

19th International Vascular Biology Meeting

Neurovascular Disease

T001

Identification of novel neuroprotective loci modulating ischemic stroke

Lee, Han Kyu; Marchuk, Douglas A.

Duke University Medical Center, Durham, NC, USA

- Ischemic stroke
- Neuroprotection
- wild-derived mouse strain

T002

A novel diagnostic to detect Notch3 aggregates in CADASIL

Coupland, Kirsten G.¹; Oliveira, Daniel V.¹; Rutten, Julie W.²; Lesnik Oberstein, Saskia A.J.²; Kalaria, Rajesh N.³; Kalimo, Hannu⁴; Viitanen, Matti¹; Lendahl, Urban¹; Lundkvist, Johan⁵; Karlstöm, Helena¹

1. Karolinska Institutet, Huddinge, Sweden

2. Leiden University Medical Centre, Leiden, Netherlands

3. Newcastle University, Newcastle, United Kingdom

4. University of Helsinki, Helsinki, Finland

5. Alzecure, Huddinge, Sweden

- An assay using proximity ligation technology to examine Notch3 aggregation in CADASIL tissue
- Visualised Notch3 aggregates in human and mouse tissue. Non-aggregated Notch3 remained unstained
- Greater number of PLA dots for CADASIL vascular smooth muscle cells compared to wild-type

T003

Increased blood-brain barrier vulnerability to systemic inflammation in a mouse model of Alzheimer's disease

Takeda, Shuko; Sato, Naoyuki; Rakugi, Hiromi; Morishita, Ryuichi

Osaka University School of Medicine, Suita, Japan

- Vulnerability of blood-brain barrier contributes to the pathogenesis of Alzheimer's disease
- Peripherally evoked inflammation crosses blood-brain barrier and induces non-cognitive symptoms
- Unique microdialysis technique enabled us to monitor brain cytokine levels in a behaving mouse

T004

Prevention of ischemic stroke by andrographolide, a novel NF-κB inhibitor: the crucial mechanisms of induction of cerebral endothelial cell apoptosis

Chen, Yen Jen; Hsieh, Cheng Ying; Sheu, Joen-Rong

Taipei Medical University, Taipei, Taiwan

- Andrographolide is a novel NF-κB inhibitor
- Andrographolide induces cerebral endothelial cells apoptosis
- Andrographolide prevents ischemia stroke

T005

Characterising calcifications in two murine models of PFBC

Nahar, Khayrun

Uppsala University, Uppsala, Sweden

- Characterising calcifications in two murine models of PFBC, pdgfbRet/Ret and slc20a2-/-
- Multilayered structures associated with capillaries and consisting of several proteins
- Microglia, reactive astrocytes and pericytes might contribute to the formation of the calcification

T006

Fc-saxatilin, a disintegrin, alleviates brain vascular leakage by hypoxia through regulating occludin expression in endothelial cells

Choi, Hyun-Jung; Kwon, Il; Kim, Ja-Young; An, Sun Ho; Heo, JiHoe
Yonsei University College of Medicine, Seoul, Korea

- Fc-saxatilin prevents hypoxia-induced endothelial hyperpermeability in vitro through binding to integrin $\alpha v\beta 3$
- Fc-saxatilin inhibits leakage of the blood-brain barrier in the ischemic brain of mice
- Fc-saxatilin regulates a tight junction protein, occludin by blocking integrin $\alpha v\beta 3$ -FAK-MMP- signaling axis

Vascular Malformations

T007

Endothelial cell PI-3'Kinase dysregulation promotes defects in vascular stability and abnormal vascular morphogenesis through an mTOR-dependent mechanism

Decker, Brandee L.; Zheng, Qingxia; Pumiglia, Kevin
Albany Medical College, Albany, NY, USA

- Endothelial specific induction of PI3KCA H1047R drives vascular malformations in vivo
- Inactivation of PTEN in mouse endothelium is also sufficient to induce abnormal vascular lesions
- In vitro models demonstrate activation of RHEB/mTOR is sufficient to drive dysfunctional morphogenesis

T008

GNAQ p.R183Q mutation disrupts endothelial behavior in capillary malformations

Huang, Lan¹; Couto, Javier A.¹; Pinto, Anna¹; Mulliken, John B²; Sahin, Mustafa¹; Greene, Arin K.³; Bischoff, Joyce³
1. Boston Children's Hospital, Boston, MA, USA
2. Children's Hospital Boston, Harvard School of Dental Medicine and Harvard Medical School, Boston, MA, USA
3. Boston Children's Hospital/Harvard Medical School, Boston, MA, USA

- GNAQ p.R183Q mutant endothelial cells
- Capillary malformations/ Sturge-Weber Syndrome
- Endothelial biology

T009

Loss of CCM2 resets the endothelial response to low shear stress in part through modulating the level of expression of the mechanosensory complex

Li, Jia; Zhao, Yang; Chen, Jinbiao; Coleman, Paul; Zheng, Xiangjian; Vadas, Mathew A.; Gamble, Jennifer R.
Centenary Institute, Sydney, NSW, Australia

- CCM2-depleted ECs have high expression of mechanosensor genes and KLF2/4 only under low shear stress
- Loss of CCM2 resets EC response to low shear stress in part through altering the mechanosensor genes
- Blocking shear stress signaling by inhibition of SHP2 compensates the CCM2-depletion induced outcome

T011

Alk1 deficiency in bone marrow-derived endothelial cells leads to arteriovenous malformations

Luo, Man; Li, Qiang; Ma, Li; Zhang, Rui; Zhan, Lei; Lawton, Michael T.; Su, Hua
University of California, San Francisco, San Francisco, CA, USA

- Alk1 deficiency causes arteriovenous malformations in multiple organs in humans
- Endothelial deletion of Alk 1 results in AVM in multiple organs and the brain angiogenic region
- Deletion of Alk1 in bone marrow-derived endothelial cells is sufficient to induce AVM

T012

Thalidomide and lenalidomide treatment stabilizes the vascular wall and reduces microhemorrhage in brain arteriovenous malformations in mice

Zhu, Wan; Zou, Dingquan; Chen, Wanqiu; Bao, Chen; Zhang, Rui; Zhan, Lei; Li, Zhengxi; Zhang, Meng; Winkler, Ethan; Lawton, Michael T.; Su, Hua
University of California, San Francisco, San Francisco, CA, USA

- Brain arteriovenous malformations have an abnormal vessel wall and are prone to rupture
- Brain AVM vessels in Alk1-deficient mice have fewer mural cells
- Thalidomide and lenalidomide stabilize the bAVM vessel wall and reduce microhemorrhage in mice

T013

Deletion of KRIT1 and the development of a pro-angiogenic vascular phenotype in CCM

DiStefano, Peter V.; Glading, Angela J.

University of Rochester, Rochester, NY, USA

- Mice lacking KRIT1 exhibited increased serum levels of VEGF and increased vascular permeability
- VEGF then promoted a feed-forward mechanism that activated RhoA signaling, and increased endothelial migration
- Treatment of Krit1ec-/- mice with SU5416 reduced the formation and size of CCM-like lesions

T014

Identifying novel small molecule drugs for Cerebral Cavernous Malformation treatment

Oldenburg, Joppe

Uppsala University, Rudbeck Lab, Uppsala, Sweden

- Cerebral Cavernous Malformation (CCM) research
- Establishing High Throughput Screening (HTS) assays
- Identifying novel drugs against CCM

T015

Rapamycin (Sirolimus) inhibits proliferation and increases vascular maturation of GLUT1-positive endothelial cells from infantile hemangioma

van der Werf, Inge Margaretha¹; Huang, Lan²; Mulliken, John B.³; Bischoff, Joyce²

1. VU University Medical Center, Voorschoten, Netherlands

2. Boston Children's Hospital, Boston, MA, USA

3. Children's Hospital Boston, Harvard School of Dental Medicine and Harvard Medical School, Boston, MA, USA

- Glucose-transporter-1 (GLUT1)-positive EC are a hallmark of infantile hemangioma
- These cells were shown to have properties of facultative stem cells
- Rapamycin inhibits proliferation of GLUT1-positive EC and seems to cause the loss of its stem cell properties

T016

Defects in fetoplacental vascularization and function in EGFL7 KO mice

Stuhlmann, Heidi¹; Lacko, Laretta A.¹; Hurtado, Romulo¹; Massimiani, Mico²; Gelber, Shari E.¹; Salvi, Silvia³; Campagnolo, Luisa²

1. Weill Cornell Medical College, New York, NY, USA

2. University of Rome Tor Vergata, Rome, Italy

3. Catholic University of the Sacred Heart, Rome, Italy

- vascularization of the placenta
- ECM
- Egfl7

T017

PRDM6 mutations impair histone methylation and underlie nonsyndromic patent ductus arteriosus

Li, Na

Yale University, New Haven, CT, USA

- Patent ductus arteriosus
- Mutation
- smooth muscle cells

T018

PI3 Kinase inhibition improves vascular malformations in mouse models of Hereditary Haemorrhagic Telangiectasia

Ola, Roxana

Yale University School of Medicine, New Haven, CT, USA

- To define cellular/molecular mechanisms that cause AVMs in mice and identify novel approaches to revert them
- We provide evidence that an increase in PI3K/AKT pathway is responsible for AVM formation in our mice models
- We identified that targeting PI3K pathway might be a novel target for the treatment of AVMs in HHT2 patients

HHT

T019

Identifying PTPN14-dependent mechanisms that influence clinical manifestations of Hereditary Hemorrhagic Telangiectasia

Mamai, Ons; Vaughan, Kahlil; Trilok, Suprita; Akhurst, Rosemary J.
University of California, San Francisco, San Francisco, CA, USA

- endothelial cell
- BMP9
- PTPN14

T020

Telangiectasia-on-a-chip: An in vitro, perfused model of hereditary hemorrhagic telangiectasia

Andrejecsck, Jillian W.; Hughes, Christopher C.
University of California, Irvine, Irvine, CA, USA

- In vitro model of HHT based on vascularized micro-organ platform
- Knockdown of Alk1, mutations in which cause HHT2, results in network resembling telangiectasia
- Future use of model to study processes important in development of telangiectasias

