Ferrer, Jorge¹; Göttgens, Berthold²; Randi, Anna M.¹

1. Imperial College London, London, United Kingdom
2. Cambridge University, Cambridge, United Kingdom
3. MRC London Institute of Medical Sciences, London, United Kingdom

- ETS transcription factor ERG is essential for endothelial lineage specification and vascular development
- ChIP-seq in HUVEC identifies ERG binding to active super-enhancers, associated with core EC regulatory genes
- ERG bound super-enhancers in VCaP cells are distinct to EC, demonstrating ERG activity is cell type-specific

Coronary Vascular Development

D010

Coordinated formation of coronary vessels and cardiac lymphatics during zebrafish heart development and regeneration

Lien, Ching-Ling (Ellen); Harrison, Michael R.; Feng, Xidi Children's Hospital Los Angeles, Los Angeles, CA

- Zebrafish is a unique model to study how vasculature forms during heart development and regeneration
- CXC chemokine signaling regulates development of coronary vessels and cardiac lymphatics
- Interactions between coronary vessels and cardiac lymphatics are essential for heart development

D011

Molecular regulation of vascular smooth muscle cell recruitment to arteries during development

Stratman, Amber; Pham, Van N.; Farrelly, Olivia M.; Burns, Margaret C.; Davis, Andrew E.; Weinstein, Brant M. NICHD/NIH, Bethesda, MD

- Smooth muscle cells recruit preferentially to arteries during early development
- cxcl12 regulates pdgf-bb ligand expression
- klf2 seemingly limits expression of cxcr4 to modulate expression of pro-chemoattractant ligands for vSMC

Lymphatic Development

D012

MMP14 suppresses lymphatic endothelial cell proliferation by inhibiting ERK activation in lymphatic valve maturation and homeostasis

Shawber, Carrie; Muley, Ajit; Kitajewski, Christopher; Riitano, Gloria; Saade, Mia M.

Columbia University Medical Center, New York, NY

- MMP14 regulates lymphatic valve maturation and homeostasis
- Loss of LEC Mmp14 results in lymphatic valve defects blocking intestinal lipid uptake
- MMP14 suppresses LEC proliferation by inhibiting ERK signaling

D013

PROX1 enhances Wnt/ β -catenin signaling during lymphatic vascular development

Cha, Boksik; Sathish, Srinivasan

Oklahoma Medical Research Foundation, Oklahoma City, OK

- We have identified PROX1 as a novel regulator of Wnt/ β -catenin signaling
- PROX1 provides endothelial cell competence to respond to OSS and Wnt ligands activating FOXC2 expression
- Wnt-ligands secreted by LECs and mural cells are necessary for the development of lymphatic valves

Visit the Exhibits

Vascular Heterogeneity

D014

Requirement for NOTCH3 in stem cell to vascular smooth muscle cell transition in infantile hemangioma

Wu, June¹; Edwards, Andrew¹; Glithero, Kyle¹; Grzesik, Peter¹; Kitajewski, Alison A.¹; Munabi, Naikhoba CO¹; Hardy, Krista¹; Tan, Qian Kun¹; Schonning, Michael¹; Kangsamaksin, Thaned²; Kitajewski, Jan K.³; Shawber, Carrie J.¹

1. Columbia University, New York, NY
2. Mahidol University, Bangkok, Thailand
3. University of Illinois Chicago, College of Medicine, Chicago, IL

- Infantile hemangiomas (IHs) have mis-expression of endothelial and perivascular cell markers
- NOTCH3 is expressed in IHs and may help to stabilize pathological IH vasculature
- Inhibition of NOTCH3 in IHs inhibited IH vessel development and may be a therapeutic target

D015

A genomic address code integrates capillary, venule and tissue specific signals to control intestinal venule identity

Dinh, Thanh Theresa

Stanford University, Stanford, CA

- A phylogenetic conserved element confers segmental and tissue specific transcriptional regulation

- COUP-TFII heterodimerizes with Nkx2-3 to promote gut high endothelial cell identity
- Notch repressors, homeodomain protein Nkx2-3 and COUP-TFII coordinately regulate MAdCAM1

D016

Defining the transcriptional code that specifies sinusoidal endothelial cells in the HSC niche

Perlin, Julie¹; Hagerdorn, Elliott¹; Mao, Clara¹; Redfield, Shelby E.¹; Daily, Madeleine¹; Collins, Samantha H.¹; D'Amato, Chris R.¹; Riquelme, Raquel¹; Wattrus, Samuel¹; van Oudenaarden, Alexander²; Junker, Jan Philipp³; Zon, Leonard I.¹

1. Boston Children's Hospital, Boston, MA
2. Hubrecht Institute, Utrecht, Netherlands
3. Max Delbrück Center for Molecular Medicine, Berlin, Germany

- Spatial transcriptomics identify genes unique to sinusoid vessels in the blood stem cell niche
- Novel zebrafish transgene used to profile HSC niche endothelial cells by RNA- and ATAC-seq
- Combinatorial transcriptional code appears to specify sinusoidal vessels in the HSC niche

Bioengineering Organ Specific Vasculatures

G001

Pericyte-derived lactadherin tightens the endothelium as identified in a novel 3D microfluidic model of the blood-brain barrier

Dang, Lan¹; Obermeier, Birgit¹; Marsh, Graham¹; Shimizu, Fumitaka²; Sano, Yasuteru²; Kanda, Takashi²; Duffield, Jeremy S.³; Ransohoff, Richard¹

1. Biogen, Cambridge, MA
2. Yamaguchi University, Ube, Japan
3. Vertex Pharmaceuticals, Boston, MA

- Pericytes are key regulators of endothelial cell function at the blood-brain barrier (BBB)
- We recapitulate the BBB's unique anatomic and functional properties in a physiological flow setting
- We identified MFG-E8 as a pericyte derived factor which enhance barrier function of MVECs

G002

BBB on-a-chip: a 3D *in vitro* model of the human blood brain barrier (BBB)

Wevers, Nienke; Vught, Remko V.; Spijkers, Xandor; Wilschut, Karlijn J.; Trietsch, Sebastiaan J.; Vulto, Paul; Joore, Jos

Mimetas, Leiden, Netherlands

- Blood brain barrier model on-a-chip
- Endothelium, astrocytes and pericytes co-culture in an easy to use platform
- For fundamental BBB research and drug development studies

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Vascular Therapeutics

G003

Doxorubicin triggers endothelial cell dysfunction by suppressing KLF2/KLF4 flow-dependent programs: Opportunities for pharmacological intervention

Slegtenhorst, Bendix; Voskuil, Floris J.; Lumertz-Saffi, Marco A.; Zhang, Yuzhi; Tullius, Stefan G.; Garcia-Cardena, Guillermo
Harvard Medical School and Brigham and Women's Hospital, Boston, MA

- The use of Doxorubicin (DOX) is associated with severe long-term cardiovascular risk and mortality

- DOX suppresses the flow-mediated expression of KLF2 and KLF4 in human endothelial cells
- Agents that sustain endothelial KLF2/KLF4 in the presence of Dox may benefit cancer patients

Engineering Vascular Morphogenesis

G004

YAP/TAZ-CDC42 signaling regulates vascular tip cell migration

Xin, Mei¹; Sakabe, Masahide¹; Fan, Jieqing¹; Odaka, Yoshinobu¹; Liu, Ning²; Hassan, Aishlin¹; Duan, Xin¹; Stump, Paige¹; Byerly, Luke¹; Donaldson, Megan¹; Hao, Jiakuan³; Fruttiger, Marcus⁴; Lu, Richard^{1,3}; Zheng, Yi¹; Lang, Richard A.¹

1. Cincinnati Children's Hospital Medical Center, Cincinnati, OH
 2. UT Southwestern Medical Center, Dallas, TX
 3. University of Cincinnati, Cincinnati, OH
 4. UCL Institute of Ophthalmology, London, United Kingdom
- Regulation of retinal angiogenesis by the Hippo Signaling Pathway
 - Gene dosage requirements of YAP and TAZ for endothelial cell proliferation and migration
 - Cytoplasmic YAP functions in promoting cell migration by activating CDC42

G005

Slug is a SDF1a downstream effector during angiogenesis

Hultgren, Nan; Ziegler, Mary E.; Welch-Reardon, Katrina; Hughes, Christopher C.
University of California, Irvine, Irvine, CA

- SDF1a treatment induces Slug but not Snail expression in EC during angiogenic sprouting
- The angiogenic effect of SDF1a is strongly impaired in Slug deficient retina explants
- SDF1a activates MEK5/ERK5 signaling, which turns on Slug transcription in EC

G006

Endothelial APLNR regulates tissue fatty acid uptake and is essential for apelin's glucose lowering effects

Chun, Hyung
Yale University School of Medicine, New Haven, CT

- Apelin's glucose lowering effect is highly dependent on endothelial APLNR signaling
- Apelin regulates endothelial FABP4 expression, which in turn determines transendothelial fatty acid transfer
- Pharmacologic inhibition of FABP4 rescues the impaired glucose utilization in apelin disrupted state

G007

Endothelial cell-derived factors controlling pericyte invasion and endothelial-pericyte tube co-assembly

Kemp, Scott; Davis, George E.
University of Missouri-Columbia School of Medicine, Columbia, MO

- Investigating pericyte invasion during EC-pericyte tube co-assembly
- PDGF-BB and PDGF-DD stimulate pericyte-only invasion, while ET-1 synergizes with either factor
- Blockade of PDGF-BB, PDGF-DD, and ET-1 markedly inhibits pericyte recruitment to EC-lined tubes

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G008
Mechanical cues control morphogenesis and longevity of vascular networks

Haase, Kristina; Kamm, Roger D.

Massachusetts Institute of Technology, Cambridge, MA

- Simulating dynamics of the myocardium allows for investigation of vascular recovery *in vitro*
- Interstitial flow promotes network connectivity during the initial stages of vasculogenesis
- Cyclic compressive strain (~10%) inhibits early vasculogenesis, and results in significant remodeling

G009
Engineering 3D microvessels with biomimetic continuous curvature and diameter

Mandrycky, Christian; Zheng, Ying

University of Washington, Seattle, WA

- Technique to rapidly form long 3D vessels *in vitro* with continuous curvature
- Vessels can be formed in gel or PDMS for flow and remodeling studies
- Support the incorporation of parenchymal populations to mimic more complex tissues

Vasculata 2018

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Organizers: *Gwendalyn Randolph and Kyunghye Choi, Washington University*

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Michael Davis, University of Missouri – Columbia

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Save the date!

July 23-26, 2018



**Abstracts due
June 1, 2018**

MONDAY - OCTOBER 16, 2017

7:00-10:00 PM - Fred Farr Forum and Kiln

Vascular Progenitors

001

Determining the role of Eglf7 in the hemogenic endothelium

Arqueta, Lissenvy¹; Bambino, Kathryr²; Stuhlmann, Heidi¹

1. Weill Cornell Medical College, New York, NY
2. Icahn School of Medicine at Mount Sinai, New York, NY

- Endothelial-restricted gene Eglf7 is expressed at sites of budding hematopoietic stem progenitors
- Sox17 is a potential upstream regulator of Eglf7 in the hemogenic endothelium
- EGFL7 signals through NOTCH and EGFR in embryonic endothelial cells

002

Expandable arterial endothelial precursors derived from human CD34+ progenitors differ in their propensity to undergo an endothelial-to-mesenchymal transition

Vereide, David¹; Miller, Auston¹; Ingram, Patrick²

1. Morgridge Institute for Research, Madison, WI
2. University of Wisconsin-Madison, Madison, WI

- MYCN and SOX17 expand human arterial endothelial precursors *in vitro*
- Some arterial precursors readily transition to a mesenchymal state, while others do not
- The precursors that become mesenchymal reveal phenotypes associated with vascular disease

003

Alternative progenitor cells compensate to rebuild the coronary vasculature in Elabela- and Apj-deficient hearts

Sharma, Bikram

Stanford University, Stanford, CA

- ELA-APJ is required for coronary vessel (CV) sprouting from the sinus venosus (SV)
- Endocardial-derived CVs can expand to rescue defective SV sprouting
- The existence of two progenitor sources provides robustness to coronary development

004

A Xeno-Free culture system for efficient derivation and amplification of human endothelial colony-forming cells from umbilical cord blood

Marchetti, Valentina¹; Lee, Kelsey¹; Wagey, Ravenska¹; Peters, Carrie¹; Sakimoto, Susumu²; Aguilar, Edith²; Friedlander, Martin²; Thomas, Terry¹; Eaves, Allen¹; Szilvassy, Stephen¹; Louis, Sharon¹

1. StemCell Technologies, Vancouver, Canada
2. The Scripps Research Institute, La Jolla, CA

- Endothelial Progenitor Cells Endothelial Colony Forming Cells
- Xeno-free culture system for derivation and expansion of ECFCs
- Oxygen induced retinopathy *in vivo* model of eye disease

Stem Cells in Vascular Biology

006

Capillary origin of new endothelium in immune angiogenesis

Rajaraman, Anusha¹; Szade, Agata A.¹; Lazarus, Nicole¹; Rahman, Milladur¹; Dermadi Bebek, Denis¹; Pan, Junliang²; Vestweber, Dietmar³; Kawashima, Hiroto⁴; Butcher, Eugene C.⁵

1. Stanford University, Stanford, CA
2. Palo Alto Veterans Institute for Research, Palo Alto, CA
3. Max-Planck Institute for Molecular Biomedicine, Munster, Germany
4. Chiba University, Chiba, Japan
5. Stanford University Med Ctr, Stanford, CA

- Lymph node blood endothelial cells expand during inflammation but their precursors remain unclear
- Our analysis shows a transitional blood endothelial phenotype during inflammation
- Antibody tagged fate-mapping reveals that capillaries give rise to high endothelial venules

007

Cx43-containing gap junctions between endothelial cells and NSC in the adult brain subventricular zone maintains NSC quiescence

Genet, Nafiisha¹; Zhi-Ming Ma, Gerry²; Lee, Seyoung¹; Chintanaphol, Michelle¹; Fang, Jennifer S.¹; Baker, Kasey¹; Bhatt, Neha¹; Bourdieu, Antonin¹; Vasavada, Hema¹; French-Constant, Charles²; Thomas, Jean-Leon¹; Hirschi, Karen K.¹

1. Yale Cardiovascular Research Center, New Haven, CT
2. MRC Centre for Regenerative Medicine, Edinburgh, United Kingdom

- *In vivo* study of neural stem cells (NSC) and endothelial cells (EC) interaction via connexins (Cx) in the SVZ
- *In vitro* modeling of NSC and EC interaction in a touch transwell co culture manner
- Cx43 is involved in NSC regulation in the murine adult SVZ niche

Vascular Signaling

008

The inhibitory protein PMEPA1, but not SMAD7, inhibits BMP signaling in endothelial cells

Citrin, Kathryn; Mouillesseaux, Kevin P.; Wylie, Lyndsay; Bautch, Victoria L.

University of North Carolina at Chapel Hill, Chapel Hill, NC

- SMAD7 knockdown does not significantly affect endothelial cell responsiveness to BMP6 stimulation
- PMEPA1 knockdown significantly increases endothelial cell responsiveness to BMP6 stimulation
- PMEPA1 knockdown decreases the proliferation of endothelial cells in culture

009

The role of NRP1 in pharyngeal arch artery morphogenesis

Navarro-Aragall, Ariadna Gador; Plein, Alice; Fantin, Alesandro; Dentí, Laura; Scambler, Peter; Ruhrberg, Christiana
University College London, London, United Kingdom

- Pharyngeal arch arteries (PAAs) are essential for normal aortic arch development
- NRP1 is important for formation and development of PAAs
- Semaphorin signalling through NRP1 is important for PAAs remodelling

011

CXCL12-CXCR4 signaling plays an essential role in proper patterning of aortic arch and pulmonary arteries

Oh, S. Paul¹; Kim, Bo-Gyeong²; Stanley, Edward L.¹; Lee, Young Jae²

1. University of Florida, Gainesville, FL

2. Gachon University, Incheon, Korea, Republic of

- Using a novel Cxcl12-LacZ reporter line, Cxcl12 expression was visualized at systemic and pulmonary arteries
- CXCL12-deficiency resulted in aberrant vertebral artery and abnormal systemic arterial supply to lungs
- Tie2-Cre but not Wnt1-Cre mediated Cxcr4 deletion phenocopied the aortic arch and pulmonary artery patterning

012

Chloride Intracellular Channel proteins function in Sphingosine-1-phosphate signaling to regulate endothelial cell behavior and angiogenesis

Mao, De Yu¹; Jilishitz, Irina²; Komarova, Yulia¹; Hla, Timothy²; Kitajewski, Jan K.¹; Kleinjan, Matt¹

1. University of Illinois Chicago, College of Medicine, Chicago, IL

2. Columbia University Medical Center, New York, NY

3. Boston Children's Hospital, Harvard Medical School, Boston, MA

- CLIC4 and CLIC1 function downstream of S1P1 receptor in endothelial cells
- CLIC1, not CLIC4, functions downstream of S1P2 receptor in endothelial cells
- C-terminus of CLIC proteins is responsible for its function in endothelial S1P signaling

013

A mouse model for tracking and auditing endothelial cell-derived extracellular vesicles in cancer

McCann, James¹; Lannigan, Joanne²; Erdbruegger, Uta²; Dudley, Andrew C.²

1. University of North Carolina, Chapel Hill, NC

2. The University of Virginia, Charlottesville, VA

- Extracellular vesicles (EVs) are important vectors for exchanging information between different cell types

- Tumor-derived endothelial cells shed abundant EVs with unique protein payloads
- Endothelial lineage-traced mice stably transport ZSGreen into EVs allowing us to track and audit EC-derived EV

014

Investigating the role of BMP9 in the development of superior cavopulmonary anastomosis-associated pulmonary arteriovenous malformations

Treggiari, Davide¹; Capasso, Teresa¹; Hindes, Morgan LM²; Bloch, Jamie L²; Cook, Stephen²; Trucco, Sara²; Roman, Beth L.¹

1. University of Pittsburgh, Pittsburgh, PA

2. Children's Hospital of Pittsburgh, Pittsburgh, PA

- PAVMs are a common consequence of bidirectional cavopulmonary anastomosis
- Decreased BMP9 availability might contribute to PAVM development in bidirectional cavopulmonary anastomosis
- BMP9 levels significantly decrease in individuals undergoing bidirectional cavopulmonary anastomosis

Regulation of Epithelial and Endothelial Junctions

015

Csk strengthens endothelial barrier function via tyrosine 685 of VE-cadherin

Spring, Kathleen

Max Planck Institute for Molecular Biomedicine, Münster, Germany

- Endothelial barrier regulation
- Inflammation and leukocyte extravasation
- endothelial permeability

016

Caveolin-1 is required for Th1 cell infiltration but not tight junction remodeling at the blood-brain barrier

Lutz, Sarah¹; Smith, Julian²; Kim, Dae³; Olson, Carl V.³; Ellefsen, Kyle³; Bates, Jennifer M.³; Gandhi, Sunil P.³; Agalliu, Dritan²

1. University of Illinois at Chicago, Chicago, IL

2. Columbia University Medical Center, New York, NY

3. University of California, Irvine, Irvine, CA

- Intravital two-photon microscopy shows that TJ remodeling precedes the onset of EAE
- Caveolar transcytosis is not required for endothelial TJ remodeling *in vivo*
- Caveolar transcytosis is required for Th1 but not Th17 cell infiltration into the CNS

Vascular Smooth Muscle Cell Biology 017

Matrix stiffness regulates vascular smooth muscle cell osteogenic potential

Tsakali, Sofia Serena¹; Warren, Derek²; Shanahan, Catherine M.¹

1. Kings College London, London, United Kingdom
2. University of East Anglia, Norwich, United Kingdom

- Vascular calcification
- Mechanotransduction
- Vascular smooth muscle cells

018

Identification of novel vascular smooth muscle cell markers by *in vivo* transcriptional profiling

Cleuren, Audrey; van der Ent, Martijn A.; Hunker, Kristina; Jiang, Hui; Ginsburg, David; Ganesh, Santhi

University of Michigan, Ann Arbor, MI

- *In vivo* transcriptional profiling of SMCs
- Identification/validation new vSMC markers
- Transgelin-Cre mouse model comparison

019

Loss of contractile SMCs in TAA of mouse model of Marfan syndrome is compensated by recruitment of collagen depositing cell types

Gharraee, Nazli; Lessner, Susan M.

University of South Carolina, Columbia, SC

- Diameter of ascending aorta increases significantly between 6 and 9 months in Fbn1 C1039G heterozygotes
- There is a loss of SM-MHC but not SMA in the media of ascending aorta in Fbn1 Hets vs WT
- Collagen deposition in the media and aortic annulus of Het mice increases with time compared to WT

020

Smooth muscle cell migration and polarization in response to vascular injury

Khogali, Shiema

University of Toronto, Toronto, ON, Canada

- Smooth muscle cell migration and polarization
- Mechanotransduction in smooth muscle cell polarization
- Smooth muscle cell biology

021

Withdrawn

022

Structure and function of resistance arteries from cardiovascular disease patients are differentially influenced by risk factors and patient characteristics

Bloksgaard, Maria¹; De Mey, Jo¹; Leurgans, Thomas¹; Riber, Lars²; Rasmussen, Lars M.²

1. University of Southern Denmark, Odense C, Denmark
2. Odense University Hospital, Odense C, Denmark

- The media-to-lumen ratio (M:L) of resistance arteries (RA) is increased in hypertension and diabetes
- We evaluated the relationship between structure and function of human RA
- Structure and function of hRA is differentially influenced by disease, drugs and risk factors

Vascular Biology

023

Correction for shrinkage during histological processing allows retrieval of the wall to lumen ratio of biobanked human resistance arteries

Bloksgaard, Maria¹; Rosenstand, Kristoffer¹; Nissen, Inger¹; Marcussen, Niels²; De Mey, Jo¹

1. University of Southern Denmark, Odense C, Denmark
2. Odense University Hospital, Odense C, Denmark

- Structural remodeling of resistance arteries is predictive of future adverse cardiovascular events
- Assessment of remodeling requires measuring the dimensions of the live resistance artery (RA)
- Correcting for histo-processing artifacts allows future research on biobanked RA segments

025

Long non-coding RNAs are dynamically regulated and influence the progression of endothelial-to-mesenchymal transition (EndMT) *in vitro*

Caudrillier, Axelle; Rodor, Julie; Monteiro, João; Deng, Lin; Kok, Fatma; Baker, Andrew H.

University of Edinburgh, Edinburgh, United Kingdom

- Endothelial-to-mesenchymal transition
- Long non-coding RNA
- Vascular remodeling

026

A novel role for prostaglandin-mediated developmental programming in the ductus arteriosus

Yarboro, Michael

Vanderbilt University, Nashville, TN

- PGE2 is a known regulator of DA tone. PGE2 infusion keeps the DA relaxed; COX inhibition causes DA closure
- Unexpectedly, chronic PGE2 inhibition leads to persistent ductus patency (PDA) instead of constriction

- PGE2 appears to mediate a time-dependent developmental program crucial for postnatal function of the DA

027

Role of reactive oxygen species in regulation of contractility of isolated lymphatic vessels

Nepiyushchikh, Zhanna; Mukherjee, Anish; Razavi, Mohammad; Dixon, J. Brandon
Georgia Institute of Technology, Atlanta, GA

- Lymphatic Vessels Dysfunctions. Lymphedema
- Reactive Oxygen Species in Regulation of Collecting Lymphatic Vessels Contractility
- Reactive Oxygen Species and Impaired functions of lymphatic vessels

028

Requisite endothelial reactivation and effective siRNA nanoparticle targeting of Etv2/Er71 in tumor angiogenesis

Kabir, Ashraf Ul¹; Lee, Tae-Jin¹; Pan, Hua²; Berry, Jeffrey C.¹; Krcma, Karen¹; Wu, Jun¹; Hinman, Kristina¹; Novack, Deborah V.¹; Mecham, Robert P.¹; Wickline, Samuel A.²; Miller, Mark J.¹; Choi, Kyunghee¹

1. Washington University School of Medicine in St. Louis, St. Louis, MO

2. University of South Florida, Morsani College of Medicine, Tampa, FL

- Etv2 is a unique marker for tumor endothelial cells and required for tumor angiogenesis
- Etv2 is a redox sensitive transcription factor, which links hypoxia and VEGF mediated tumor angiogenesis
- Systemic delivery of Etv2 siRNA nanoparticles inhibited tumor angiogenesis without cardiovascular side effects

029

Molecular mechanism of differential VEGF signaling regulation by Epsin and Dab2 for neovascularization

Rahman, Habibunnabi

Boston Children's Hospital, Boston, MA

- Epsin mediated endocytosis
- VEGFR2 dependent angiogenesis
- Therapies modulating neovascularization

030

Mimicking physiological shear stress conditions *in vitro* by using the versatile ibidi Perfusion System

Wagner, Helga¹; Öffner, Wolfgang²; Zantl, Roman¹

1. ibidi GmbH, Martinsried, Germany

2. ibidi GmbH, Plankstadt, Germany

- Flow conditioning is a substantial parameter to approach physiological conditions in EC culture
- Defined flow conditions of the experimental setup are important for reproducible results

- The ibidi Perfusion System is an easy-to-use solution to obtain striking new results in vascular biology

031

Understanding the role of oxidative stress in altering cardiovascular disease severity in elastin insufficiency

Troia, Angela¹; Halabi, Carmen²; Danback, Joshua²; Kovacs, Attila²; Kozel, Beth A.¹

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

2. Washington University School of Medicine, St. Louis, MO

- Elastin insufficiency induced hypertension and vascular stiffness
- Elastin insufficiency is associated with increased vessel wall oxidative stress
- Genetic and drug manipulations that reduce NOX activity improve HTN and functional stiffness

032

Characterizing the role of RHOA in regulating cranial vascular integrity

Pillay, Laura¹; Butler, Matthew G.¹; Davis, Andrew E.¹

Castranova, Daniel A.¹; Gore, Aniket V.¹; Swift, Matthew R.¹; Iben, James R.¹; Stan, Radu V.²; Weinstein, Brant M.¹

1. NIH, Bethesda, MD

2. Dartmouth Medical School, Lebanon, NH

- A dominant mutation in zebrafish "Bloody Mary" mutants generates an intracranial hemorrhage phenotype
- The causative mutation in "Bloody Mary" is likely a missense mutation in a zebrafish RHOA orthologue
- Vascular integrity in developing zebrafish is highly sensitive to either decreased or increased RHOA dosage

033

Development of the pectoral fin vasculature in zebrafish embryos

Paulissen, Scott; Castranova, Daniel A.; Weinstein, Brant M.