Diseases

T021

MT1-MMP endothelial deletion improves vascular response and ameliorates colitis

Esteban, Sergio¹; Gonzalo, Pilar¹; Colmenar, Angel¹; Seiki, Motoharu²; López Otín, Carlos³; Garcia Arroyo, Alicia¹
1. Centro Nacional de Investigaciones Cardiovasculares Carlos III(CNIC), Madrid, Spain
2. Institute of Medical Science, University of Tokyo, Tokyo, Japan
3. Instituto Universitario de Oncología, Universidad de Oviedo, Oviedo, Spain

- The MT1-MMP is required for endothelial cell migration and tubulogenesis during sprouting in vitro
- Endothelial deletion of MT1-MMP ameliorates intestinal inflammation in mice treated with 1% DSS
- Our data uncover MT1-MMP as a novel player in intussusceptive angiogenesis

T022

Anti-vascular endothelial growth factor treatment normalizes tuberculosis granuloma vasculature and improves small molecule delivery

Datta, Meenal¹; Via, Laura²; Kamoun, Walid¹; Liu, Chong¹; Chen, Wei¹; Seano, Giorgio¹; Weiner, Danielle²; Schimel, Danief²; England, Kathleen²; Martin, John¹; Gao, Xing¹; Xu, Lei¹; Barry, Clifton²; Jain, Rakesh K.¹
1. Massachusetts General Hospital, Boston, MA, USA
2. National Institute of Allergy and Infectious Disease, Bethesda, MD, USA

- Pulmonary tuberculosis granulomas feature a structurally and functionally abnormal vasculature
- Anti-VEGF treatment can “normalize” the granuloma vasculature, improving the structural morphology
- Anti-VEGF treatment reduces hypoxia and improves the delivery of small molecules in tuberculosis granulomas

T023

Cerebral microvascular calcification in the mouse model for primary familial brain calcification is caused by ossification of capillaries

Zarb, Yvette; Kirschenbaum, Daniel; Aguzzi, Adriano; Keller, Annika
University Hospital of Zurich, Zurich, Switzerland

- Investigation of the pathomechanism of cerebral microvascular calcification using mouse PDGFB hypomorphs
- Evidence that microvascular mineralisation in mouse PDGFB hypomorphs is a result of osteogenic calcification
- Aiding in understanding the role of PDGFB hypomorphism in the development of bone forming cells in the brain

T024

Tumor-induced neutrophil extracellular traps (NETs) impair vascular function and induce systemic inflammation in mice with cancer

Cedervall, Jessica; Zhang, Yanyu; Huang, Hua; Zhang, Lei; Femel, Julia; Dimberg, Anna; Olsson, Anna-Karin
Uppsala University, Uppsala, Sweden

- Tumors induce systemic intravascular NETosis in mice with cancer and impair peripheral vessel function
- Tumor-induced NETs cause endothelial activation and inflammation in distant organs of mice with cancer
- NETosis is potentially a cause of organ dysfunction in individuals with cancer

T025

Change in VEGF-A165b / VEGF-A ratio as an indicator of cell therapy efficacy in patients with CLI

Kikuchi, Ryoosuke¹; Kondo, Kazuhisa¹; Hayashida, Ryu¹; Shibata, Rei¹; Walsh, Kenneth²; Murohara, Toyooki¹

1. Nagoya University, Nagoya, Japan
2. Boston University School of Medicine, Boston, MA, USA

- Therapeutic angiogenesis
- anti-angiogenic VEGF-A splice isoform
- Adipose-derived regenerative cells

T026

Distinct requirement of Alk2/ACVR1 and Alk3/BMPR1A in bone morphogenetic protein induced retinal angiogenesis

Lee, Heon-Woo

Yale University, New Haven, CT, USA

- Each BMP receptors have distinct expression pattern and function in endothelial cells
- BMP signaling mediated by coordination of ALK2, ALK3, and BMPR2 as an essential pro-angiogenic cue
- ALK1, ALK2 ALK3 and BMPR2 iEC knock out mice have distinct phenotype

Heart

T027

Mitochondrial fusion-related protein predicts the response to the treatment of heart failure among patients with idiopathic dilated cardiomyopathy

Jiao, Shuang; Shimizu, Ippei; Watanabe, Tohru; Kashimura, Takeshi; Yoshida, Yohko; Hanawa, Haruo; Ozaki, Kazuyuki; Minamino, Tohru

Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

- Mitochondrial fusion-related protein
- beta-1 adrenergic receptor-mediated signaling pathway
- ventricular myocytes

T028

Brown adipose tissue has a critical role in the maintenance of metabolic homeostasis in failing heart

Yoshida, Yohko¹; Shimizu, Ippei¹; Walsh, Kenneth²; Minamino, Tohru¹

1. Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan
2. Boston University School of Medicine, Boston, MA, USA

- BAT dysfunction develops with heart failure
- BAT dysfunction promotes cardiac remodeling by inducing systemic metabolic dysfunction
- Maintenance of BAT homeostasis is critically important for heart failure therapy

T029

Selective blockade of periostin exon-17 ameliorates heart failure after myocardial infarction

Sanada, Fumihiko; Taniyama, Yoshiaki; Muratsu, Jun; Otsu, Rei; Rakugi, Hiromi; Morishita, Ryuichi

Osaka University Graduate School of Medicine, Suita, Japan

- Regulation of extracellular matrix protein, periostin, for the treatment of heart failure
- Splicing variants of periostin in C-terminal have different role in cardiac remodeling
- Neutralizing antibody against periostin exon 17 might offer new therapeutic option for AMI

T030

VEGFR2 signaling mediates endothelial cell to cardiomyocyte crosstalk in cardiac hypertrophy

Kivelä, Riikka¹; Amudhala Hemanthakumar, Karthik²; Robciuc, Marius¹; Alitalo, Kari³

1. University of Helsinki and Wihuri Research Institute, Helsinki, Finland

2. University of Helsinki, Helsinki, Finland

3. Biomedicum Helsinki/Univ Helsinki, Helsinki, Finland

- Endothelial VEGFR1 deletion induces cardiomyocyte hypertrophy similarly as its ligands VEGF-B and PIGF
- Blocking or deleting endothelial VEGFR2 inhibits the VEGF-B and PIGF induced cardiac hypertrophy
- We identified endothelial VEGFR2 signaling as an important regulator of cardiomyocyte growth

T031

Treatment with anti-RANKL antibody reduces infarct size and attenuates dysfunction impacting on neutrophil-mediated injury

Carbone, Federico¹; Brandt, Karim J.²; Mach, Francois³; Montecucco, Fabrizio¹

1. University of Genoa, Genoa, Italy

2. University of Geneva, Geneva 4, Switzerland

3. University Hosp, Geneva Med School, Geneva, Switzerland

- RANKL
- Infarct
- Neutrophil

Organ Specific Vascular Beds

T032

Analysis of the effect of the nucleolin targeting pseudopeptide N6L in retinopathy diseases

Darche, Marie¹; Cossutta, Melissande¹; Courty, José¹; Paques, Michel²; Cascone, Ilaria¹

1. CRRET laboratory, Créteil, France

2. Centre d'investigations clinique, Paris, France

- N6L is a peptidic antagonist of Nucleolin located at the cell surface of activated endothelial cells
- Study of N6L in Oxygen-Induced Retinopathy and Laser-Induced Choroidal Neovascularization models
- N6L showed antiangiogenic efficiency at low doses by systemic administration in retinopathies models

T033

S. aureus alpha toxin activates Notch1 in retinal endothelial cells and induces retinal angiogenesis in vivo

Hernandez, Sonia L.; Defnet, Ann M.; Naina, Bagrodia; Lec, Bianca; Bubeck-Wardenburg, Juliane; Kandel, Jessica J.

The University of Chicago, Chicago, IL, USA

- S. aureus, via Hla toxin is a significant bacterial cause of morbidity and mortality in the human population
- Hla toxin is known to activate Notch via ADAM10, a modulator of retinal angiogenesis.
- Hla induced Notch activation in retinal angiogenesis, as well as increased density of retinal vasculature

T034

Activation of ARF6 by two ARF-GEFs differentially controls VEGFR2 trafficking and signal transduction

Rich, Bianca E.; Winter, Jacob M.; Shi, Dallas; Zhu, Weiquan; Li, Dean Y.

University of Utah, Salt Lake City, UT, USA

- ARNO activates ARF6 to stimulate VEGFR2 internalization
- GEP100 activates ARF6 to promote VEGFR2 recycling via NRP1, co-receptor, binding
- Targeting ARF6 can inhibit VEGFR2 trafficking and consequent pathological signaling

T035

The Dll4-Notch axis and organic anion transporters cross-regulate indoxyl sulfate-induced macrophage activation: a novel mechanism for atherogenesis in chronic kidney disease

Nakano, Toshiaki¹; Chen, Mingxian¹; Pestana, Diego¹; Katsuki, Shunsuke¹; Kum, Angelo¹; Kuromoto, Rodrigo¹; Irvin, Whitney¹; Aikawa, Elena²; Aikawa, Masanori²

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

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

- Indoxyl sulfate mediates inflammation in macrophages via Dll4 Notch signaling
- Dll4-Notch signaling induces atherosclerosis in CKD
- OATP2B1 is expressed in macrophages and mediates indoxyl sulfate-induced inflammation

T036

Role of TGF-beta and BMP-7 in the acquisition of endothelial to mesenchymal transition (EndMT), vascular disorganization and fibrosis during cirrhosis progression

Morales-Ruiz, Manuel¹; Ribera, Jordi²; Pauta, Montse²; Melgar-Lesmes, Pedro²; Cordoba, Berna²; Bosch, Anna³; Calvo, Maria³; Rodrigo, Daniel²; Sancho, Pau²; Jimenez, Wladimiro¹

1. Hospital Clinic of Barcelona, IDIBAPS/CIBERehd/University of Barcelona, Barcelona, Spain

2. IDIBAPS/CIBERehd, Barcelona, Spain

3. School of Medicine, Centres Científics i Tecnològics, University of Barcelona, Barcelona, Spain

- A subpopulation of endothelial cells from cirrhotic patients and mice undergo EndMT
- BMP-7 blocks the acquisition of EndMT in vitro, induced by TGF-b, and in vivo in cirrhotic mice
- BMP-7 treatment improves liver dysfunction by reducing fibrosis and vascular disorganization

T037

Nitric oxide and prostacyclin in progression of Liver Sinusoidal Endothelial Cells (LSECs) dysfunction induced by Non-Alcoholic Fatty Liver Disease (NAFLD)

Kus, Edyta¹; Patrycja, Kaczara¹; Mateuszuk, Lukasz¹; Gregorius, Aleksandra¹; Czyzynska-Cichon, Izabela¹; Kaczor, Dawid¹; Selmi, Anna¹; Czarnowska, Elzbieta²; Chlopicki, Stefan¹

1. Jagiellonian University, Krakow, Poland

2. The Children's Memorial Health Institute, Warszawa, Poland

- The structural, biochemical and metabolic changes of LSECs during NAFLD progression were studied
- Impaired NO synthesis was not associated with LSECs defenestration but compensated by PG12 production
- Mitochondrial respiration seems to be the main source of energy over glycolysis in LSECs

T038

Endothelial PlexinD1 is a requisite regulator of Vegf and Notch signaling during lung organogenesis

Deckelbaum, Ron A.; Lerner, Iuliia; Tong, Chunxiang; Hughes, Virginia C.; Nuwayhid, Samer; Walls, Johnathon; Rajamani, Saathyaki; Zambrowicz, Brian; Murphy, Andrew J.; Gale, Nicholas

Regeneron Pharmaceuticals, Tarrytown, NY, USA

- Functional relationship between endothelial cells and organogenesis
- Identification of PlexinD1 as a regulator of lung and kidney development
- PlexinD1 regulates VegfA and Notch signaling during lung development

T039

Experimental Lung Injury reduces KLF2 to increase endothelial permeability via regulation of RAPGEF3-Rac1 signaling

Huang, Ru-Ting¹; Wu, David¹; Meliton, Angelo¹; Jain, Mukesh K.²; Birukova, Anna¹; Kress, John¹; Birukov, Konstantin¹; Mutlu, Gokhan¹; Fang, Yun¹

1. University of Chicago, Chicago, IL, USA

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

- KLF2 is significantly reduced both in animal and in vitro lung injury models
- KLF2 activates small GTPase Rac1 via transcriptional regulation of RAPGEF3 and stabilizes the vascular barrier
- KLF2 plays a central role in regulating many genes associated with ARDS identified by GWAS

Brain

T040

Microfluidics to model the human blood-brain barrier for study of barrier function, drug penetration, and leukocyte-endothelial interactions in the context of neurodegenerative diseases

Obermeier, Birgit¹; Marsh, Graham¹; Huang, Angela¹; Fisher, Ken²; Zumpano, Danielle³; Cottle, Anne C.¹; Shimizu, Fumitaka⁴; Sano, Yasuteru⁴; Kanda, Takashi⁴; Duffield, Jeremy¹; Ransohoff, Richard¹

1. Biogen, Cambridge, MA, USA

2. Nortis, Inc., Seattle, WA, USA

3. Nortis, Inc., Woodinville, WA, USA

4. Yamaguchi University, Ube, Japan

- Neurodegenerative diseases are often characterized by a compromised blood-brain barrier (BBB)

- We have established a novel 3D microfluidic model of the human BBB that is of high physiological relevance
- We obtain a tight barrier that discriminates between substrates and responds to inflammatory stimuli

T042

Characterisation of a transcellular leakage pathway at the Blood-Brain/Retinal Barriers

Chang, Jui-Hsien; Kenny, Bridget-Ann; Turowski, Patric

University College London, London, United Kingdom

- Dysfunctional vascular blood-brain/retinal barriers at the origin of many neuronal and retinal diseases
- Pathophysiological conditions render cerebral endothelial cells permissive to transcellular permeability
- Paracellular and transcellular leakage pathways can coexist in response to most permeability inducing factors

T043

PDGFR β plays a key role in the ectopic migration of neuroblasts along with blood vessels in cerebral stroke

Yamamoto, Seiji¹; Ishii, Yoko¹; Hamashima, Takeru¹; Sato, Hikaru²; Azuma, Erika¹; Sasahara, Masakiyo¹

1. University of Toyama, Toyama, Japan

2. Tokyo General Hospital, Tokyo, Japan

- PDGFR β plays a key role in the ectopic migration of neuroblasts
- Migrating neuroblasts are along with blood vessels
- CXCL12 and integrin $\alpha 3$ are involved in ectopic migration of neuroblasts in N-PR β -KO

Transcriptions and Epigenetics

T044

Epigenetic regulation of necroptosis in developing mesenteric lymphatics

Menendez, Matthew; Podsiadlowska, Joanna; Drozd, Anna; Griffin, Courtney T.

Oklahoma Medical Research Foundation, Oklahoma City, OK, USA

- Brg1 mutant embryos die during mid-gestation with blood-filled and hemorrhagic mesenteric lymphatics
- Ripk3 levels are increased in Brg1 mutant LECs in vivo and in vitro due to a misregulated miRNA
- Ripk3 deletion rescues Brg1 mutant embryos

T046

Exploring the transcriptomic atlas of the mammalian cardiovascular system

Tsang, Hiu Gwen²; Clark, Emily L.¹; Bush, Stephen J.¹; Hume, David A.¹; Corcoran, Brendan M.³; MacRae, Vicky E.¹; Summers, Kim M.¹

1. The Roslin Institute, Midlothian, United Kingdom

2. The Roslin Institute, University of Edinburgh, Midlothian, United Kingdom

3. The University of Edinburgh, Hospital for Small Animals, Midlothian, United Kingdom

- This work describes the first cardiovascular-wide transcriptomic atlas of the mammalian cardiovascular system
- Novel gene networks were identified showing specialised roles and region-specific functions
- This comprehensive dataset will facilitate the understanding of the functions of key cardiovascular genes

T047

The role of miRNA in fine tuning the haemodynamic regulation of endothelial cell epigenetic mechanisms

Wallace, Robert G.¹; Twomey, Laura¹; Orr, A. Wayne²; Moyna, Niall¹; Cummins, Philip M.¹; Murphy, Ronan P.¹

1. Dublin City University, Dublin, Ireland

2. LSU Health Sciences Center - Shreveport, Shreveport, LA, USA

- Epigenetic drift
- miRNA
- Atherosclerosis

T048

Functional dissection of a MAPK-ERG-p300 transcriptional network activated by VEGF signaling

Fish, Jason E.¹; Dang, Lan T.¹; Khyzha, Nadiya¹; Chen, Zhiqi¹; Cheng, Henry S.²; Khor, Melvin¹; Veitch, Shawn¹; Antounians, Lina³; Cantu Gutierrez, Manuel⁴; Njock, Makon-Sebastien¹; Boudreau, Emilie¹; Wilson, Michael D.³; Wythe, Joshua D.⁴

1. University Health Network, Toronto, ON, Canada

2. University of Toronto, Toronto, ON, Canada

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

4. Baylor College of Medicine, Houston, TX, USA

- Induction of DLL4 in response to VEGF stimulation requires dynamic MAPK/ERK activation of the ETS factor, ERG
- A network of VEGF-dependent genes require MAPK/ERG/p300 for induction
- A highly conserved ERG-bound enhancer is required for VEGF induction of the angiogenic gene, HLX

T049

Uncovering VEGF-stimulated variable epigenome landscape in primary cultured endothelium –endothelium specified epigenetic modifiers regulated accurate transcription on the bivalent histone marked angiogenic genes

Kanki, Yasuharu¹; Suehiro, Jun-ichi¹; Osawa, Tsuyoshi¹; Wada, Youichiro¹; Nagai, Nao²; Kodama, Tatsuhiko¹; Aird, William C.³; Minami, Takashi²

1. The University of Tokyo, Tokyo, Japan

2. Kumamoto University, Kumamoto, Japan

3. Beth Israel Deaconess Med Center, Boston, MA, USA

- Global mapping on NFAT bindings, as well as major histone-code profiling in VEGF-stimulated ECs with ChIP-seqs
- Angiogenic transcription factors exclusively obtained ES-like bivalent epigenetic marks via VEGF stimuli
- NFAT associated epigenome modifier transactivated bivalent genes by H3K4me3-accelerator over H3K27me3-brake

T050

Excessive plasmin activity causes endothelial cell necroptosis and 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, USA

- Embryos with excessive plasmin have elevated Ripk3 in endothelial cells lining rupture-prone blood vessels
- Genetically reducing either plasmin activation or Ripk3 rescues Chd4 mutant embryos from vascular rupture
- Cultured endothelial cells treated with plasmin display upregulated Ripk3 transcription

T051

A network of long noncoding RNAs regulated by inflammatory signaling in endothelial cells

Khyzha, Nadiya¹; Wilson, Michael²; Fish, Jason¹

1. University Health Network, Toronto, ON, Canada

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

- Investigating how the NF-kB pathway is fine-tuned via a network of noncoding RNA
- Identifying lncRNA-mRNA neighboring pairs regulated by NF-kB signalling in endothelial cells
- Elucidating potential functional targets of NF-kB regulated lncRNAs

T052

Transcriptional regulation of the smooth muscle-specific, hypertension-associated gene, GRAF3, by RBPJ and TEF-1

Mangum, Kevin D.; Taylor, Joan; Mack, Chris

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

- GRAF3 is a smooth muscle-selective RhoGAP that inhibits SMC contraction and hypertension
- DHS2 within the first intron of the GRAF3 gene exhibits marked SMC-specific transcription activity
- A core sequence within DHS2 binds transcription factors RBPJ and TEF-1 to regulate GRAF3 transcription

T053

SoxF factors induce Notch1 expression via arterial-specific enhancers during early vascular development

Chiang, Ivy¹; Fritzsche, Martin²; Pichol-Thievend, Cathy¹; Neal, Alice²; Holmes, Kelly³; Legendijk, Anne Karine¹; Overman, Jeroen¹; D'Angelo, Donatella⁴; Omini, Alice⁴; Hermkens, Dorien⁵; Liu, Ke⁶; Ratnayaka, Indrika²; Corada, Monica⁷; Bou-Gharios, George⁶; Carroll, Jason³; Dejana, Elisabetta⁴; Schulte-Merker, Steffan⁵; Hogan, Benjamin M.⁸; Beltrame, Monica⁴; De Val, Sarah²; Francois, Mathias¹