NICHHD, NIH, Bethesda, MD

- Vascular development
- Zebrafish
- Lumenization

034

Determine the mechanism that governs CD151-mediated inhibition of vascular hyperpermeability

Chen, Junxiong

OUHSC, Oklahoma City, OK

- CD151 regulate endothelial barrier function
- CD151 is associated with extracellular matrix deposition
- CD151 may regulate COX-2-PGE2 via JAK/STAT signaling pathway

035

Biomarkers of cerebral small vessel endotheliopathy*Elahi, Fanny¹; Altendahl, Marie²; Staffaroni, Adam²; Casaletto, Kaitlin²; Neuhaus, John¹; Goetzl, Edward³; Kramer, Joef*

1. University of California, San Francisco, San Francisco, CA
2. Memory and Aging Center, UCSF, San Francisco, CA
3. Geriatric Research Center, UCSF, San Francisco, CA

- biomarker discovery for cerebral small vessel endotheliopathy
- exosome-derived cargo proteins as biomarkers of vascular endotheliopathy
- diagnosis of cerebral small vessel disease

036

Jagged1-Notch signaling increases metastatic behavior in tumor cells*Herts, James; Chaudhri, Reyhaan A.; Du, Jing; Gordon, Benjamin; Kitajewski, Jan K. University of Illinois Chicago, College of Medicine, Chicago, IL*

- Ligand-specific Notch Decoys exhibit differential effects on sprouting angiogenesis
- In tumor cells, Jag1 and Dll4 differentially regulate EMT-related genes and adhesion molecules
- Jag1/Notch blockade reduces tumor cell metastatic behavior

037

Hemogenic endothelium in human fetal liver?*Choi, Yoon Jung¹; Hayes, Brian²; Hadland, Brandon²; Zheng, Ying¹*

1. University of Washington, Seattle, WA
2. Fred Hutchinson Cancer Research Center, Seattle, WA

- Human fetal liver hematopoiesis
- Human fetal liver-specific angiocrine factors
- Hematopoietic populations present in the human fetal liver

038

AAV-mediated delivery of virus-derived apoptosis and inflammasome inhibitors reduces liver allograft vasculopathy and LPS-induced ascitic inflammation in mice*Ambadapadi, Sriram¹; Ildefonso, Cristhian J.²; Yaron, Jordan R.¹; Dornstauder, Quinn¹; Zhang, Liqiang¹; Lewin, Alfred S.²; Lucas, Alexandra¹*

1. Arizona State University, Tempe, AZ
2. University of Florida, Gainesville, FL

- Myxomavirus-derived apoptosis and inflammasome inhibitors reduce renal allograft vasculopathy
- AAV-mediated delivery of Myxomavirus-derived anti-inflammatories is an effective mode for delivery
- Myxomavirus-derived apoptosis and inflammasome inhibitors reduce LPS-induced inflammation in the ascites

Vascular Tissue Engineering

039

Micropatterning induced morphological and functional alterations of endothelial colony forming cells (ECFCs)*Hagen, Matthew; Hinds, Monica T. Oregon Health & Science University, Portland, OR*

- ECFCs from circulating progenitors have an endothelial phenotype suitable for tissue engineering
- Micropatterning drives fluid shear-like athero-protection in ECs. It has not been studied in ECFCs
- We have generated durable ECFC micropatterns. Further study on MPECFC function is needed

040

Reactive ion etching of vascular graft materials enhances endothelialization*Hinds, Monica¹; Jurney, Patrick¹; Anderson, Deirdre EJ¹; Pohan, Grace²; Yim, Evelyn KF²*

1. Oregon Health & Science University, Portland, OR
2. University of Waterloo, Waterloo, Canada

- Modification of PVA biomaterials is required to support endothelialization of the surface
- Reactive ion etching of PVA with O₂ and N₂ increased the Nitrogen content and hydrophilicity of the surface
- Etching of PVA with O₂ and N₂ increased the available amines and supported endothelial cell attachment

041

Islet-on-a-Chip: A vascularized micro-organ approach to enhance islet function ex vivo*Bender, Hugh¹; Wortham, Matthew²; Sander, Maik²; Hughes, Christopher C.¹*

1. University of California, Irvine, Irvine, CA
2. University of California, San Diego, San Diego, CA

- Pancreatic islets survive poorly and do not respond to glucose stimulation when maintained in culture
- We have developed a vascularized, islet-on-a-chip platform to enhance islet survival and function ex vivo
- Islets within the platform secrete insulin in response to glucose and pharmacologic stimulation

042

Characterizing human induced pluripotent stem cell-derived endothelial cells under fluid flow-induced shear stress: comparisons to primary endothelial cell types

Soos, Agnes; Fitzsimmons, Ross E.; Santerre, J Paul; Simons, Craig A.

University of Toronto, Toronto, ON, Canada

- Induced pluripotent stem cell-derived endothelial cells respond to extended fluid shear conditioning
- iPSC-derived endothelial cells demonstrate some similarity to primary vascular endothelial types
- Ability to form sprouts and networks supports angiogenic potential of iPSC-derived endothelial cells

043

Raman microspectroscopy for the marker-free characterization of smooth muscle cells from different tissue origins

Marzi, Julia¹; Brauchle, Eva¹; Schenke-Layland, Katja¹; Rolle, Marsha W.²

1. University of Tuebingen, Tuebingen, Germany

2. Worcester Polytechnic Institute, Worcester, MA

- label-free characterization of smooth muscle cells in situ
- vascular tissue engineering
- Raman microspectroscopy

044

Modeling fibrin and von Willebrand factor binding within bioengineered microvessels

Rayner, Samuel¹; Gunnarsson, Celina¹; Chen, Junmei²; Chung, Dominic²; Lopez, Jose²; Zheng, Ying¹

1. University of Washington, Seattle, WA

2. Bloodworks Northwest Research Institute, Seattle, WA

- Characterize fibrin binding to VWF fibers within a microvessel model
- Explore whether fibrin may play a role in the pathogenesis of thrombotic microangiopathies
- Understand the optimal flow conditions under which VWF-fibrin binding occurs

046

Assembly of modular tissue engineered blood vessels for modeling focal pathologies

Strobel, Hannah¹; Piola, Marco²; Fiore, Gianfranco B.³; Soncini, Monica²; Alsborg, Eben⁴; Rolle, Marsha W.¹

1. Worcester Polytechnic Institute, Worcester, MA

2. Politecnico di Milano, Milano, Italy

3. Dipartimento di Elettronica, Informazione e Bioingegneria, Milano, Italy

4. Case Western Reserve University, Cleveland, OH

- Developed modular TEBV from ring sub-units with localized regions of microsphere incorporation
- Fabricated custom luminal flow bioreactor for TEBV culture, which also enables endothelialization

- This modular system may potentially be used for fabricating focal disease models

047

The key role of fibronectin in the maturation of tissue engineered blood vessels

Di Paolo, Joseph¹; Pezzoli, Daniele²; Kumra, Heena¹;

Candiani, Gabriele²; Mantovani, Diego²; Reinhardt, Dieter¹

1. McGill University, Montreal, Canada

2. Université Laval, Quebec City, Canada

- Addition of plasma fibronectin increases the elastic modulus of tissue engineered blood vessels
- It also increase the production of tropoelastin and elastic fiber related proteins
- It enhanced the deposition and assembly of tropoelastin and other elastic fiber related proteins

048

Withdrawn

Mechanotransduction

049

Withdrawn

050

Endothelial Piezo1 and Gq/G11 mediate inflammatory signaling induced by disturbed flow

Albarran Juarez, Julian¹; Althoff, Till F.²; Wang, Sheng-Peng¹; Wettschureck, Nina¹; Offermanns, Stefan¹

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

2. Charité Berlin, Berlin, Germany

- Investigate the role that Piezo1 and Gq/G11-mediated signaling play in endothelial responses to disturbed flow
- knockdown of Piezo1 and Gq/G11 inhibited induction of NF-kB activation both *in vitro* and *in vivo*
- Endothelial Piezo1 and Gq/G11 are not only essential for sensing laminar flow but also disturbed flow

051

Phosphoproteomic analysis revealed that ultrasound induces phosphorylation of adherens junctional proteins in cardiac endothelial cells

Emechebe, Uchenna¹; Ammi, Azzdine Y.¹; Davies, Catherine M.¹; Lyon, Kristin¹; Jacobs, Jor²; Alkayed, Nabil¹; Barnes, Anthony¹; Kaul, Sanjiv¹

1. Oregon Health and Science University, Portland, OR

2. Pacific Northwest National Laboratory, Richland, WA

- We used a global proteomics approach to understand how ultrasound alters vascular function

- Our approach yielded ~200 phosphopeptides that are significantly altered by ultrasound in cardiac endothelia
- Ultrasound increased the phosphorylation of adherens junctional proteins, including beta catenin

052

Filamin A stabilizes a mechanosensitive complex containing VE-cadherin and PECAM-1 at the endothelial surface to promote angiogenesis

Duran, Camille¹; Torrie, Melanie²; Abbey, Colette A.¹; Kaunas, Roland¹; Essner, Jeffrey J.²; Bayless, Kayla¹

1. Texas A&M Health Science Center, College Station, TX
2. Iowa State University, Ames, IA

- Filamin A complexes and colocalizes with the mechanosensitive proteins, VE-Cadherin and PECAM-1
- Silencing Filamin A inhibits EC sprouting and VE-Cadherin and PECAM-1 localization within junctions
- CRISPR/Cas-9-generated Filamin A mutant zebrafish are reduced in size

053

Biomechanical regulation of stem cell differentiation for vascularized tissue regeneration

Sligar, Andrew; Lee, Jason; Deb, Chaarushena; Le, Victoria; Baker, Aaron B.

The University of Texas at Austin, Austin, TX

- Applied shear stress alters vascular marker expression in mesenchymal stem cells
- Applied shear stress creates synergistic activation of various transcription factors
- Rats treated with conditioned MSCs showed increased vascularity and perfusion

054

Endothelial cell shear stress mechanotransduction impacts glucose metabolism

Clyne, Alisa; Basehore, Sarah; Garcia, Jonathan

Drexel University, Philadelphia, PA

- Little is known about how blood flow regulates endothelial glucose metabolism in health and disease
- Our data show that steady laminar and oscillating disturbed flow differentially regulate glucose metabolism
- Endothelial cells in oscillating disturbed flow maintain eNOS O-GlcNAcylation, which inhibits phosphorylation

Vascular Mechanics

055

3D-Registration of MRI, histology and computational fluid dynamics data of human carotid plaques

Moerman, Astrid M.; Dilba, Kristine; Postema, Erik Jan; van Gaalen, Kim; Gijzen, Frank J.; Wentzel, Jolanda; van der Lugt, Aad; Rouwet, Ellen V.; Poot, Dirk H.J.; Klein, Stefan; van der Steen, Antonius F.W.; van der Heiden, Kim

Erasmus Medical Center Rotterdam, Rotterdam, Netherlands

- Changes in wall shear stress (WSS) during plaque progression affect underlying plaque composition
- Patient specific flow and geometry data were obtained by *in vivo* MRI to create a 3D WSS map
- A tool was created to register the 3D WSS map to 2D histological sections of human carotid plaques

056

Effect of lowering heart rate on wall shear stress and atherosclerosis

Xing, Ruoyu¹; Moerman, Astrid M.¹; Ridwan, Yanto¹; van der Steen, Antonius FW¹; Evans, Paul²; Gijzen, Frank JH¹; van der Heiden, Kim¹

1. Erasmus Medical Center, Rotterdam, Netherlands

2. University of Sheffield, Sheffield, United Kingdom

- Ivabradine reduced heart rate in atherosclerotic mice
- Ivabradine increased normalized peak flow and WSS level during systole in atherosclerotic mice
- Ivabradine did not induce changes in plaque composition

057

Characterizing heterogeneity of venous material properties in porcine central venous thrombosis model

Vekilov, Dragoslava¹; Schwein, Adeline²; Bismuth, Jean²; Grande-Allen, K. Jane¹

1. Rice University, Houston, TX

2. Houston Methodist Hospital, Houston, TX

- Characterizing material properties of healthy porcine vein tissue
- Assessing material properties of venous wall in porcine central venous thrombosis model
- Analyzing the time scale of changes to central venous system vessel wall in response to thrombosis

058

Aged coronary resistance microvessels undergo adverse remodeling similar to early Type 2 diabetes

Trask, Aaron; McCallinart, Patricia; Sunyecz, Ian L. The Research Institute at Nationwide Children's Hospital, Columbus, OH

- Coronary Microvascular Disease
- Type 2 Diabetes
- Aging

059

The effect of G protein-coupled estrogen receptor deletion on the common carotid artery mechanical properties