1. University of Queensland, Brisbane, QLD, Australia

2. University of Oxford, Oxford, United Kingdom

3. University of Cambridge, Cambridge, United Kingdom

4. Università degli Studi di Milano, Milano, Italy

5. University of Münster, Münster, Germany

6. University of Liverpool, Liverpool, United Kingdom

7. IFOM, Milan, Italy

8. Institute for Molecular Bioscience, Brisbane, QLD, Australia

- SoxF dependent Notch 1 enhancer is identified
- Functional SoxF is required for endogenous notch1b expression
- SoxF modulates Notch1 expression through arterial specific enhancers

T054

Transcription Factor EB regulates (TFEB) VEGFR2 functions in embryo and adult life

Doronozzo, Gabriella¹; Astanina, Elena¹; Cora, Davide¹; Noghero, Alessio¹; Chiabotto, Giulia²; Neri, Francesco²; Comunanza, Valentina¹; Puliafito, Alberto³; Primo, Luca¹; Camussi, G.¹; Ballabio, Andrea⁴; Oliviero, Salvatore²; Bussolino, Federico¹

1. University of Torino, Candiolo, Italy

2. University of Torino, Torino, Italy

3. Candiolo Cancer Institute, Candiolo, Italy

4. Telethon Institute of Genetics and Medicine, Pozzoli, Italy

- TFEB deletion in endothelium impairs embryo vascular remodelling and maturation of retinal and renal vessels
- TFEB targets VEGFR2 by silencing its transcript and regulating its membrane trafficking
- The molecular mechanism requires miR 15a/16-and the motor myosin MYOC1

Tissue Engineering

T055

Hybrid collagen-alginate microspheres scaffolds for localized growth factor release to induce neovascularization in cardiac implants

Munarin, Fabiola; Coulombe, Kareen LK

Brown University, Providence, RI, USA

- Collagen-alginate microsphere hybrid scaffold promotes neovascularization of cardiac engineered tissues
- Immobilization of proangiogenic factors in the hybrid scaffold leads to recruitment of host endothelial cells
- Formation of vascular networks is quantified by 2D and 3D in vitro assays and by implants on infarcted hearts

T056

Brain microvascular mimics using human iPS cells

Sundaram, Sumati¹; DeVito, Kyle²; Adams, Andre²

1. George Mason University, Fairfax, VA, USA

2. Naval Research Laboratory, Washington DC, USA

- Derivation of brain microvascular endothelial cells from hiPS cells
- Creating microvascular vessels using hiPS-derived brain microvascular endothelial cells
- Characterization of hiPS-derived brain microvascular endothelial cells and engineered microvascular mimics

T057

Angiogenic peptide nanofibers enhanced post-infarction arteriogenesis and cardiac remodeling

Abdul Jalil, Rufaihah¹; Yasa, Ceren I.²; Ramanujam, Vaibavi¹; Cheyyatraivendran Arularasu, Suganya¹; Kofidis, Theo¹; Guler, Mustafa O.²; Tekinay, Ayse B.²

1. National University of Singapore, Singapore, Singapore

2. Bilkent University, Ankara, Turkey

- Heparan Sulfate-Mimetic Peptide Nanofiber Injection Salvaged Cardiac Muscle and Regulated Infarct Expansion
- The Peptide Nanofiber Treatment Enhanced the Degree of Post-infarction Arteriogenesis
- The Peptide Nanofiber Treatment Resulted in Significant Improvement in Cardiac Output And Contractility

T058

Bone marrow mononuclear cell seeding prevents luminal thrombosis within tissue-engineered vascular grafts directly following implantation in mice

Reinhardt, James W.; Best, Cameron A; Yi, Tai; Shinoka, Toshiharu; Breuer, Christopher K.

Nationwide Children's Hospital, Columbus, OH, USA

- Our murine TEVG model develops partial thrombosis within 1 day after implantation
- BM-MNCs might be antithrombotic; seeded scaffolds show less thrombosis than unseeded scaffolds
- In vitro experiments suggest the mechanism is not mediated by PGE2 or NO

T059

Characterization of a novel 3D perfused blood-brain barrier model

Tsubota, Yoshiaki; Ketsawatsomkron, Pimonrat

Nortis, Inc., Seattle, WA, USA

- Nortis' microfluidic technology established perfusable 3D blood-brain barrier (BBB) model
- Our model recapitulates in vivo BBB-like architectures, permeability, and leukocyte trafficking
- Our model will serve as a research tool for testing drug transport and cell migration across the BBB

T060

Inducing vascularization of engineered tissues in vitro and in vivo

Levenberg, Shulamit

Technion, Haifa, Israel

- Vasculogenic dynamics in 3D engineered tissue constructs
- Morphogenesis of 3D vascular networks is regulated by tensile forces.
- Integration of engineered vessel networks in vivo

T061

Functional ultrathorax biomaterials to enhance vascular stents

Howell, David; Duran, Camille; Bondos, Sarah; Bayless, Kayla

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

- Ultrathorax (Ubx) biomaterials are functionalized with VEGF, bFGF, and SDF-1a
- Functionalized Ubx biomaterials promote endothelial attachment, survival, and downstream signaling in vitro.
- VEGF-Ubx biomaterials attract outgrowing sprouts in aortic ring assay and induce vessel formation in CAM assay

T062

A new ex vivo tool for stem cell fate and functional studies in cultured microvascular networks

Murfee, Walter Lee; Katakam, Prasad V.; Bunnell, Bruce; Azimi, Mohammad S.; Motherwell, Jessica

Tulane University, New Orleans, LA, USA

- The rat mesentery culture model offers a new tool for investigating angiogenesis
- This study demonstrates application of the model for evaluating stem cell fate and vasoreactivity
- Our results suggest new hypotheses for angiogenesis research

T063

Examining the role of metabolism using in vitro 3D microtumors supported by perfused vascular networks

Sobrinho Gregorio, Aqua; Phan, Duc; Datta, Rupsa; Gratton, Enrico; Hughes, Christopher

University California, Irvine, Irvine, CA, USA

- tissue engineering

- cancer metabolism
- vasculogenesis

T064

Specification of arterial-venous identity in engineered vascularized tissues requires perivascular cells and is impaired in diabetes

Altalhi, Wafa

University Health Network, Toronto General Research Institute, Toronto, ON, Canada

- Tissue engineering: We are using 3D implantation model made from microvascular fragments
- Diabetes: We are comparing vascular maturation in diabetic vs healthy mice
- Arterial and Venous Identity: acquisition arterial and venous identity microvasculature

T065

A microphysiological system to model the human neurovascular unit

Phan, Duc T.; Craver, Brianna M.; Flanagan, Lisa A.; Hughes, Christopher C.

University of California, Irvine, Irvine, CA, USA

- An in vitro microphysiological model of human neurovascular unit supported by perfused, living microvessels
- Preliminary studies indicated that ECFC-EC take on BBB characteristics in the platform
- Development of this in vitro model will further BBB pathological studies

T066

Modular fabrication of self-assembled vascular tissue from smooth muscle cells and growth factor-loaded degradable microspheres

Strobel, Hannah¹; Dikina, Anna D.²; Alsberg, Eben²; Rolle, Marsha W.¹

1. Worcester Polytechnic Institute, Worcester, MA, USA

2. Case Western Reserve University, Cleveland, OH, USA

- We generated 3D vascular tubes from self-assembled, scaffold free tissue ring units
- TGF-beta-loaded microspheres incorporated within self-assembled rings stimulate contractile protein expression
- Cells maintain position within ring units to produce spatial heterogeneity along tubes for disease modelling

T067

Treatment of refractory cutaneous ulcers with mixed sheets consisting of peripheral blood mononuclear cells and fibroblasts

Ueno, Koji; Takeuchi, Yuriko; Samura, Makoto; Tanaka, Yuya; Nakamura, Tamami; Nishimoto, Arata; Murata, Tomoaki; Hosoyama, Tohru; Hamano, Kimikazu

Yamaguchi University Graduate School of Medicine, Ube, Japan

- the therapeutic effects of mixed sheets consisting of peripheral blood mononuclear cells and fibroblasts
- vascular endothelial growth factor (VEGF) secretion in mixed cell sheets
- a promising therapeutic material for refractory cutaneous ulcers

Immunity

T068

Sequential chemotactic cues guide neutrophils through distinct cellular barriers of blood vessel walls during inflammation

Girbl, Tamara; Voisin, Mathieu-Benoit; Nourshargh, Sussan

Barts and The London School of Medicine, Queen Mary University of London, London, United Kingdom

- Chemokines CXCL1 & CXCL2 exhibit non-redundant functions during TNF-induced neutrophil trafficking
- CXCL1 is essential for neutrophil adhesion to endothelial cells & crawling on pericytes in vivo
- CXCL2 plays a key role in mediating neutrophil migration through endothelial cell junctions

T069

Angiopoietins and Angiopoietin-like proteins bind to LILRA/B receptors and activate innate immune responses in human monocytes

Fryxell, Dan

Bio-Techne, Minneapolis, MN, USA

- Angiopoietins and ANGPTL proteins bind to multiple LILRA and LILRB (ILT/CD85) family proteins
- LILRs are expressed on antigen presenting cells and can promote or inhibit monocyte activation
- Angiopoietins and ANGPTL proteins offer additional ways to regulate monocytes and innate immunity

T070

Host neutrophils mediate tissue graft revascularization

Lin, Rwei-Zeng¹; Lee, Chin Nien²; Melero-Martin, Juan M.²

1. Boston Children's Hospital, Brookline, MA, USA

2. Boston Children's Hospital, Boston, MA, USA

- Inadequate revascularization remains a frequent outcome in surgical grafting
- Revascularization of transplanted grafts is mediated by host neutrophils
- Harnessing the potential of host neutrophils can significantly improve surgical grafting

T071

Suppressive effect of inflammatory regulator mCAP-18 on CD4 T effector memory cell population in ApoE(-/-) mice

Mihailovic, Peter M.; Lio, Wai Man; Yano, Juliana; Zhao, Xiaoning; Zhou, Jianchang; Chyu, Kuang-Yuh; Shah, Prediman K.; Cercek, Bojan; Dimayuga, Paul C.

Cedars-Sinai Medical Center, Los Angeles, CA, USA

- Stimulation with mCAP-18 suppresses CD4+ effector and central memory cell population in ApoE^{-/-} mice
- CD4+ effector memory cell suppression occurs in mice fed normal or high fat diet
- Stimulation with mCAP-18 has no effect on CD4+ T regulatory cells from ApoE^{-/-}/FoxP3-GFP mice

T072

Long noncoding RNA Inc-FAM164A1 modulates macrophage activation through NF-κB signaling: a novel potential therapeutic target for inflammatory diseases

Wang, Jian-Guo¹; Nihira, Keishi¹; Decano, Julius L.²; Mattson, Peter C.¹; Amaral, Gabriela³; Mojcher, Alexander¹; Lee, Lang Ho Ho¹; Singh, Sasha²; Zhang, Hengmin¹; Aikawa, Masanori⁴

1. Center for Interdisciplinary Cardiovascular Sciences, Brigham and Women's Hospital, Boston, MA, USA

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

3. Brigham and Womens Hospital, Brookline, MA, USA

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

- We identified a novel long noncoding RNA (Inc-FAM164A1) in activated human macrophages
- Lnc-FAM164A1 regulates LPS-induced expression of pro-inflammatory cytokines and modulates NF-κB signaling
- LPS challenge increased the expression of Inc-FAM164A1 in blood leukocytes and spleen in humanized mice

T073

Immunoglobulin G monoclonal autoantibody LO9 targets a cryptic adhesion-dependent epitope on ApoB trapped in the arterial wall in LDL-receptor deficient atherosclerotic mice and stimulates macrophage TNF alpha release

Khamis, Ramzi¹; Woollard, Kevin¹; Caga-Anan, Mikhail¹; Kojima, Chiari¹; Hyde, Gareth¹; Chang, Shang-Hung¹; Johns, Michael²; Bicknell, Colin¹; Boyle, Joseph J.¹; Johnson, Jason L.³; Matthews, Paul¹; Haskard, Dorian¹

1. Imperial College London, London, United Kingdom

2. NHLI, L5, ICTEM, Imperial College, London, United Kingdom

3. University of Bristol, Bristol, United Kingdom

- LO9 shows that a neoepitope for an autoantibody appears following arterial wall trapping of LDL
- Stimulation of TNF release shows possible pathogenicity of this autoantibody in atherosclerosis
- In vivo NIRF imaging of atherosclerosis with LO9 shows its potential as an in vivo targeting vehicle

T074

Humoral immunity and oxidized LDL clearance: a transient increase and then loss of plasma oxidized LDL levels occurs dynamically in parallel with IgG anti-MDA-LDL depletion and a reduction on oxLDL-IgG complexes during cardio-pulmonary bypass

Kojima, Chiari¹; Ammari, Tareq¹; Caga-Anan, Mikhail¹; Nguyen, Bao¹; Anderson, Jon²; Evans, Paul³; Johns, Michael⁴; Lynham, Steven⁵; Haskard, Dorian¹; Khamis, Ramzi¹

1. Imperial College London, London, United Kingdom
2. Imperial College Healthcare NHS Trust, London, United Kingdom
3. University of Sheffield Medical School, Sheffield, United Kingdom
4. NHLI, L5, ICTEM, Imperial College, London, United Kingdom
5. King's College London, London, United Kingdom

- Plasma LDL is oxidized but rapidly cleared during cardio-pulmonary bypass surgery
- The fall in IgG anti-MDA-LDL and oxLDL-IgG complexes suggests oxLDL clearance is antibody-mediated
- This provides a model for the studying the role of humoral immunity in oxLDL clearance in humans

T075

Implication of NOD1 expressing smooth muscle cell in vascular inflammation and atherosclerosis

Jiang, Xintong

Karolinska Institute, Stockholm, Sweden

- Lesion resident SMC NOD1 singling is highly involved in vascular inflammation and atherosclerosis in mice
- NOD1 activation leads to cytokine production in human atherosclerosis, and is identified in lesions SMC
- Rat neointimal SMCs exert rigorous inflammatory activity in response to NOD1 stimulation

T076

Regulation of the phosphorylation of VE-cadherin Y731 under basal and inflammatory conditions

Holm, Maren; Nyamay'Antu, Alengo; Vestweber, Dietmar

Max-Planck Institute for Molecular Biomedicine, Munster, Germany

- Y731 phosphorylation occurs before VEC reaches the cell surface and is protected under basal conditions
- Leukocyte triggered dephosphorylation of VEC Y731 is directly mediated by SHP2
- Leucocytes trigger recruitment of SHP-2 to the VEC complex and dissociation of SHP-2 from PECAM

T077

Activated β 2 integrins restrict neutrophil recruitment during acute respiratory infection with *Pseudomonas aeruginosa*

Wilson, Zachary S.¹; Serratelli, William S.²; Ahn, Lawrence²; Sen, Mehmet³; Lefort, Craig T.²

1. Brown University, Providence, RI, USA
2. Rhode Island Hospital, Providence, RI, USA
3. University of Houston, Houston, TX, USA

- Neutrophils with defective integrin activation exhibit enhanced recruitment during respiratory infection
- Emigration from pulmonary vasculature into interstitium is the step that is delayed by active β 2 integrins
- Small molecule inhibitor of β 2 integrin activation promotes neutrophil entry into interstitial and airspaces

T078

ADAM10-mediated cleavage of ICAM-1 is required for neutrophil release from the endothelial surface and enter the diapedesis step

Rademakers, Timo¹; Brouns, Sanne²; van Stalborch, Annemarike²; Donners, Marjo³; van Buul, Jaap D.¹

1. Sanquin Research and Landsteiner Laboratory, Amsterdam, Netherlands
2. University of Amsterdam, Amsterdam, Netherlands
3. Maastricht University, Maastricht, Netherlands

T079

Critical role of complement C5a and neutrophils during high-fat diet-induced vascular inflammation

Osaka, Mizuko¹; Honda, Masaki²; Inomata, Yukihiro²; Yoshida, Masayuki¹

1. Tokyo Medical and Dental University, Tokyo, Japan
2. Kumamoto University, Kumamoto, Japan

- Neutrophils play an important role in the early phase of vascular inflammation by high-fat diet feeding
- Excessive high-fat diet feeding increase serum C5a level
- Elevation of serum C5a induces neutrophil adhesion in femoral artery

T080

Recruitment of circulating inflammatory monocytes by TNF/IL-6-Induced expression of vascular cell adhesion molecule 1 (VCAM-1) drives valvular inflammation and fibrosis in K/B.g7 mice

Meier, Lee A.; Auger, Jennifer; Engelson, Brianna; Boyer, Joshua; Breed, Elise; Binstadt, Bryce A.

University of Minnesota, Minneapolis, MN, USA

- Atherosclerosis and valvular heart disease are manifestations of fibrosis
- The K/B.g7 mouse develops spontaneous fibrotic valvular heart disease with complete penetrance
- We demonstrate a TNF/IL6-VCAM1-a4 β 1 axis mediating valve fibrosis in the K/B.g7 line

T081

Suppression of the gut microbiome accelerates lethal herpesviral infection and reduces efficacy of immune modulating therapy

Ambadapadi, Sriram; Thomas, Ryan; Jobin, Christian; Karst, Stephanie; Tibbetts, Scott; Morshed, Sufi; McFadden, Grant; Lucas, Alexandra

University of Florida, Gainesville, FL, USA

- Microbiome and vasculitis
- Immunomodulatory proteins from myxomavirus
- anti-inflammatory peptides

T082

Lung vaso-occlusion in sickle cell disease mediated by arteriolar neutrophil-platelet micro-emboli

Sundd, Prithu; Bennewitz, Margaret; Jimenez, Maritza; Vats, Ravi; Kato, Gregory; Gladwin, Mark

University of Pittsburgh, Pittsburgh, PA, USA

- First ever in vivo real-time video microscopic evidence of lung vaso-occlusion in sickle mice
- Neutrophil-platelet embolic aggregates occlude lung arterioles to promote lung vaso-occlusion in sickle mice
- Blocking platelet P-selectin resolves lung vaso-occlusion by attenuating neutrophil-platelet aggregates

Stem Cells

T083

Diabetic mesenteric stem cells from PAD patients have decreased ERK phosphorylation

Brewster, Luke P.

Emory Clinic, Decatur, GA, USA

- human MSCs from diabetic patients are not well studied. we have found them to be robust angiogens
- However their expansion is limited in culture
- we have identified decreased erk1/2 phosphorylation in stimulation by FGF-2 that may be part of this problem

T084

Transplantation of human induced pluripotent stem cell-derived endothelial cells (iPSC-ECs) in a murine model of wound healing; can a polycaprolactone/gelatin scaffold enhance their therapeutic potential?