Clark, Gabrielle; Abshire, Caleb; Lindsey, Sarah; Miller, Kristin

Tulane University, New Orleans, LA

- G protein-coupled estrogen receptor
- Arterial Mechanics
- Constitutive modeling

060

The role of shear stress in localization and progression of atherosclerosis in porcine coronary arteries

Hoogendoorn, Ayla¹; Kok, Annette M.¹; Hartman, Eline M.J.¹; Casadonte, Lorena²; Peters, Ilona¹; Visser - te Lintel Hekker, Maaike¹; van Gaalen, Kim¹; van der Heiden, Kim¹; Gijzen, Frank J.¹; Duncker, Dirk-Jan¹; van der Steen, Antonius F.W.¹; Wentzel, Jolanda¹

1. Erasmus Medical Center, Rotterdam, Netherlands

2. Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands

- Serial and spatial analysis of the influence of shear stress on coronary plaque growth in pigs
- Surprisingly, there are fast and slow responding pigs that show big differences in plaque morphology
- Low wall shear stress predicts coronary plaque growth

061

The role of type VIII collagen in arterial vessel stiffening

Mohabeer, Amanda¹; Hou, Guangpei¹; Zhang, Hangjun¹; Kroetsch, Jeffrey¹; Bolz, Steffen-Sebastian¹; Heximer, Scott¹; Assoian, Richard K.²; Bendeck, Michelle P.¹

1. University of Toronto, Toronto, ON, Canada

2. University of Pennsylvania Health System, Philadelphia, PA

- Collagen-VIII (Col8) is upregulated in CVD and inhibits the Rho GTPase RhoA
- Vasoconstriction to phenylephrine was enhanced in Col8^{-/-} relative to Col8^{+/+} murine carotids
- Pressure-dependent increases in diameter were significantly greater in Col8^{-/-} murine carotids

Other Vascular Matrix Biology and Bioengineering

062

Obesity adversely impacts lymphatic function in lymphedema through a loss in pumping pressure

Nelson, Tyler¹; Nepiyushchikh, Zhanna²; Dixon, J. Brandon²

1. Georgia Institute of Technology, Atlanta, GA

2. Georgia Tech, Atlanta, GA

- Obesity and lymphedema
- Lymphatic function and remodeling
- Inflammation and lymphedema development

063

Protein-engineered hydrogels for transplantation of induced pluripotent stem cell-derived endothelial cells in a mouse model of peripheral arterial disease

Foster, Abbygail; Dewi, Ruby E.; Cai, Lei; Hou, Luqia; Strassberg, Zachary; Alcazar, Cynthia; Heilshorn, Sarah C.; Huang, Ngan F.

Stanford University, Stanford, CA

- Injectable hydrogel, SHIELD, provides mechanical protection from cell membrane damage during transplantation
- SHIELD enhances iPSC-EC proliferation and proangiogenic factor secretion during *in vitro* hypoxic culture
- SHIELD enhances *in vivo* iPSC-EC retention and promotes improved re-vascularization of the ischemic limb

064

Engineering 3D vascular networks through tunable bio-ink design

Seymour, Alexis; Dubbin, Karen; Berry, Alex; Hori, Yuki; Heilshorn, Sarah

Stanford University, Stanford, CA

- A fundamental limitation of tissue engineering is the inability to create scalable, vascularized constructs
- While 3D printing allows complex scaffold architectures, many bio-inks do not adequately mimic native matrix
- We have created a family of highly tunable bio-inks for 3D printing of endothelial and support cells

065

Evaluation of endothelial cell phenotype in the rat mesentery culture model

Motherwell, Jessica¹; Murfee, Walter Lee^{1,2}

1. Tulane University, New Orleans, LA

2. University of Florida, Gainesville, FL

- Challenges in tissue engineering biomimetic models include recapitulating physiological complexity

- EC sprouts in *ex vivo* tissue culture model are similar to *in vivo* EC sprouts from *in vivo* wound healing model
- Novel *ex vivo* rat mesentery culture model to study angiogenesis and microvascular networks

066

Systems biology approaches identify a new disease pathway in mice with severe Marfan syndrome

Caescu, Cristina; Ramirez, Francesco

Icahn School of Medicine at Mount Sinai, New York, NY

- Limited pharmacological options for thoracic aortic aneurysm (TAA), a major manifestation of Marfan syndrome
- Experimental and bioinformatics approaches in mice identify a new TAA- related pathway
- Characterization of MFS mice with postnatal inactivation of Hpk2 indicates a new contributor to TAA

067

Evaluating human umbilical cord perivascular cells as an alternative to bone marrow-derived mesenchymal stromal cells for heart valve tissue engineering

Parvin Nejad, Shouka; Simmons, Craig A.

University of Toronto, Toronto, ON, Canada

- Serum-free expansion of mesenchymal stromal cells
- Self-renewal and differentiation capacity of serum-free expanded mesenchymal stromal cells
- *Ex vivo* extracellular matrix synthesis in serum- and xeno-free culture

068

Hemodynamic perturbations alter the mechanical properties of chick dorsal aorta in development

Espinosa, Gabriela; Taber, Larry; Wagenseil, Jessica E.

Washington University in St. Louis, St. Louis, MO

- Vitelline vein ligation reduces of blood flow both immediately and 7 days post-surgery
- Decreased blood flow reduces elastin content in the developing dorsal aorta
- Altered extracellular matrix changes the viscoelastic properties of the dorsal aorta

069

Imaging cellular glycan epitopes and glycoproteins using glycosyltransferases

Wu, Zhengliang; Person, Anthony; Fryxell, Dan

Bio-Techne, Minneapolis, MN

- We describe here a method for enzyme-based glycan imaging using glycosyltransferases

- this method offers precise detection of target glycans
- highly specific technique will facilitate the detection and characterization of biologically important glycans

Vascular Cell Biology I

070

Secretion of the TLR4 ligand, NAMPT is essential to NAMPT-mediated resistance to cytokine-induced lung cell apoptosis and to enhanced acute NFκB-mediated inflammation

Garcia, Joe G.N.; Chaing, Sara; Oita, Radu

University of Arizona, Tucson, AZ

- NAMPT is an important cytozyme involved in vascular influences
- NAMPT regulates endothelial cell apoptosis
- NAMPT cleavage is critical to NAMPT secretion and pro-inflammatory effect via TLR4 binding

071

Junction-based lamellipodia drive endothelial cell rearrangements via a VE-cadherin/F-actin based oscillatory ratchet mechanism *in vivo*

Belting, Heinz-Georg¹; Paatero, Ilkka¹; Sauter, Loic¹; Lee, Mink-Young¹; Lagendijk, Anne Karine²; Heutschi, Daniel¹; Hogan, Benjamin M.²; Affolter, Markus¹

1. Universitaet Basel, Biozentrum, Basel, Switzerland

2. University of Queensland, St Lucia, Brisbane, QLD, Australia

- We have analyzed dynamics and function of junctional components during vascular remodeling *in vivo*
- Morphogenetic EC behaviors are driven by polarized and oscillating junction-based lamellipodia (JBL)
- JBL function as ratchet via VE-cad/F-actin interaction and provide the physical means for cell rearrangements

072

Endothelial cell autophagy in angiogenesis and solid tumor progression

Monkkonen, Teresa; Marsh, Timothy; Debnath, Jayanta

University of California, San Francisco, San Francisco, CA

- Autophagic flux is present in endothelial cells of pancreatic neuroendocrine tumors
- Ablation of endothelial autophagy may promote extravasation of PyMT breast cancer cells
- Endothelial cell autophagy may maintain vascular integrity and barrier function

073

Shaping waves of BMP Inhibition during vascular growth

Guihard, Pierre

University of California, Los Angeles, Los Angeles, CA

- vasculogenesis is controlled by waves of BMP inhibition

- Controlled by a BMP9/ALK/Endoglin Signaling
- Disruption of these inhibitors leads to abnormal vasculature and AVMs

074

Excess centrosomes affect endothelial cell junctions and polarity

Berlin, Danielle; Kushner, Erich J.; Bautch, Victoria L. University of North Carolina at Chapel Hill, Chapel Hill, NC

- Role of centrosome homeostasis in interphase endothelial cells and sprouting angiogenesis
- Effects of excess centrosomes on adherens junctions
- Effects of excess centrosomes on cell repolarization

075

Laminin-dystroglycan signaling regulates retinal arteriogenesis

Biswas, Saptarshi; Bachay, Galina; Hunter, Dale D.; Brunken, William J.

SUNY Upstate Medical University, Syracuse, NY

- Laminins in the vascular basement membrane
- Dystroglycan
- Dll4/Notch signaling and arteriogenesis

076

Vascular thiol isomerase ERp72 is critical for endothelial injury-induced thrombus formation

Wu, Yi

Soochow University, Suzhou, China

- Vascular ERp72 is critical for endothelial cells-injury-induced thrombosis
- The second and third CGHC motifs of ERp72 are important
- ERp72 is a dual regulator of thrombin generation and platelet accumulation

077

Disruption of the regulator of G protein signaling 14; A novel mechanism inhibiting vasoconstriction

Zhang, Jie; Guers, John; Yoon, Seonghun; Vatner, Dorothy E.; Vatner, Stephen F.

Rutgers University, New Jersey Medical School, Newark, NJ

- RGS14
- Hypertension
- Angiotensin II

078

Macrophage-thrombus interactions mediate repair after vascular injury

Clay, Hilary

University of California, San Francisco, San Francisco, CA

- Thrombus removal is rate limiting during vascular repair

- Macrophages are required for clearing the cellular components of the thrombus
- Macrophage phagocytosis of cellular debris at the injury site is mediated by plasma coagulation Factor XIII

079

Endothelial actin dynamics during blood vessel morphogenesis

Phng, Li-Kun

RIKEN Center for Developmental Biology, Kobe, Japan

- Endothelial cells are highly plastic in shape
- Endothelial cells generate diverse actin cytoskeleton structures during angiogenesis *in vivo*
- Actin cytoskeleton of different subcellular localization and dynamics drive distinct steps of angiogenesis

080

The transcription factor Foxc1 is required for proper vascular development during postnatal retinal angiogenesis

Norden, Pieter; Liu, Ting; Kume, Tsutomu

Northwestern University School of Medicine, Chicago, IL

- The role of Foxc1 & Foxc2 in postnatal angiogenesis is not well understood
- Foxc1 is required for postnatal retinal angiogenesis
- Foxc1 & Foxc2 regulate expression of key genes related to several signaling pathways involved in angiogenesis

081

Nck adaptor proteins modulate atherogenic endothelial activation in response to disturbed flow

Alfaidi, Mabruka; Green, Jonette M; Orr, A. Wayne

LSU Health Sciences Center - Shreveport, Shreveport, LA

- Hemodynamic shear stress induces atherogenic endothelial activation
- Pak2 regulates NF-kB activation by flow
- Nck1 but not Nck2 plays a dominant role in flow induced Pak2 and NF-kB activation

082

The increased Angiopoietin-1 released from isolated mouse lung pericytes following stimulation with hemorrhage-primed neutrophils is significantly suppressed in endothelial cell:pericyte co-culture

Lomas-Neira, Joanne; Petitpas, Kaitlyn; Chung, Chun-Shiang

Rhode Island Hospital/Brown University, Providence, RI

- Primed neutrophils increase pericyte Angiopoietin-1 release into culture supernatant
- In EC:pericyte co-culture, primed neutrophils significantly reduced Angiopoietin-1 release
- EC:pericyte interactions alter their individual responsiveness to primed neutrophils

083

Phosphate transport and mineral deposition at the vascular maternal-fetal interface

Wallingford, Mary¹; Neradugomma, Naveen K.¹; Chalek, Julian²; Rincon, Monica³; Pereira, Leonardo³; Mao, Qingcheng¹; Giachelli, Cecilia M.¹

1. University of Washington, Seattle, WA

2. Metis, Seattle, WA

3. Oregon Health & Science University, Portland, OR

- Phosphate dysregulation can severely impact vascular function and is poorly understood in placenta
- We used molecular biology and histology to examine Pi in tissues, cell lines, and biological fluids
- Herein, we present the first comparative characterization of phosphate biology at the M-F interface

084

Excessive plasmin activity promotes endothelial Ripk3 transcription and murine embryonic vascular rupture

Colijn, Sarah; Ingram, Kyle; Menendez, Matthew; Muthukumar, Vijay; Silasi-Mansat, Robert; Lupu, Florea; Griffin, Courtney T.

Oklahoma Medical Research Foundation, Oklahoma City, OK

- Embryos with excessive plasmin activation have elevated RIPK3 in endothelial cells at midgestation
- Genetically reducing either plasmin activation or Ripk3 rescues embryos from lethal vascular rupture
- Plasmin works through PAR4 to upregulate Ripk3 transcription in cultured endothelial cells

Other Developmental Vascular Biology and Genetics

085

Investigation of PTPN14 interactions in balancing vascular integrity and angiogenesis

Mamai, Ons; Akhurst, Rosemary J.