Clayton, Zoe E.¹; Sadeghipour, Sara¹; Tan, Richard¹; Wong, Jack WT²; Bursill, Christina¹; Wise, Steven G.¹; Cooke, John P.²; Sanjay, Patel¹

1. Heart Research Institute, Sydney, NSW, Australia

2. Houston Methodist Research Institute, Houston, TX, USA

- This study aims to test the pro-angiogenic properties of iPSC-ECs in the context of wound healing
- iPSC-ECs may enhance angiogenesis in wound healing, but direct application leads to variable cell survival
- iPSC-ECs can be pre-seeded on PCL+gelatin scaffolds. These scaffolds appear to promote wound closure

T085

Peg3/PW1 is a marker of a subset of vessel associated endothelial progenitors

Malinverno, Matteo

IFOM - The FIRC Institute of Molecular Oncology, Milano, Italy

- Vessel associated endothelial progenitors
- Endothelial to Mesenchymal transition
- RNA sequencing

T086

Arterialization of endothelial cells derived from embryonic stem cells by upregulation of Notch1 signaling and application to the repair of ischemic injury

Jang, Il Ho; Do, Eun Kyoung; Park, Jaekyung; Heo, Soon Chul; Kwon, Yang Woo; Kim, Jae Ho
Pusan National University School of Medicine, Yangsan, Korea

- Arterialization of endothelial cells
- Embryonic stem cell differentiation
- Cell therapy for ischemic limb disease

T087

Tip cell/stalk cell characterization of Nrp1 endothelial progenitors derived from embryonic stem cells

Kim, Diana; Dai, Guohao
Rensselaer Polytechnic Institute, Troy, NY, USA

- We optimized an in vitro protocol for differentiation of Nrp1-positive vascular tip cells from ESCs
- Nrp1+ vascular progenitors exhibit higher proliferative ability and migratory behavior than Nrp1- cells
- VECad+Nrp1+ cells show up-regulated tip cell markers and down-regulated stalk cell markers

T088

Cellular and molecular characterisation of human endothelial progenitors in vivo defined based on self-renewal and colony forming potential identifies Notch signalling as a key pathway

Shafiee, Abbas; Patel, Jatin; Fisk, Nicholas M.; Khosrotehrani, Kiarash
The University of Queensland, Brisbane, Australia

- human endothelial progenitors
- notch
- placenta

T089

Priming of endothelial colony forming cells using mesenchymal stem/stromal cells improves engraftment and vasculogenic potential by initiating mesenchymal transition orchestrated by NOTCH signalling

Shafiee, Abbas¹; Patel, Jatin¹; Huttmacher, Dietmar W.²; Fisk, Nicholas M.¹; Khosrotehrani, Kiarash¹
1. *The University of Queensland, Brisbane, Australia*
2. *Queensland University of Technology, Brisbane, Australia*

- endothelial colony forming cells
- mesenchymal stem cells
- vasculogenesis

T090

Normal and neoplastic stem cells

Weissman, Irving
Stanford University, Stanford, CA, USA

- Identified methods to isolate and purify pure hematopoietic stem cells (HSCs)
- Followed the progression from hematopoietic stem cells (HSCs) to myelogenous leukemias
- Identified a dominant method of cancer cells to avoid programmed cell removal

T091

Leukotriene signaling and its regulation of integrin $\alpha 4$ controls the transition of hematopoietic niche from vasculature to liver

Jiang, Xuan; Hawkins, John; Lee, Jerry; Lizama, Carlos; Bos, Frank L.; Zape, Joan P.; Ghatpande, Prajakta; Louie, Justin; Lagna, Giorgio; Ann, Zovein C.; Hata, Akiko
University of California, San Francisco, San Francisco, CA, USA

- Endothelial loss of Drosha (cKO) in mice results in a complete loss of hematopoietic stem cells
- Upregulation of the LTB4/Itga4 in cKO attenuates cell fate specification and mobilization of HSPC
- Genetic or pharmacological inhibition of LTB4/Itga4 rescues the hematopoietic defects in cKO

T092

Transplantation of mouse ESC derived endothelial cells supports expansion and recovery of hematopoietic stem and progenitor cells

Palikuqi, Brisa

Weill Cornell Medicine, New York, NY, USA

- We successfully differentiated endothelial cells from mouse embryonic stem cells
- These cells were used in vitro to expand hematopoietic stem and progenitor cells
- Transplantation of mESC-ECs resulted in recovery of hematopoiesis and vascularity in irradiated VEGFR2ko mice

T093

Cell to cell communication via gap junctions (connexins) in the brain subventricular zone

Baker, Kasey¹; Fang, Jennifer S.²; Lauridsen, Holly M.³; Gonzalez, Anjelica³; Khoyrattee, Nafiisha²; Gillis, Noelle¹; Hirschi, Karen K.²

1. Yale Cardiovascular Research Center, New Haven, CT, USA

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

3. Yale University, New Haven, CT, USA

- Cx40 and Cx43 are highly expressed in the brain subventricular zone
- NCS-EC communication via Cx43 may regulate adult brain neurogenesis
- Cx40 may regulate NSC maintenance. We are creating a co-culture system for NSC and EC on PEG-hydrogel membrane

Hypertension/Endothelial-dependent Responses

T094

LCZ696, an angiotensin receptor neprilysin inhibitor, attenuates renal fibrosis and glomerular injury in a mouse model of salt-sensitive hypertension using angiotensin 1 receptor knockout mouse

Ohtsu, Rei; Taniyama, Yoshiaki; Sanada, Fumihiko; Muratsu, Jun; Shibata, Kana; Brule, Kawako May; Rakugi, Hiromi; Morishita, Ryuichi

Osaka University, Suita, Japan

T095

Impaired endothelium-dependent relaxation of coronary arterioles after cardioplegic-ischemia/reperfusion in pig with metabolic syndrome

Liu, Yuhong; Chu, Louis M.; Sabe, Ashraf; Sellke, Frank; Feng, Jun

Rhode Island Hospital, Providence, RI, USA

- Coronary microcirculation Endothelial Function Coronary arterioles
- Metabolic syndrome Obesity
- calcium activated potassium channels Cardioplegia Ischemia and reperfusion

T096

Evaluation of endothelial function-associated clinical parameters and whole blood PCR array analysis in patients with lifestyle-related diseases

Morimoto, Kana¹; Takahashi, Yuka¹; Yamashita, Saori¹; Yoshida, Sumiko¹; Ishikawa, Kazue¹; Uemoto, Ryoko¹; Yuasa, Tomoyuki¹; Azuma, Hiroyuki²; Aihara, Ken-ichi¹

1. Tokushima University, Tokushima, Japan

2. Anan Kyohei Hospital, Anan, Japan

- Endothelial function
- Whole blood PCR array analysis
- Lifestyle-related diseases

T097

Towards understanding the variability of patient pericardial resistance artery contractility

Bloksgaard, Maria¹; Leurgans, Thomas¹; Rosenstand, Kristoffer¹; Nissen, Inger¹; Irmukhamedov, Akhmadjon²; Rasmussen, Lars M.²; De Mey, Jo¹

1. University of Southern Denmark, Odense C, Denmark

2. Odense University Hospital, Odense C, Denmark

- max active wall tension

- media cross sectional area
- pharmacotherapy

Animal Models of Disease

T098

Repetitive postprandial glucose/triglyceride spikes activate p53 in bone marrow progenitor cells and induce premature aging of bone marrow

Horitani, Keita; Iwasaki, Masayoshi; Kishimoto, Hiroshi; Wada, Kensaku; Nakano, Miyuki; Shiojima, Ichiro
Kansai Medical University, Hirakata, Japan

- How does altered glucose/lipid metabolism in T2DM affects the homeostasis of stem cells in bone marrow?
- Repetitive postprandial glucose/triglyceride spikes induce premature aging of bone marrow cells
- bone marrow stem cells maintain their homeostasis via PDK2 upregulation against repetitive glucose spikes

T099

Vascular permeability alternations induced by uremic toxin p-cresyl sulfat

Chen, Shih-Chieh¹; Wang, Chao-Ping²; Tai, Pei-Yang²; Tang, Wei-Hua¹; Liang, Shih-Shin¹; Chung, Fu-Me²

1. Kaohsiung Medical University, Kaohsiung, Taiwan

2. E-Da Hospital, I-Shou University, Kaohsiung, Taiwan

- High levels of PCS are associated with increased mortality of cardiovascular diseases in CKD patients
- Increased vascular permeability induced by PCS was dose and duration dependent
- In situ exposure to high concentration of PCS may produce vascular dysfunction (vascular leakage) in vivo

T100

High cholesterol diet and angiotensin II induces spontaneous atherothrombotic occlusion of balloon-injured rabbit iliac arteries; Effects of lipid-lowering therapies

Honda, Katsuya¹; Matoba, Tetsuya¹; Nakano, Kaku²; Egashira, Kensuke¹

1. Kyushu University, Fukuoka City, Japan

2. Department of Cardiovascular Medicine, Fukuoka City, Japan

- We established a valid animal model of spontaneous atherothrombotic occlusion in rabbits
- Oral treatment with Ezetimibe not Rosuvastatin reduced the incidence of atherothrombotic occlusion
- 7-KC inhibited the proliferation and migration of HUVECs and induced TF on cultured SMCs

T101

Macrophage dynamin-related protein1 promotes neointima formation after mechanical injury in mouse femoral arteries

Umezumi, Ryuta¹; Koga, Jun-ichiro¹; Wang, Lixang¹; Nomura, Masaki²

1. Kyushu University, Fukuoka, Japan

2. Department of Medicine and Bioregulatory Science, Fukuoka, Japan

- Femoral arterial wire injury was performed in macrophage selective Drp1-deficient mice
- Deletion of macrophage Drp1 decreased intimal thickening and macrophage accumulation
- Inhibition of Drp1 attenuated induction of IL-1 β and MCP-1 by LPS+IFN γ in "M1" macrophages

T102

Bone marrow and endothelial cell senescence induced by excessive adrenergic signaling promotes cardiac remodeling

Katsuami, Goro; Shimizu, Ippei; Yoshida, Yohko; Suda, Masayoshi; Yuka, Hayashi; Jiao, Shuang; Minamino, Tohru

Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan

- Excessive adrenergic signaling induces p53 dependent cellular senescence in bone marrow and endothelial cell
- Bone marrow and endothelial cell senescence induced by adrenergic signaling promotes cardiac remodeling
- Genetic suppression of bone marrow and endothelial senescence ameliorates cardiac remodeling

T103

Rabbit model for a preclinical comparison of coronary stent types in-vivo

Yang, Han-Mo¹; Lee, Joo Myung¹; Lee, Sahmir²; Kim, Hyo-Soo¹

1. Seoul National University Hospital, Seoul, Korea

2. Asan Medical Center, Seoul, Korea

- More precise and convenient method in vivo
- Useful tool for assessing and comparing the efficacy of new coronary stents with conventional stent systems
- Advantage of rabbit iliac model

T104

Accelerated oxygen-induced retinopathy is a reliable model of ocular angiogenesis

Villacampa Alcubierre, Pilar; Menger, Katja; Abelleira, Laura; Ribeiro, Joana; Duran, Yanai; Smith, Alexander J.; Ali, Robin R.; Luhmann, Ulrich F.; Bainbridge, James W.

UCL Institute of Ophthalmology, London, United Kingdom

- Oxygen-induced retinopathy (OIR) in mice is a widely used model of ocular angiogenesis
- We compared conventional OIR in mice with an alternative, accelerated protocol
- The accelerated protocol is similar in severity but more rapid in evolution

T105

A DBA/2J haplotype on distal chromosome 2 reduces Mertk expression, curtails efferocytosis, and increases susceptibility to atherosclerosis

Kayashima, Yukako; Maeda, Nobuyo N.

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

- We have placed an athero-promoting Aath4 QTL of DBA/2J onto a 129S6-Apoe^{-/-} background (D10I)
- D10I males develop larger plaques and D10I macrophages showed reduced apoptotic cell uptake
- Lower Mertk expression, rather than protein variation, causes restricted efferocytosis in D10I

T106

Endothelial specific deletion of NF1 results in myeloproliferative disease

Li, Qing-fen; Zheng, Qingxia; Pumiglia, Kevin

Albany Medical College, Albany, NY, USA

- A mouse model of endothelial specific, tamoxifen inducible deletion of NF1
- Mice loss of NF1 in endothelium had normal vasculature but suffered from significant myeloproliferation
- Expanded populations lacked Cre expression, suggesting a microenvironment driven myeloproliferation

T107

Developed novel rodent model of diabetic retinopathy after conditional Pdgfrb gene targeting

Kitahara, Hideyuki¹; Yamamoto, Seiji¹; Kajikawa, Sayaka¹; Azuma, Erika¹; Hamashima, Takeru¹; Ishii, Yoko¹; Sato, Hikari²; Shimada, Yutaka¹; Sasahara, Masakiyo¹

1. University of Toyama, Toyama, Japan

2. Tokyo General Hospital, Tokyo, Japan

- Novel rodent DR model via conditional Pdgfrb gene targeting was developed
- The DR model efficiently reproduced DR through early to advanced stages
- VEGF-A, PIGF and PDGF-B were upregulated that may contribute to the progress of DR

Vascular Biology

T108

Omental endothelial dysfunction Precedes type 2 diabetes in obesity

Bakhamis, Aysha¹; Orié, Nelson¹; Raees, Asmaa¹; Bashah, Moataz²; Alsayrafi, Muhammad¹; Mohamed-Ali, Vidya¹

1. Anti doping Lab Qatar, Doha, Qatar

2. Hamad Medical Corporation, Bin Omran Area, Doha, Qatar

- Obesity and the associated state of insulin resistance are major risk factor for many other diseases
- Omental adipose tissue depot which is considered more pathogenic compared with the subcutaneous adipose depot
- Omental adipose tissue depot more damaging impact on the endothelial functions of embedded arteries

T109

The CUL3-SPOP-DAXX axis is a novel regulator of VEGFR2 expression in endothelial cells

Sakaue, Tomohisa; Fujisaki, Ayako; Izutani, Hironori; Higashiyama, Shigeki
Ehime University, Toon, Japan

- Neddylated-CUL3 is essential for VEGF-induced endothelial cell activation
- CUL3-SPOP targets DAXX that is a key regulator of VEGFR2 mRNA expression
- CUL3-SPOP-DAXX axis plays crucial roles in endothelial cell functions

T110

MnTBAP protects against vascular inflammation through BMP-dependent signaling

Zhou, Qian; Einert, Michaela; Schmitt, Hanah; Esser, Jennifer; Pankratz, Franziska; Bode, Christoph; Moser, Martin
Heart Center, University of Freiburg, Freiburg, Germany

- Vascular inflammation
- Leukocyte adhesion
- BMP signaling

T111

Preparation of a simple more physiologically relevant microfluidic model to study of vascular inflammation

Vitecek, Jan¹; Cernik, Marek²; Kolarova, Hana²; Kubala, Lukas¹

1. St. Anne's University Hospital Brno, Brno, Czech Republic
2. Institute of Biophysics AC CR, Brno, Czech Republic

- Circular cross-section of microfluidic channels was found to be superior to parallel plate concept
- Silicone based chip having channels with circular cross section were prepared
- These chips were successfully colonized with endothelium cells

T112

Genetic analysis of peri-endothelial development in zebrafish

Grosse, Ann¹; Shih, Yu-Huan¹; Kok, Fatma O.¹; Yu, Jun¹; Stone, Oliver²; Stainier, Didier²; Zhu, Julie¹; Lawson, Nathan D.¹

1. University of Massachusetts Medical School, Worcester, MA, USA
2. Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

- Periendothelial cells are important for the maturation and function of the circulatory system
- Pdgfrb signaling is crucial for periendothelial cells development in zebrafish
- RNA-Seq on Periendothelial cells provides insights into the ontogeny of periendothelial cells lineages

T113

Role of CD93 in endothelial cell function and glioma angiogenesis

Lugano, Roberta; Vemuri, Kalyani; Langenkamp, Elise; Dimberg, Anna
Uppsala University, Uppsala, Sweden

- CD93 regulates endothelial cell dynamics and functions
- Rho-GTPases are involved in the effects of CD93 on endothelial cell functions
- CD93 interacts with proteins that regulate endothelial cell function, angiogenesis and vessel permeability

T114

CLEC14A determines the offset of VEGFR2- and VEGFR3- dependent signals during angiogenesis and lymphangiogenesis

Lee, Sungwoon; Park, Hyojin; Kwon, Young-Guen
Yonsei University, Seoul, Korea

- CLEC14A acts in vascular homeostasis by fine tuning of VEGFR-2 and VEGFR-3 signalling in ECs
- CLEC14A controls angiogenesis and lymphangiogenesis during development
- CLEC14A modulates tumour vasculature and survival of tumour-bearing mice

T115

Activated platelets release microparticles containing functional miRNA, which can be internalized by vascular smooth muscle cells and induce their differentiation

Tang, Wai Ho; Zeng, Zhi; Chen, Yinshuang
Guangzhou Women and Children's Medical Center, Guangzhou, China

- Platelet-derived microparticles
- Vascular smooth muscle cell differentiation

- microRNA-143/145

T116

PDGFR α protein level in hepatic stellate cells is regulated by a balance of autophagic degradation and release via extracellular vesicles

Kostallari, Enis; Hirsova, Petra; Shah, Vijay H.

Mayo Clinic, Rochester, MN, USA

- Extracellular Vesicles/Microparticles/Exosomes
- Autophagy and how it is related to Extracellular Vesicles
- Regulation of RTK receptor levels in pericyte-like cells

T117

Serum anti-vimentin antibody in association with interstitial fibrosis and tubular atrophy in renal transplants

Oh, Eun-Jee; Lee, Hyeyoung; Chung, Byung Ha; Yang, Chul Woo

Catholic University of Korea, Seoul, Korea

- In pre-renal transplant sera, anti-vimentin antibodies were positive in 64.8% of patients
- IgG-AVA levels were increased following transplantation in both IFTA(+) and IFTA(-) patients
- The increased levels of IgG-AVA in post-transplant sera suggest contribution of AVA in IFTA

T118

Detection of PARP14-dependent STAT1 ribosylation using the Q Exactive high resolution accurate mass spectrometer

Higashi, Hideyuki¹; Maejima, Takashi²; Singh, Sasha²; Aikawa, Masanori³

1.Center for Interdisciplinary Cardiovascular Sciences, Boston, MA, USA

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

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

- STAT1 can be ADP-ribosylated by PARP14
- Using mass spectrometry, three glutamates of STAT1 were found to be ADP-ribosylated
- Two independent treatments of the peptides facilitated identification of the ADP-ribosylation sites

T119

Development of LC/MS/MS based targeted metabolomic method to study the effects of carbon monoxide and nitric oxide on endothelial cell metabolism

Kus, Kamil; Patrycja, Kaczara; Walczak, Maria; Chlopicki, Stefan

Jagiellonian University, Krakow, Poland

- A quantitative metabolomics to assess 168 endogenous polar endothelial metabolites was developed
- CO and NO treatment of endothelial cells led to marked changes in intracellular metabolites concentrations
- Major changes included glycolysis, TCA, PPP, redox state of cells and methionine-homocystine cycle

T120

Characterization of angiogenic factors in human skeletal muscle pericytes and endothelial cells

Hoier, Birgitte; Hanskov, Dorte; Jorgensen, Maria; Hellsten, Ylva

University of Copenhagen, Copenhagen O, Denmark

- Characterization of angiogenic factors in human skeletal muscle pericytes and endothelial cells in training
- Similar amount of VEGF in both cell types whereas VEGFR2 and TSP-1 levels were 10 fold higher in ECs vs. PCs
- Low levels of VEGFR2 in PCs compared to ECs suggest that VEGF contained in PCs may primarily affect ECs

T121

Retinoic acid regulates vascular pericyte coverage in the developing brain via WNT signaling and the WNT target Sox17

Bonney, Stephanie; Wendlandt, Megan; Peterman, Eric; Siegenthaler, Julie

University of Colorado Denver - AMC, Aurora, CO, USA

- Retinoic acid modulation of neurovascular Wnt signaling
- Retinoic acid as a novel regulator of CNS pericyte coverage through Wnt signaling
- Sox17 as a regulator of pericyte coverage and angiogenic events in the CNS

T122

microRNAs control cells homeostatic adaptation to ECM stiffness

Moro, Albertomaria¹; Driscoll, Tristan¹; Zhang, Jing²; Donghoon, Lee²; Gu, Mengting²; Gerstein, Mark²; Schwartz, Martin A.¹; Nicoli, Stefania³

1. Yale University School of Medicine, New Haven, CT, USA
2. Yale University, New Haven, CT, USA
3. Yale University Cardiovascular Research Center, New Haven, CT, USA

- miRNAs activity in endothelial cell
- Mechanotransduction regulation
- cell adaptation to ECM stiffness

T123

Identification of novel intracellular modulators of angiogenesis through the BERG Interrogative Biology® Platform; a Multi-Omic systems biology approach to disease modeling and drug discovery

*Bourdelais, Justin J.; Spencer, Carrie; Shah, Chahan; Akmaev, Slava; Rodrigues, Leonardo; Gesta, Stephane; Vishnudas, Vivek; Sarangarajan, Rangaprasad; Narain, Niven
Berg LLC, Framingham, MA, USA*

- Systems biology was utilized to contrast angiogenic endothelial cells and quiescent cells
- Novel drivers of angiogenesis were identified as potential targets for anti-angiogenic therapy
- Targets have been validated through in vitro studies and are progressing towards drug development