University of California, San Francisco, San Francisco, CA

- HHT patient phenotype
- angiogenesis
- modifiers gene

086

Cell proliferation in fetal elastin heterozygous mice suggests mechanism underlying Williams Syndrome cardiac disease

Watson, Anderson; Levin, Mark; Yu, Zu-Xi; Kozel, Beth A. NIH/NHLBI, Bethesda, MD

- Elastin insufficiency is associated with increased risk of sudden death in humans
- Eln+/- coronaries reveal increased SMC proliferation from E9.5, persisting later into gestation
- No prenatal differences in endothelial cell proliferation were noted in Eln+/- vs WT coronaries

087

The phenotypic and functional properties of mouse yolk-sac-derived embryonic macrophages

Yosef, Neila¹; Vadakkan, Tegy J.¹; Park, June Hee²; Poche, Ross¹; Thomas, Jean-Leon²; Dickinson, Mary E.¹

1. Baylor College of Medicine, Houston, TX

2. Yale School of Medicine, New Haven, CT

- Established an *in vitro* model of mouse yolk-sac-derived embryonic macrophages
- EMs have a higher pro-angiogenic potential compared to adult macrophages
- EMs preferentially matured into microglia when co-cultured with mouse neural stem cells

088

The Wnt inhibitor Apccd1 coordinates vascular remodeling and barrier maturation in retinal blood vessels

Mazzoni, Jenna¹; Smith, Julian R.¹; Cutforth, Tyler¹; Shahriar, Sanjid¹; Ceja, Bernardo²; Agalliu, Dritan¹

1. Columbia University Medical Center, New York, NY

2. University of California at Irvine, Irvine, CA

- Apccd1 is expressed in retinal endothelial cells during angiogenesis and barrier formation
- Apccd1 precisely modulates Wnt/Norrin signaling activity in the retinal endothelium
- Apccd1 coordinates the timing of vascular pruning and barrier maturation in retina

089

Tissue specific origin of endothelial cells

Yao, Jiayi; Guihard, Pierre; Blazquez-Medela, Ana; Hoang, Jonathan; Bostrom, Kristina; Yao, Yucheng

UCLA, Los Angeles, Los Angeles, CA

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- ECs play multiple roles in organogenesis and involve in the regulation of biological processes
- tissue-specific ECs display the morphological distinction and specific gene signatures
- tissue-specific ECs express tissue-specific markers at early developmental stages in lungs, brain and liver

090

Thrombospondin1 (TSP1) replacement prevents cerebral cavernous malformations

Lopez-Ramirez, Miquel Alejandro¹; Fonseca, Gregory¹; Zeineddine, Hussein A.²; Girard, Romuald²; Moore, Thomas²; Pham, Angela¹; Lagarrigue, Frederic¹; Lawler, Jack³; Glass, Christopher K.¹; Awad, Issam A.²; Ginsberg, Mark H.¹

1. University of California, San Diego, La Jolla, CA
2. The University of Chicago Medicine and Biological Sciences, Chicago, IL
3. Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

- Krit1 inactivation in brain endothelium changes the expression of genes involved in cardiovascular development
- Loss of Krit1 results in dramatic suppression of TSP1, a potent endogenous angiogenesis inhibitor
- Suppression of TSP1 is an important downstream effect of the elevation in KLF4 that follows loss of KRIT1

091

GATA2 maintains the identity of lymphovenous valve-forming endothelial cells

Mahamud, Md Riaj

University of Oklahoma Health Science Center, Oklahoma City, OK

- Lymphatic vasculature development
- Mutation in GATA2 causes lymphatic vasculature defect
- GATA2 maintain the identity of lymphovenous valve-forming cells

092

ALK1 ligands in zebrafish cardiovascular development

Capasso, Teresa; Li, Bijun; Roman, Beth L.

University of Pittsburgh, Pittsburgh, PA

- We are interested in HHT and the ALK1 signaling pathway, specifically looking the BMP ligands for ALK1
- We are using zebrafish as a model system and have mutated the alk1 ligands, bmp9, bmp10, bmp10-like
- We found that loss of bmp10 causes cardiac abnormalities and vascular and cardiac abnormalities in adulthood

093

Elucidating the role of EphB4/EphrinB2 signaling in zebrafish endocardial morphogenesis

Fontana, Federica¹; Haack, Timm²; Moghtadaei, Motahareh²; Abdellilah-Seyfried, Salim²

1. Universität Potsdam Abteilung, Potsdam, Germany
2. Hannover Medical School, Hannover, Germany

- EphrinB2a expression is restricted to endocardial cells at the junction of the atrium and ventricle
- EphrinB2a is involved in establishing endocardial chamber boundaries
- Loss of EphrinB2a causes defects in cardiac chamber morphogenesis and valve leaflet formation

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Lymphatic Development

101

Deciphering the role of JUNB in lymphangiogenesis

Gutierrez Miranda, Laura¹; Tempelhof, Hanoch²; Angel, Peter¹; Yaniv, Karina²; Schorpp-Kistner, Marina¹

1. German Cancer Research Center, Heidelberg, Germany
2. Weizmann Institute of Science, Rehovot, Israel

- Morpholino-mediated downregulation of junba/junbb revealed the role of JUNB in zebrafish lymphangiogenesis
- Generation and characterization of junba/junbb zebrafish mutants using the CRISPR-Cas system
- JUNB is upregulated during an "in vitro" differentiation system of mESCs into LECs

102

Mechanisms regulating lymphangiogenesis in physiology and pathology

Chen, Hong

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

- hyperglycemia induces VEGFR3 degradation and impairs lymphangiogenesis
- epsin upregulation causes enhanced degradation of VEGFR3 in diabetes
- sustained VEGFR3 signaling upon epsin loss is crucial for restoring impaired lymphangiogenesis in diabetes

103

Transcriptional regulation of postnatal lymphatic valve maturation and maintenance by Foxc1 and Foxc2

Norden, Pieter; Liu, Ting; Shackour, Tarek; Kume, Tsutomu
Northwestern University School of Medicine, Chicago, IL

- Mechanisms of lymphatic valve formation, maturation, and maintenance are not well understood
- Foxc1 and Foxc2 have a key role in postnatal valve maintenance and maturation
- Identifying mechanisms regulated by Foxc1 and/or Foxc2 will help to treat lymphedema patients

104

Tightly balanced S1P-S1PR1 signaling is required for proper lymphatic vessel development

Ochsenbein, Alexandra; Wilmering Wetter, Barbara; Leonhard, Sabine; Chang, Lena; Beerli, Christian; Guibourdenche, Christel; Seuwen, Klaus; Jurisic, Giorgia
Novartis, Basel, Switzerland

- lymphangiogenesis, molecular regulators
- in vivo, murine, development
- sphingosine-1-phosphate (S1P), S1PR1

105

Sphingosine-1-phosphate receptor 1 regulates lymphatic vascular patterning

Genq, Xin¹; Yanagida, Keisuke²; Hla, Timothy³; Srinivasan, Sathish¹

1. Oklahoma Medical Research Foundation, Oklahoma City, OK

2. Harvard Medical School, Boston, MA

3. Boston Children's Hospital, Harvard Medical School, Boston, MA

- Lymphatic development
- Shear Stress
- S1p/S1pr1 signaling

106

Emerging roles of the chromatin-remodeling SWI/SNF ATPase BRG1 in omental lymphatic development

Menendez, Matthew; Drozd, Anna M.; Chmielewska, Joanna J.; Griffin, Courtney T.

Oklahoma Medical Research Foundation, Oklahoma City, OK

- Macrophage expression of BRG1 is required to maintain blood-lymphatic separation in the omentum
- BRG1 suppresses necroptosis in omental macrophages by inhibiting RIPK3 expression
- Genetic reduction of Ripk3 rescues blood entry into developing Brg1 mutant omental lymphatics

107

ERK5 is a novel regulator of lymphatic development

Kim, Ah-Ra

Gwangju Institute of Science and Technology, Gwangju, Republic of Korea

- ERK5 is essential regulator for lymphatic development
- ERK5 activity is regulated by cGMP-PKG-MEKK3 signaling cascade during lymphatic development
- PDE5 appears to promote inactivation of ERK5

108

An in vivo screen using zebrafish to identify small molecules that inhibit lymphatic vessel growth

Shih, Yu-Huan¹; Portman, Daneal E.¹; Welsh, Christofer M.²; Shin, Masahiro³; Lawson, Nathan D.¹

1. University of Massachusetts Medical Sch, Worcester, MA

2. Worcester Polytechnic Institute, Worcester, MA

- Lymphatic vessels are essential for fluid homeostasis and involved in pathogenic processes
- Identification of small molecules with anti-lymphatic activity using phenotype-based screen in zebrafish

- Small molecules selectively inhibiting lymphangiogenesis are potential leads for therapeutics

109

A novel sox18 zebrafish mutant showing subtle lymphatic defects, highly enhanced under perturbed Vegf-C signaling

Moleri, Silvia; D'Angelo, Donatella; Pezzotta, Alex; Brix, Alesia; Beltrame, Monica

Universita' degli Studi di Milano, Milano, Italy

- a novel sox18 mutant allele causes subtle defects in thoracic duct formation in homozygous state
- when challenged with perturbed VegfC signaling, TD defects are exacerbated even in sox18 hets
- our data reinforce the notion of an involvement of sox18 in zebrafish lymphatic development

110

RASA1 regulates endothelial cell export of the vascular basement membrane protein collagen IV to control development of the lymphatic and blood vascular systems

King, Philip; Chen, Di; Lapinski, Philip

University of Michigan Medical School, Ann Arbor, MI

- RASA1 is required for developmental lymphangiogenesis and angiogenesis in mice
- RASA1 promotes LEC and BEC survival during developmental lymphangiogenesis/angiogenesis
- RASA1 is required for EC export of the basement membrane protein collagen IV

**Transcriptional Control/
Gene Regulation**

111

Mef2 transcription factors are essential for endothelial function

Lu, Yao Wei; Schwarz, John

Albany Medical College, Albany, NY

- Combined deletion of endothelial Mef2a/c/d leads to lung hemorrhage and death
- Mef2a/c/d deletion results in a highly proliferative endothelium
- Endothelial Mef2a/c/d are redundantly required for Klf2 and Klf4 expression

112

VEGF Regulates gene expression through a MAPK-ERG-p300 transcriptional network

Wythe, Joshua¹; Cantu-Gutierrez, Manuel¹; Khyzha, Nadiya²; Wilson, Michael D.³; Fish, Jason E.²

1. Baylor College of Medicine, Houston, TX

2. University Health Network, Toronto, ON, Canada

3. Hospital for Sick Children, Toronto, ON, Canada

- VEGF stimulation of DLL4 transcription requires MAPK/ERK phosphorylation of the ETS family member, ERG
- Like DLL4, transcription of a network of VEGF-dependent genes require MAPK/ERG/p300
- A highly conserved ERG-bound enhancer is required for VEGF induction of the angiogenic gene, HLX

113

Profiling the endothelial translome *in vivo* using "AngioTag" zebrafish

Miller, Mayumi¹; Gildea, Derek²; Monzo, Kathryn¹; Williams-Simons, Lisa¹; Pham, Van¹; Aloji, Natalie¹; Baxevanis, Andreas²; Weinstein, Brant¹

1. NICHD, Bethesda, MD

2. NHGRI, Bethesda, MD

- Endothelial translome
- TRAP RNAseq
- Novel vascular genes

114

Antagonistic roles for the chromatin remodeling enzymes CHD4 and BRG1 in plasmin activation and embryonic hepatic vascular integrity

Wu, Meng Ling; Griffin, Courtney T.

Oklahoma Medical Research Foundation, Oklahoma City, OK

- Excessive plasmin activity degrades hepatic extracellular matrix and compromises vascular integrity
- The chromatin remodeler CHD4 transcriptionally suppresses plasmin activation in the embryonic liver
- BRG1 acts antagonistically to CHD4 to transcriptionally balance embryonic hepatic plasmin activation

115

Long-term activation of cyclic AMP pathway in vascular cells leads to R-Ras transcriptional repression and endothelial barrier destabilization

Perrot, Carole; Komatsu, Masanobu

Sanford Burnham Prebys Medical Discovery Institute, Orlando, FL

- Transcriptional regulation of R-Ras in vascular cells
- Cyclic AMP pathway and endothelial barrier stability
- Endothelial cells and pericytes

116

Transcriptional profiling of capillary (CAP) and high endothelial cells (HEC) from human lymphoid tissues

Szade, Agata; Brulois, Kevin F.; Lee, Mike; Lazarus, Nicole H.; Dermadi, Denis; Rahman, Miladur; Butcher, Eugene C. Stanford University, Palo Alto, CA

- Lymphocyte homing into lymphoid is controlled by high endothelial cells (HEC)
- Comparison of HEC and capillary EC transcriptomes reveals subset and tissue-specific pathways
- Genes whose differential expression in HEC is conserved define core functions in lymphocyte homing

117

Withdrawn

118

Endothelial regeneration of adult arteries requires upregulation of a subset of metabolic genes

Uebelhoer, Melanie; Shirali, Aditya; Iruela-Arispe, Luisa University of California, Los Angeles, Los Angeles, CA

- Mouse model to monitor endothelial regeneration during wound healing
- Endothelial regeneration involves transcriptional changes related to stress, proliferation and ECM
- Expression of specific metabolic genes is altered during proliferative phases of wound healing

119

Somatic activating KRAS mutations in the endothelium drive MAPK/ERK/Notch signaling and brain arteriovenous malformations

Fish, Jason¹; Nikolaev, Sergey²; Vetiska, Sandra¹; Frosen, Juhana³; Wythe, Joshua³; Radovanovic, Ivan¹

1. University Health Network - Toronto Western Hospital, Toronto, ON, Canada

2. University of Geneva Medical School, Geneva, Switzerland

3. Baylor College of Medicine, Houston, TX

- Somatic activating KRAS mutations identified in the majority of brain arteriovenous malformations
- Mutations were restricted to the endothelium of lesions and activated MAPK/ERK signaling
- Activated KRAS dysregulates angiogenic genes, including components of the Notch signaling pathway

120

miR26a targets smad1 to control vascular smooth muscle differentiation

Watterston, Charlene; Zeng, Lei; Onobadejo, Abidemi; Childs, Sarah J.

University of Calgary, Calgary, AB, Canada

- Loss of miR26 leads to hemorrhage and loss of vascular stability
- Loss of microRNA26 results in upregulation of vSMC marker genes
- miR26 represses Smad1 expression downstream of BMP signaling and promote vSMC differentiation

121

Transcriptional regulation and functional role of Etv2

Singh, Bhairab

University of Minnesota, Minneapolis, MN

- Functions of Dicer are important in Etv2+ vascular angioblast
- miR-130a is a critical regulator of angiogenesis and vascular patterning
- Etv2-miR130a-Jarid2 cascade is a novel network operational during vascular development

122

Withdrawn

123

Role of endothelial cell cis-acting DNA elements in regulating hemodynamic-mediated changes in gene expression *in vivo*

Dubinsky, Michelle; Ku, Kay K.H.; Sukumar, Aravin N.; Lee, John J.Y.; Knight, Britta K.; Steer, Brent M.; Marsden, Philip A.

University of Toronto, Toronto, ON, Canada

- Shear stress responsive endothelial gene
- Genetic and epigenetic regulation
- *in vivo* mouse promoter-reporter construct

Vascular Cell Biology II

124

STAT1 is a negative regulator of the vascular smooth muscle to myfibroblast transition in response to vascular injury

Medley, Shayna¹; He, Chaoyong²; Olson, Lorin E.¹

1. Oklahoma Medical Research Foundation, Oklahoma City, OK

2. State Key Laboratory of Natural Medicines, Nanjing, China

- STAT1^{-/-} vascular smooth muscle cells show increased proliferation & extracellular matrix production *in vitro*
- Vascular smooth muscle cell-specific STAT1 deletion exacerbates the injury response to carotid artery ligation
- STAT1 opposes the vascular smooth muscle to myfibroblast transition following vascular injury

125

The role of the VEGFR-1:VEGFR-2 heterodimer in vascular network assembly

Cudmore, Meli

University of Edinburgh, Edinburgh, United Kingdom

- Identification of a function of the VEGFR-1:VEGFR-2 Heterodimer
- Localisation of VEGFR-1:VEGFR-2 Heterodimer
- Angiogenesis using the embryoid body model

126

Splitting (intussusceptive) angiogenesis in human melanoma metastases and 3D cell culture – are matrix metalloproteinases (MMPs) required for pillar formation?

Levin, Max¹; Ekstrand, Matias¹; Ewald, Andrew J.²; Pandita, Ankur¹; McMahon, Martin³; Ny, Lars¹; Werb, Zena⁴; Borén, Jan¹; Mostov, Keith⁴

1. University of Gothenburg, Gothenburg, Sweden

2. Johns Hopkins University School of Medicine, Baltimore, MD

3. Huntsman Cancer Institute, Salt Lake City, UT

4. University of California, San Francisco, San Francisco, CA

- Splitting (intussusceptive) angiogenesis starts with formation of a slender intravascular pillar
- We characterized pillars in melanoma metastases and in 3D culture
- MMP inhibition stopped pillar formation in 3D by stopping cell migration and matrix remodeling

127

Positive-feedback confers robustness of angiogenesis to variable VEGF signal

Herbert, Shang¹; Page, Donna J.¹; Thuret, Raphael¹; Bentley, Katie²

1. University of Manchester, Manchester, United Kingdom

2. University of Uppsala, Uppsala, Sweden

- Vegf signaling induces tm4sf1 expression selectively in sprouting ECs in zebrafish embryos

- Vegf-induced Tm4sf1 expression feeds back to amplify Vegfr-mediated signaling *in vitro* and *in vivo*
- Tm4sf1-mediated positive feedback confers robustness of angiogenesis to variable Vegfr activity

128

Manipulation of microtubule dynamics markedly inhibits endothelial tip cell formation and branching tube morphogenesis

Salvador, Jocelynda; Davis, George E.

University of Missouri-Columbia School of Medicine, Columbia, MO

- Endothelial tip cell formation and network branching is blocked by manipulation of microtubule (MT) dynamics
- The MT stabilizing and disrupting agents, taxol and vinblastine, respectively inhibit EC tip cell formation
- Vinblastine, but not taxol, inhibits lumen expansion, suggesting unique differences in required MT dynamics

129

Vascular SMAD6 regulation of EC migration

Ruter, Dana L.; Mouillesseaux, Kevin P.; Bautch, Victoria L.

University of North Carolina at Chapel Hill, Chapel Hill, NC

- Loss of SMAD6 enhances endothelial cell migration *in vitro*
- Loss of SMAD6 enhances cellular alignment near the wound in a classical scratch wound assay
- SMAD6-mediated migration inhibition is driven through the canonical BMP pathway

130

N-cadherin regulation of vascular smooth muscle cells; the role of DDR1 and Rho GTPases

Xu, Songyi; Bendeck, Michelle P.

University of Toronto, Toronto, ON, Canada

- N-cadherin regulation is important to establish VSMC migratory arrest and prevent intimal thickening
- DDR1 stabilizes N-cadherin adhesion without affecting its total membrane levels or association with catenins
- Establishment of N-cadherin-mediated adhesion in VSMCs suppresses Cdc42 activation

131

Collaboration of Derlin-2 and Derlin-1 in mediating cyclooxygenase-2 degradation through ERAD: Role of N-glycosylation

Shyue, Song-Kun; Chen, Shu-Fen; Wu, Chun-Hu

Academia Sinica, Taipei, Taiwan

- Derlin-2 is upstream of Derlin-1 in mediating COX-2 degradation
- Caveolin-1 prefers to interact with glycosylated COX-2

- COX-2 degradation is mediated through the Derlin-2/Derlin-1/caveolin-1/p97 pathway

132

A new mechanism that controls cardiac fibroblast to endothelial cell fate transition involving protein methylation

Jackson-Weaver, Olan¹; Wu, Jian¹; Chen, Yibu; Li, Meng¹; Jin, Jian²; Sucov, Henry¹; Xu, Jian¹

1. University of Southern California, Los Angeles, CA
2. Mount Sinai, New York, NY

- Vascular cell fate determination
- Transcription control and gene expression
- Signal transduction

133

Pericyte cell line isolation, validation and applications

Zhao, Huaning

Virginia Tech, Blacksburg, VA

- Pericytes isolated from NG2:DsRed transgenic mouse embryos using Fluorescence Activated Cell Sorting (FACS)
- Pericytes identification comparing with fibroblasts and endogenous pericytes *in vitro* and *ex vivo*
- Pericytes and fibroblasts behavior patterns with HUVEC co-culture in 2D and 3D conditions

134

Endothelial TGF β type I receptor ALK5 regulates vascular integrity in the central nervous system using a canonical Smad-dependent pathway

Dubrac, Alexandre; Ola, Roxana; Eichmann, Anne

Yale University, New Haven, CT

- Inhibition of endothelial TGF β signaling mimics the phenotype of Diabetic Retinopathy
- Endothelial deletion of Smad4 at P5 recapitulates the phenotypes observed in the endothelial Alk5 mutant mice
- Endothelial TGF β signalling is essential for pericyte identity and vascular stability

135

Inhibiting Nck-dependent Pericyte migration improves pathological neoangiogenesis during retinopathy

Kuenzel, Steffen; Eichmann, Anne; Dubrac, Alexandre

Yale University, New Haven, CT

- Pericyte dysfunction in pathological angiogenesis
- Pericyte function during ocular vasoproliferative disease
- Function of Nck dependent Pericyte migration

136

BMP9/10-Alk1 signaling through Smad4 is responsible for Arterial Venous Malformations in retina development

Ola, Roxana; Eichmann, Anne

Yale University School of Medicine, New Haven, CT

- Canonical Smad4 signaling triggers AVM formation downstream of BMP9/10-Alk1
- Loss of Smad4 in ECs phenocopies BMP9/10-Alk1 signaling blockade
- PI3K blockade rescues AVM formation in Smad4 deficient mice

137

Investigating mural cell activity during cerebral blood flow regulation *in vivo*

Bahrami, Nabila; Childs, Sarah J.

University of Calgary, Calgary, AB, Canada

- We identify how mural cells regulate cerebral blood flow *in vivo* using the zebrafish model
- In early development, both pericytes and vSMC-covered vessels dilate in response to vasodilators
- As vessels mature, vSMC-covered vessels continue to strongly respond to vasodilators

138

A genetic zebrafish *Rasa1* mutant model of capillary malformations- arteriovenous malformations (CM-AVM)

Greysson-Wong, Jasper; Davari, Paniz; Ryu, Jae-Ryeon; Childs, Sarah

University of Calgary, Calgary, AB, Canada

- Use of morpholino & genetic *Rasa1* mutant zebrafish models to determine role of *Rasa1* in vascular development
- AVM phenotype in *Rasa1* mutant zebrafish recapitulates AVM seen in humans with *RASA1* mutations
- Vessel size is different between morpholino and mutant model and requires further investigation

139

foxc1b as a marker of early vascular smooth muscle cells in zebrafish

Whitesell, Thomas¹; Ryu, Jae-Ryeon¹; Workentine, Matthew¹; Lawson, Nathan D.²; Childs, Sarah J.¹

1. University of Calgary, Calgary, AB, Canada

2. University of Massachusetts Medical School, Worcester, MA

- Mural cells expressing *foxc1b* wrap around endothelium in embryos and adults
- Some *foxc1b*-expressing cells co-express *acta2*, suggesting *foxc1b* marks early smooth muscle cells
- The transcriptome of *foxc1b*⁺/*acta2*⁺ cells is similar but distinct from *acta2*⁺ and *pdgfr β* ⁺ cells

140

Exploring the role of TIE2 mutation L914F in venous malformation

Boscolo, Elisa; Cai, Yuqi; Li, Xian; Goines, Jillian

Cincinnati Children's Hospital Medical Center, Cincinnati, OH

- 3D system to study vessel lumen formation in venous malformation
- HUVEC-TIE2-L914F form massively enlarged lumens in 3D fibrin gel
- HUVEC-TIE2-L914F do not interact with normal pericytes and endothelial cells in 3D fibrin gel

Vascular Therapeutics

141

ABL kinase inhibitor Ponatinib combined with rapamycin causes regression of murine Venous Malformation

Boscolo, Elisa; Li, Xian; Cai, Yuqi; Goines, Jillian

Cincinnati Children's Hospital, Cincinnati, OH

- screening for candidate drugs targeting mutant TIE2 signaling in venous malformation (VM)
- Ponatinib affects TIE2 and cABL activity downstream of mutant TIE2
- Ponatinib combined with rapamycin induces regression of mutated-TIE2 derived murine model of VM

142

Vascular cell permeant decoy peptides: A possible therapeutic approach to reverse aortic stiffness

Singh, Kuldeep; Nicholson, Christopher J.; Saphirstein, Robert J.; Gao, Yuan Z.; Li, Qian; Chiu, Joanna; Porter, Tyrone; Morgan, Kathleen G.

Boston University, Boston, MA

- The shock absorber function of proximal aorta is impaired with age because of aortic stiffening
- Decoy peptides targeted to n-WASP, VASP and Talin-Vinculin protein-protein interfaces decrease stiffness
- Decoy peptides can be packaged into microbubbles, ultrasound-targeted and released into proximal aortic tissue

143

S-Sulphydration of HuR regulates cathepsin S expression in human atheromas

Bibli, Sofia Iris¹; Hu, Jiong¹; Zukunft, Sven¹; Luck, Bert¹; Sigala, Frangiska²; Szabo, Czaba³; Pfeilschifter, Josef⁴; Papapetropoulos, Andreas²; Fleming, Ingrid⁵

1. Inst for Vascular Signaling, Frankfurt am Main, Germany

2. University of Athens, Athens, Greece

3. University of Texas Medical Branch, Galveston, TX

4. Pharmacentre Frankfurt/ZAFES, Frankfurt am Main, Germany

5. Johann Wolfgang Goethe University, Frankfurt, Germany

- HuR sulphydration
- Human atherosclerotic plaques
- hydrogen sulfide

144

Cystathionine γ lyase sulfhydrates the RNA binding protein HuR to preserve endothelial cell function

Bibli, Sofia Iris¹; Hu, Jiong¹; Sigala, Frangiska²; Luck, Bert¹; Zukunft, Sven¹; Szabo, Czaba³; Abdel Malik, Randa¹; Pfeilschifter, Josef⁴; Papapetropoulos, Andreas²; Fleming, Ingrid⁵

1. Institute for Vascular Signaling, Frankfurt am Main, Germany

2. University of Athens, Athens, Greece

3. University of Texas Medical Branch, Galveston, TX

4. Pharmacentre Frankfurt/ZAFES, Frankfurt am Main, Germany

5. Johann Wolfgang Goethe University, Frankfurt, Germany

- Endothelial Cell Activation
- Hydrogen Sulfide bioavailability
- Cystathionine Gamma Lyase ablation

145

Catalytic subunit of telomerase prevents hyperoxia induced injury of pulmonary endothelial cells by protection of mitochondrial integrity

Beyer, Andreas¹; Durand, Matt¹; Clought, Anne²; Audi, Said²; Jacobs, Elizabeth¹

1. Medical College of Wisconsin, Milwaukee, WI

2. Marquette University, Milwaukee, WI

- Hyp induced mt-damage in PEC cells in the form of increased MTT levels and mt-fragmentation
- Hyp increases expression of the dominant negative splice variant of TERT, β -del TERT
- Elevated TERT protects against Hyp PEC damage while inhibition of TERT augments effects of Hyp

146

Targeted delivery of miR-145 to atheroprone vasculature by platelet-mimetic nanoparticles

Wang, Kuei-Chun; Zhang, Liangfang; Chien, Shu

University of California, San Diego, La Jolla, CA

- Therapeutic microRNAs
- Atherosclerosis
- Drug delivery

147

Activation of VEGFR1 post VEGF165b inhibition induces truncated miR17-92 cluster that targets Regulator of Calcineurin-3 to enhance perfusion in preclinical Peripheral Arterial Disease

Ganta, Vijay; Choi, Min; Luu, Victoria; Annex, Brian

University of Virginia, Charlottesville, VA

- VEGFR1 activation post VEGF165b inhibition induces miR17, miR20a levels in ischemic muscle vs. IgG
- Increased miR17-20a levels post VEGF165b inhibition inversely correlate with RCAN3 levels in ischemic muscle
- Hypoxia serum starved VR1+/- endothelium have significantly higher RCAN3 levels vs. VR1+/- endothelium

Bioengineering Organ-Specific Vasculatures

148

High-Throughput permeability assay on perfused 3D microvessels *in vitro*

Duinen, Vincent¹; Vught, Remko V.¹; Ramakers, Christian¹; Trietsch, Sebastiaan J.¹; van Zonneveld, Anton Jan²; Hankemeier, Thomas²; Vulto, Paul¹

1. Mimetis, Leiden, Netherlands

2. LUMC, Leiden University, Leiden, Netherlands

- *in vitro* perfused 3D microvessels
- Barrier integrity quantified by the diffusion fluorescent dextrans
- Fundamental research, drug testing

149

Perfusable 3D angiogenesis in high throughput microfluidic culture platform

Duinen, Vincent¹; Vught, Remko V.¹; Ramakers, Christian¹; Trietsch, Sebastiaan J.¹; van Zonneveld, Anton Jan²; Hankemeier, Thomas²; Vulto, Paul¹

1. Mimetis, Leiden, Netherlands

2. LUMC, Leiden University, Leiden, Netherlands

- Perfusable 3D angiogenesis in high throughput
- Microfluidic culture platform that allows precisely controlled gradients, perfused blood vessels
- *in vitro* screening platform to unravel the important drivers in angiogenesis and vasculogenesis

150

A microphysiological system to model the human neurovascular unit and glioblastoma progression *in vitro*

Phan, Duc; Hughes, Christopher C.

University of California, Irvine, Irvine, CA

- An *in vitro* model of the BBB with perfused vasculature that allows for studies of permeability
- Brain environment induces ECFC-EC to take on BBB characteristics such as gene expression and less permeability
- Observe drug delivery, and the pathological changes associated with cancer development (glioma) in the CNS

151

Of the vasculature... if we had a “Google Map” for the human body?

Galis, Zorina S.

NIH/NHLBI, Bethesda, MD

- Assessing the status of single vascular cell research: What are the biggest challenges?
- The transformative effects of building ONE multidimensional, multi-scale, integrated map of human vasculature

- Key contributions that mapping the vasculature could make to the human body “Google Map”

Animal Models of Vascular Diseases

152

Withdrawn

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pGTAG and pPRISM: two expanded tool sets for using short regions of homology for precise DNA integration in zebrafish

Essner, Jeffrey¹; Torrie, Melanie E.¹; Wierson, Wesley A.¹; Welker, Jordan M.; Almeida, Maira; Mann, Carla¹; Bullard, Cassandra²; Duran, Camille L.³; Kwan, Kristen M.⁴; Chien, Chi-Bin⁴; Balciunas, Darius⁵; Dobbs, Drena¹; Bayless, Kayla³; Ekker, Stephen C.²; Clark, Kar²; McGrail, Maura A.¹

1. Iowa State University, Ames, IA

2. Mayo Clinic, Rochester, MN

3. Texas A&M Health Science Center, College Station, TX

4. University of Utah, Salt Lake City, UT

5. Temple University, Philadelphia, PA

- gene targeting in zebrafish
- CRISPR Cas9
- genome engineering

154

Characterization of a novel Smad4 mouse model of Hereditary Hemorrhagic Telangiectasia (HHT)

Crist, Angela; Meadows, Stryder M.

Tulane University, New Orleans, LA

- Deletion of Smad4 in a murine retinal model causes arteriovenous malformations
- Smad4 mutants exhibit increases in artery and vein diameter and a reduction in vascular outgrowth
- Loss of Smad4 leads to a distortion of artery-vein identity and altered mural cell coverage

155

Studying the *in vivo* effects of Lox inhibition on aortic aneurysm formation via high throughput mRNA sequencing

van der Ent, Martijn; Hunker, Kristina; Cleuren, Audrey; Ginsburg, David; Jiang, Hui; Ganesh, Santhi

University of Michigan, Ann Arbor, MI

- Lysyl oxidase
- *In vivo* transcriptome profiling
- Aortic aneurysm

156

Endothelial Sirt6 deficiency increases arterial thrombosis by upregulating tissue factor and pro-inflammatory cytokines

Gaul, Daniel¹; Calatayud, Natacha¹; Bonette, Nicole¹; van Tits, Lambertus J. ¹; Weber, Julien¹; Pasterk, Lisa¹; Camici, Giovanni G. ¹; Lüscher, Thomas F. ¹; Matter, Christian M. ^{1,2}

1. University of Zurich, Zurich, Switzerland
2. University Hospital Zurich, Zurich, Switzerland

- Arterial Thrombosis
- Sirt6
- Tissue Factor

157

Endothelial-specific CDC42 deletion elicits cerebral vascular malformations

Castro, Marco¹; Laviña Siemsen, Barbara¹; Brakebush, Cord ²; Gaengel, Konstantin ³

1. Uppsala Universitet, Uppsala, Sweden
2. University of Copenhagen, Copenhagen, Denmark
3. Karolinska Institutet, Stockholm, Sweden

- Angiogenesis
- Cerebral vascular malformations
- Cdc42 and Cell migration

158

MHV68-induced vasculitis model is accelerated by microbiome suppression and alleviated by modified myxomavirus serpin reactive center loop-derived peptides

Ambadapadi, Sriram¹; Yaron, Jordan R. ¹; Mahon, Brian P. ²; Thomas, Ryan M. ³; Jobin, Christian³; Gharaibeh, Raad³; Karst, Stephanie M. ³; Tibbetts, Scott A. ³; Keinan, Shahar⁴; Varsani, Arvind¹; Zhang, Liqiang¹; McFadden, Grant¹; Lucas, Alexandra¹

1. Arizona State University, Tempe, AZ
2. National Institutes of Health, Bethesda, MD
3. University of Florida, Gainesville, FL
4. Cloud Pharmaceuticals, Research Triangle Park, NC

- MHV68-induced vasculitis is worsened by microbiome suppression with antibiotics
- Myxomavirus Serine Protease Inhibitor-derived peptides lose anti-inflammatory activity without gut microbiome
- Modified Serine Protease Inhibitor-derived peptides regain anti-inflammatory activity

Vascular Inflammation and Immunology

159

Endothelial NDST1 knockout and treatment with a viral chemokine modulator increase heparan sulfate disaccharide (D0S6) content and reduce renal allograft rejection

Yaron, Jordan¹; Ambadapadi, Sriram¹; Chen, Hao²; Esko, Jeffrey D. ³; Zhang, Liqiang¹; Lucas, Alexandra¹

1. Arizona State University, Tempe, AZ
2. University of Florida, Gainesville, FL
3. University of California San Diego, La Jolla, CA

- Chemokine-binding glycosaminoglycans (GAGs) in the endothelial glycolcalyx alter host inflammatory responses
- Altering donor organ disaccharides and inhibiting GAG/chemokine interaction reduce renal transplant rejection
- Myxomavirus M-T7 reduces renal transplant rejection and inflammation

161

Platelet-derived calpain mediates protease-activated receptor 1-dependent vascular inflammation in diabetes

Kyselova, Anastasia¹; Elgheznawy, Amro¹; Wittig, Ilka¹; Heidler, Juliana¹; Ruf, Wolfram²; Randriamboavonjy, Voahanginirina¹; Fleming, Ingrid¹

1. Goethe University Frankfurt, Frankfurt am Main, Germany
2. Medical Center University Mainz, Mainz, Germany

- platelet-derived microparticles
- extracellular calpain
- diabetes-associated vascular inflammation

162

Effects of electrochemotherapy (ECT) on blood vessel morphology and immune cell infiltration in cutaneous melanoma metastases - a case study with multiple biopsies over time

Ekstrand, Matias; Bjursten, Sara; Jespersen, Henrik; Stierner, Ulrika; Yrlid, Ulf; Fogelstrand, Per; Ny, Lars; Levin, Max

University of Gothenburg, Gothenburg, Sweden

- Electrochemotherapy may have effects in blood vessels and immune cell infiltration in tumors
- Blood vessel morphology in tumors affects infiltration of T-cells and dendritic cells
- Recruitment of T-cells and dendritic cells to tumors increases the response rate to immunotherapy

Atherosclerosis and Restenosis

163

Ultrahigh resolution phase contrast X-ray imaging of atherosclerotic plaques

Xing, Ruoyu¹; Moerman, Astrid M.¹; Rodrigues, Daniel¹; Ridwan, Yanto¹; van der Steen, Anton FW¹; Klein, Stefan¹; Trachet, Bram²; Gijzen, Frank JH¹; van der Heiden, Kim¹

1. Erasmus Medical Center, Rotterdam, Netherlands
2. Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland

- Phase contrast X-ray imaging reveals murine atherosclerotic plaques in ultrahigh resolution (6.5µm)
- 3D visualization & quantification of plaque components in any desired orientation
- Ultrahigh resolution plaque imaging allows the delineation of related plaque features

164

Therapeutic modulation of S-nitrosylation signaling pathways to potentiate endothelial repair via Nrf2

Das, Debapria; Liu, Xin; Tesmenitsky, Yevgenia; Croce, Kevin J.

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

- GSNOR inhibition increases transcription of NRF2-regulated antioxidant genes
- GSNOR regulates vascular inflammation in part by controlling NRF2 vasculoprotective transcriptional responses
- GSNOR is an attractive therapeutic target for atherosclerotic vascular disease

165

Regulation of human atherosclerosis-induced angiogenesis by macrophages and hypoxia in an ex vivo co-culture model with rat aortic explants

Aplin, Alfred; Kohler, Ted R.; Tang, Gale L.; Nicosia, Roberto F.

University of Washington, Seattle, WA

- Human plaques stimulate angiogenesis *in vitro* and *in vivo*
- Plaque stimulatory activity correlates with the presence of intraplaque macrophages
- Plaque induced angiogenesis is maladaptive under hypoxic conditions

166

Endothelial glucocorticoid receptor (GR) modulates Wnt signaling in a mouse model of atherosclerosis

Goodwin, Julie; Zhou, Han; Sessa, William C.

Yale University School of Med, New Haven, CT

- Apo E KO/eGR KO mice have more severe atherosclerotic lesions than eGR replete animals
- Genomic experiment indicate that the Wnt signaling pathway is regulated by eGR

- Modulation of the Wnt signaling pathway may be a novel therapeutic intervention for atherosclerosis

Vascular Calcification

168

Differential cardiovascular effects of teriparatide in hyperlipidemic mice with pre-existing aortic calcification

Hsu, Jeff; Lu, Jinxiu; Umar, Soban; Lee, Jason; Kulkarni, Rajan; Ding, Yichen; Hsiai, Tzung; Demer, Linda L.; Tintut, Yin

University of California, Los Angeles, Los Angeles, CA

- We tested effects of osteoporosis therapy on pre-existing aortic calcification in hyperlipidemic mice
- Imaging showed increased x-ray attenuation by CT scan, but decreased fluoride uptake by PET
- Teriparatide did not affect progression of aortic calcification but may change surface area and stability

169

Regulation of vascular smooth muscle cell calcification by syndecan-4/FGF-2/PKCa signaling and cross-talk with TGFβ

Borland, Samantha¹; Morris, Thomas G.¹; Borland, Shona C.¹; Morgan, Mark R.²; Francis, Sheila E.³; Merry, Catherine LR⁴; Canfield, Ann E.¹

1. University of Manchester, Manchester, United Kingdom

2. University of Liverpool, Liverpool, United Kingdom

3. University of Sheffield, Sheffield, United Kingdom

4. University of Nottingham, Nottingham, United Kingdom

- To profile the expression of FGF-2 and syndecan 4 during VSMC mineralisation *in vitro* and *in vivo*
- To determine the role of FGF-2 and syndecan-4 in VSMC mineralisation
- To identify the signaling pathway(s) downstream of FGF-2 and syndecan-4 that regulates VSMC mineralisation

170

A role for telomerase in valvular calcification

Hortells, Luis; Garchar, Evelyn; Doyon, Genevieve; Bruemmer, Dennis; St Hilaire, Cynthia

University of Pittsburgh, Pittsburgh, PA

- Valvular calcification
- Aging
- Telomerase

171

Protective role of type III Sodium-Dependent Phosphate Transporter, PiT-2, against vascular calcification in a mouse model of chronic kidney disease

Yamada, Shunsuke; Wallingford, Mary C.; Leaf, Elizabeth M.; Chia, Jia Jun; Cox, Timothy C.; Speer, Mei Y.; Giachelli, Cecilia M.

University of Washington, Seattle, WA

- The aim of the study was to elucidate whether PiT-2 is protective against VC *in vivo* and *in vitro*
- PiT-2 haploinsufficiency enhanced vascular calcification in CKD mice
- PiT-2 deficiency increased matrix calcification and decreased OPG synthesis in cultured mouse VSMCs

Extracellular Matrix and Disease

172

Immunogenic matrix remodeling and myeloid cell contributions to myxomatous valve disease in a mouse model of Marfan syndrome

Kim, Andrew; Hulin, Alexia; Alfieri, Christina M.; Yutzey, Katherine E.

Cincinnati Children's Hospital Medical Center, Cincinnati, OH

- Marfan valves have matrix modification, chemokine up-regulation, and increased CD45+ leukocytes
- Valvular CD45+ leukocytes are myeloid cells that increase after pathological valve thickening
- CD206+ or MHCII+ macrophage subsets localize to regions of matrix disruption in diseased valves

173

ADAMTS6 regulates cardiac development through fibrillin-2 proteolysis

Mead, Timothy¹; Gulic, Cagri²; Wang, Lauren¹; Lo, Cecilia²; Apte, Suneel S.¹

1. Cleveland Clinic, Cleveland, OH

2. University of Pittsburgh School of Medicine, Pittsburgh, PA

- Adamts6 is expressed in murine cardiac and musculoskeletal tissue with an undefined role
- Adamts6^{-/-} embryos have cardiac, craniofacial and limb defects that are rescued by Fbn2^{+/-}
- Adamts6 is a regulator of cardiac and musculoskeletal development through fibrillin-2 cleavage

174

Lipid profiling of human carotid atherosclerotic plaque with imaging mass spectrometry (MALDI-IMS)

Moerman, Astrid M.; Visscher, Mirjam; Burgers, Peter C.; van Beusekom, Heleen M.M.; Luider, Theo M.; van der Steen, Antonius F.W.; Gijzen, Frank J.; van Soest, Gijs; van der Heiden, Kim

Erasmus Medical Center Rotterdam, Rotterdam, Netherlands

- We hypothesize that the lipid signature of a plaque is related to plaque vulnerability
- We identify the unique lipid signature of human carotid plaques by MALDI-imaging mass spectrometry
- We correlate the detailed lipid profile to established compositional markers of plaque vulnerability

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Deposition of endothelial cell-derived fibronectin by alpha5beta1 integrins mediates proinflammatory gene expression and early atherosclerosis

Orr, A. Wayne¹; Al Yafeai, Zaki¹; Yurdagul, Arif¹; Green, Jonette M.¹; Murphy, Patrick A.²

1. LSU Health Sciences Center - Shreveport, Shreveport, LA

2. UConn Health, Farmington, CT

- Oxidized LDL induces $\alpha 5\beta 1$ -dependent fibronectin deposition
- Endothelial $\alpha 5$ knockout mice show reduced endothelial activation and early atherosclerosis
- Cell-derived but not plasma-derived fibronectin mediates EDA/EDB-dependent endothelial activation

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Vascular smooth muscle EphA2 signaling regulates fibrillar adhesion formation to modulate fibronectin deposition

Finney, Alexandra¹; Green, Jonette¹; Rana, MOhammad¹; Alexander, J. Steven¹; Lim, Ssang-Taek²; Traylor, James G.¹; Orr, A. Wayne¹

1. LSU Health Sciences Center - Shreveport, Shreveport, LA

2. University of South Alabama Sch of Medicine, Mobile, AL

- EphA2 positively regulates multiple matrix-associated genes and is localized in focal adhesions
- EphA2-deficient smooth muscle cells attenuate fibrillar adhesion formation and contractility
- Vascular smooth muscle cells signal through fibronectin-binding integrins to upregulate EphA2

Visit the Exhibits

177

Talin1-dependent integrin activation is required for flow- and oxidized LDL-induced endothelial proinflammatory responsesAl-Yafeai, Zaki¹; Yurdagul Jr, Arif²; Petrich, Brian G³; Orr, A. Wayne¹

1. LSU Health Sciences Center - Shreveport, Shreveport, LA
2. Columbia University, New York, NY
3. Emory University, Atlanta, GA

- Our knowledge of Integrin affinity in endothelial cell (EC) activation is limited
- We used Talin1 L325R EC to specifically test the role of Integrin activation in EC proinflammatory response
- Blocking integrin activation blunts flow and oxidized LDL-induced proinflammatory responses

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Cell receptor interactions of fibulin-4 and latent transforming growth factor- β binding protein-4Reinhardt, Dieter; Hakami, Hana; Kumra, Heena; Pagliuzza, Amelie; Djokic, Jelena; Lee, Kungjun; Lee, Chae Syng
McGill University, Montreal, PQ, Canada

- The interaction of FBLN4 with cells is mediated via cell surface heparan sulfate
- FBLN4 multimers, but not monomers, interact with cells
- LTBP-4 interacts with cells in the absence of an RGD site

179

Functional relevance of Fibulin-4 interactions with latent transforming growth factor beta binding protein-4 in the context of fibronectin and fibrillin-1Reinhardt, Dieter; Kumra, Heena; Nelea, Valentin; Pagliuzza, Amelie; Hakami, Hana

McGill University, Montreal, PQ, Canada

- Fibulin-4 interact with fibronectin and is directly dependent on fibronectin for its assembly
- Interaction of fibulin-4 with LTBP-4 induces a conformational change
- This induces functional changes in LTBP-4 assembly and its binding to other ECM proteins

180

Elastin haploinsufficiency results in disordered calcium homeostasis in cardiomyocytesLevin, Mark; Kozel, Beth A.
NIH/NHLBI, Bethesda, MD

- Elastin haploinsufficiency results in disordered calcium homeostasis
- Elastin haploinsufficiency gives rise to ECG abnormalities
- Cardiomyocytes from elastin haploinsufficient mice have increased whole cell calcium currents

182

miR-145 regulates cardiac fibrosis through selective inhibition of TGF β signalingSawant, Dwitiya; Lowe, Megan; Marosis, Samantha; Trask, Aaron J.; Lilly, Brenda

The Research Institute at Nationwide Children's Hospital, Columbus, OH

- miR-145 has multiple targets in the fibrotic pathway and it directly suppresses TGF β signaling
- To determine whether miR-145 alleviates cardiac fibrosis by its conditional expression in mouse models
- To characterize the mechanisms by which miR-145 regulates signaling pathways involved in cardiac fibrosis

183

Integrin $\alpha 5 \beta 1$ and fibronectin are essential for regulating the formation of pharyngeal arch arteriesJubran, Ali

Thomas Jefferson University, Philadelphia, PA

- Endothelium of the pharyngeal arch arteries (PAAs) is derived from the second heart field (SHF)
- Integrin $\alpha 5$ and Fn1 regulate PAA morphogenesis from SHF-derived precursors
- Integrin $\alpha 5$ regulates the deployment of endothelial progenitors and their assembly into the PAA

184

Impact of genetic GPER deletion on baseline cardiovascular parametersAbshire, Caleb; Clark, Gabrielle L.; Miller, Kristen S.; Lindsey, Sarah H.

Tulane University School of Medicine, New Orleans, LA

- The novel estrogen receptor GPER is a potential target for postmenopausal cardiovascular disease
- Genetic GPER deletion reduced nighttime blood pressure in mature, healthy mice, independent of sex
- GPER deletion did not impact baseline *ex vivo* passive properties of carotid arteries

185

Alternative splicing of fibronectin regulates arterial matrix compositionMurphy, Patrick¹; Jailkhani, Noor²; Del Rosario, Amanda M.²; Levine, Stuart²; Begum, Shahinoor²; Hynes, Richard O.²

1. UCONN Medical School, Farmington, CT

2. MIT, Cambridge, MA

- Flow responsive alterations in matrix composition *in vivo* including recruitment of blood proteins
- Quantitative *in vitro* analysis of the recruitment of blood proteins to the endothelial extracellular matrix

- Alternative splicing effects on extracellular matrix composition and recruitment of blood proteins

186

TGF β mediated up-regulation of serpine1 via suppression of miR-30c coordinates vascular-directed fibrinolysis, sprouting angiogenesis, and tumor growth

McCann, James¹; Xiao, Lin²; Khan, Omar³; Kowalski, Piotr³; Anderson, Daniel G.^{3,4}; Pecot, Chad¹; Parker, Joel¹; Tsai, Yihsuan¹; Wolberg, Alisa¹; Mackman, Nigel¹; Dudley, Andrew C.⁵

1. UNC Chapel Hill, Chapel Hill, NC

2. National Cancer Institute, Bethesda, MD

3. MIT, Cambridge, MA

4. Harvard Medical School, Cambridge, MA

5. The University of Virginia, Charlottesville, VA

- Endothelial cell heterogeneity in tumors
- TGF β and fibrin-mediated angiogenesis
- Maladapted tumor-specific endothelial cells

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Excessive plasmin compromises postnatal hepatic vascular integrity after liver injury

Gao, Siqi; Griffin, Courtney T.

University of Oklahoma Health Science Center/Oklahoma Medical Research Foundation, Oklahoma City, OK

- Plasmin activity peaks 6 hr after APAP overdose
- ECM components around hepatic vasculature are diminished after APAP overdose and plasmin elevation
- Partial reduction of plasmin activity stabilizes vascular integrity after APAP overdose

188

Improved aortic elastogenesis driven by adipose-derived mesenchymal stem cell secreted factors

Ramaswamy, Aneesh; Sides, Rachel E.; Weinbaum, Justin S.; Vorp, David A.

University of Pittsburgh, Pittsburgh, PA

- Adipose-derived MSC delivery to elastase-induced mouse aneurysm slows growth and preserves elastin
- Do MSCs secreted factors (SF) elevate adult aortic SMC elastic fiber production and organization?
- In 3D fibrin gels, SF induced 3x SMC insoluble elastin after 20 days, networked elastin after 30 days

189

Combined chronic treatment with β -blocker and inhibitor of the renin-angiotensin system decreases resistance artery stiffness in hypertensive patients

Bloksgaard, Marja¹; Leurgans, Thomas¹; Rasmussen, Lars M.²; Riber, Lars²; Irmukhamedov, Akhmadjon²; De Mey, Jo¹

1. University of Southern Denmark, Odense C, Denmark

2. Odense University Hospital, Odense C, Denmark

- RAAS inhibitors (ACEI/ARB) but not β -blockers can reverse resistance artery (RA) remodeling
- The effect of chronic drug treatment on RA stiffness was evaluated in RA from CVD patients
- Combined treatment with ACEI/ARB and β -blocker decreases wall stiffness (vs. either treatment alone)

**190 - presenting on board 24 on Monday
Development of a decellularized tissue model of early heart valve lesions**

Maleki, Hoda; Simmons, Craig A.

University of Toronto, Toronto, ON, Canada

- Valve cells express osteochondral genes in early valve lesions with distinct ECM
- Established an *in vitro* decellularized ECM model that preserves valve ECM mechanics and composition
- This model is being used to assess pathological cell responses to early valve lesion ECM

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Lysyl oxidase mutation in vascular disease

Lee, Vivian; Mecham, Robert

Washington University in St. Louis, St. Louis, MO

- Lysyl oxidase is required for crosslinking tropoelastin and collagen in developing vessels
- Mutations in lysyl oxidase leads to thoracic aortic aneurysm and dissection
- Mutant lysyl oxidase is retained in the endoplasmic reticulum

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Tissue-specific role of fibulin-4 in maintaining arterial wall integrity

Halabi, Carmen; Lin, Michelle; Broekelmann, Thomas J.; Mecham, Robert P.

Washington University School of Medicine in St. Louis, St. Louis, MO

- Fbln4(E57K) mice serve as a model for autosomal recessive cutis laxa type 1B
- Elastic, but not muscular arteries, are affected by the homozygous E57K mutation in fibulin-4
- The normal desmosine content of Fbln4 (E57K) vessels challenges fibulin-4's role in elastin assembly