T124

An automated workflow for parallel reaction monitoring mass spectrometry-enabled apoA-I in vivo metabolism unveils an updated picture of HDL metabolism

Lee, Lang Ho Ho¹; Andraski, Allison B.²; Pieper, Brett³; Higashi, Hideyuki¹; Sacks, Frank M.²; Aikawa, Masanori⁴; Singh, Sasha⁵

1. Center for Interdisciplinary Cardiovascular Sciences, Boston, MA, USA
2. T.H. Chan Public Health School of Harvard University, Boston, MA, USA
3. Center for Interdisciplinary Cardiovascular Science, Brigham and Women's Hospital and Harvard Medical School, Boston, MA
4. Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
5. Brigham and Women's Hospital, Boston, MA, USA

- We developed highly accurate method using mass spectrometry to explore high density lipoprotein metabolisms
- Using our method, we made enrichment profile of apolipoproteins from high-abundant APOA1 to very little LCAT
- Our method can improve understanding of high density lipoprotein metabolism and anti-atherogenic mechanisms

Atherosclerosis I

T125

Deficiency of macrophage epsins impedes atherosclerosis by inhibiting LRP-1 internalization and degradation

Brophy, Megan L.¹; Dong, Yunzhou¹; Song, Kai¹; Wu, Hao¹; Rahman, Ashiqur¹; Tessneer, Kandice L.²; Pasula, Satish²; Cai, Xiaofeng³; Ley, Klaus F.⁴; Chen, Hong⁵

1. Boston Children's Hospital, Boston, MA, USA
2. Oklahoma Medical Research Foundation, Oklahoma City, OK, USA
3. University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA
4. La Jolla Institute for Allergy & Immunology, La Jolla, CA, USA
5. Boston Children's Hospital/Harvard Medical School, Boston, MA, USA

- Macrophage epsins promote atherosclerosis
- Macrophage epsins bind to LRP-1
- Deficiency of macrophage epsins enhances LRP-1 protein expression

T126

Angiogenic factor AGGF1 activates autophagy with an essential role in therapeutic angiogenesis for heart disease

Yao, Yufeng¹; Chen, Qiuyun²; Qiuyun, Lu¹; Wang, Qing K.²

1. Huazhong University of Science and Technology, Wuhan, China

2. Cleveland Clinic, Cleveland, OH, USA

- AGGF1 is a novel, master regulator of autophagy in endothelial cells and many other cells
- AGGF1 activates autophagy by activating JNK, which leads to activation of the Vps34 lipid kinase
- The angiogenic factor AGGF1 is a novel target and agent that can successfully treat coronary artery disease

T127

Apoptotic cells trigger mitochondrial fission in macrophages and promote efficient apoptotic cell internalization

Yurdaqul, Arif¹; Subramanian, Manikandan¹; Wang, Ying¹; Lorenzi, Valeria²; Maxfield, Frederick²; Nomura, Masatoshi³; Tabas, Ira¹

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

2. Weill Cornell Medical College, New York City, NY, USA

3. Kyushu University, Fukuoka, Japan

- Mitochondrial Fission Promotes Continuing Efferocytosis
- Loss of the Fission Protein, Drp1, Delay Apoptotic Cell Internalization
- Macrophage-Specific Deletion of Drp1 Reduces Efferocytosis in Advanced Atherosclerosis

T128

Reducing PCSK9, VLDL, and collagen secretion by inhibiting dynamin-related protein 1

Rogers, Maximilian A.¹; Hutcheson, Joshua D.¹; Goetsch, Claudia¹; Singh, Sasha¹; Higashi, Hideyuki²; Aikawa, Masanori¹; Aikawa, Elena¹

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

2. Center for Interdisciplinary Cardiovascular Sciences, Boston, MA, USA

- DRP1 inhibition reduces PCSK9 secretion in human liver cells and mice
- DRP1 inhibition reduces APOCIII secretion in human liver cells
- DRP1 inhibition reduces smooth muscle cell collagen secretion and attenuates cardiovascular calcification

T129

Inhibition of lysophosphatidic acid receptors 1/3 attenuates atherosclerosis development in LDL-receptor deficient mice

Kritikou, Eva¹; van Puijvelde, Gijis²; van der Heijden, Thomas²; van Santbrink, Peter²; Swart, Maarten²; Schaftenaar, Frank²; Kröner, Mara²; Kuiper, Johan²; Bot, Ilze¹

1. LACDR/Leiden University, Leiden, Netherlands

2. Leiden University, Leiden, Netherlands

- LPA1/3 receptor antagonism attenuated atherosclerosis development in LDL-receptor deficient mice
- Inhibition of LPA1/3 receptors lowered the inflammatory immune responses
- Pharmacological blockade of LPA1/3 receptors mildly reduced LDL cholesterol levels in the plasma

T130

Specific inhibition of the NLRP3 inflammasome reduces atherosclerotic lesion development in the carotid artery

van der Heijden, Thomas¹; Bot, Ilze²; Kritikou, Eva²; Foks, Amanda¹; Venema, Wouter¹; Kuiper, Johan¹; Duijn, Janine van¹; Slütter, Bram¹

1. Leiden University, Leiden, Netherlands

2. LACDR/Leiden University, Leiden, Netherlands

- MCC950 inhibited IL-1 β release after combined stimulation with LPS and cholesterol crystals in BMMFs and BMDCs
- Developed carotid artery plaque was reduced by 26% in MCC950 treated mice
- MCC950 reduced the amount of macrophages in the carotid artery plaque by 42%

T131

IL-35 reduces atherosclerotic lesion development in the carotid artery by possible increasing the number of Tregs

van der Heijden, Thomas¹; Bot, Ilze²; Foks, Amanda¹; Kritikou, Eva²; van Puijvelde, Gijls¹; Amersfoort, Jacob¹; Douna, Hidde¹; Kröner, Mara¹; Kuiper, Johan¹

1. Leiden University, Leiden, Netherlands

2. LACDR/Leiden University, Leiden, Netherlands

- Developed carotid artery plaque was reduced by 38% in IL-35 treated mice
- Relative necrotic area in IL-35 treated mice was reduced by 13% and plaque stability was not affected
- The number of splenic regulatory T cells was increased 2-fold in IL-35 treated mice

T132

Oral metformin profoundly suppresses atherosclerotic lesion development in vivo independently of glucose-lowering in a mild hyperlipidemic model via AMPK

Seneviratne, Anusha; Carling, David; Haskard, Dorian; Boyle, Joseph J.

Imperial College London, London, United Kingdom

- Metformin prevents lesion development in vivo in mice
- Metformin has a direct mechanism independent on blood glucose or lipids
- Metformin acts via plaque macrophages and in part via macrophage HO-1 induction

T133

Complement reduced foam cell formation via a CR3-AMPK pathway

Huo, Yilin; Carling, David; Haskard, Dorian; Boyle, Joseph J.

Imperial College London, London, United Kingdom

- Complement reduces foam cell formation in human and mouse
- This requires complement receptor CR3 (receptor for iC3b)
- This pathway also requires AMPK

T134

Lipid loading of human macrophages induces FasL expression via aryl hydrocarbon receptor (AhR)

Seneviratne, Anusha; Haskard, Dorian; Schukraft, Sara; Davis, Heather; Boyle, Joseph J.

Imperial College London, London, United Kingdom

- Oxidised low density lipoproteins induce macrophage expression of Fas-Ligand
- OxLDL induced FasL is dependent on aryl hydrocarbon receptors
- Other ligands of the AHR also induce macrophage FasL

T135

Endothelium-specific deletion of epsins attenuates atherosclerosis in ApoE-deficient mouse model through the stabilization of IP3 Receptor 1 and ER homeostasis

Dong, Yunzhou¹; Brophy, Megan²; Wen, Aiyun¹; Wu, Hao¹; Song, Kai¹; Rahman, Ashiqur¹; Yu, Lili³; Liu, Xiaolei³; Wong, Scott¹; Chen, Ju⁴; Chen, Hong¹

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

2. Boston Children's Hospital, Boston, MA, USA

3. Oklahoma Medical Research Foundation, Oklahoma City, OK, USA

4. University of California, San Diego, San Diego, CA, USA

- Loss of epsins in endothelium in ApoE-deficient mouse model (EC-iDKO/ApoE^{-/-}) attenuates atherosclerosis
- Loss of epsins in endothelium stabilizes IP3 receptor and attenuates ER stress
- Epsins bind and modulate IP3 receptor. UIM-chimeric peptide TAME shows potential for atherosclerotic therapy

T137

Erythrocyte angiophagy promotes oxidation in early-stage atheroma in humans

Delbosc, Sandrine; Bayles, Richard; Laschet, Jamila; Ho-Tin-Noe, Benoit; Ollivier, Véronique; Morvan, Marion; Deschildre,

Catherine; Louedec, Liliane; Gouya, Laurent; Guedj, Kevin; Nicoletti, Antonino; Michel, Jean-Baptiste

INSERM, Paris, France

- Vascular smooth muscle cells phagocyte red blood cells
- Red blood cells infiltration is a trigger of foam cells formation
- Role of erythrophagy in early stages of atherosclerosis

T138

EphA2 deficiency attenuates fibroproliferative remodeling in experimental atherosclerosis

Finney, Alexandra C.; Green, Jonette; Rana, Mohammad A.; Funk, Steven D.; Alexander, J. Steven; Traylor, James G.; Orr, A. Wayne

Louisiana State University Health Sciences Center - Shreveport, Shreveport, LA, USA

- EphA2 deletion reduces atherosclerosis, fibrosis, and smooth muscle in ApoE knockout mice
- EphA2 is upregulated in synthetic smooth muscle, and EphA2 siRNA attenuates VSMC proliferation
- EphA2 deficient smooth muscle cells attenuates matrix deposition and phospho-myosin light chain

T139

Plaque neovessel maturation enhancement by VEGFR2 blockade in murine atherosclerotic vein grafts results in intraplaque haemorrhage reduction and increased lesion stability

de Vries, Margreet R.; Parma, Laura; Peters, Erna A.B.; Hamming, Jaap F.; Goumans, Marie-Jose; Quax, Paul LUMC, Leiden, Netherlands

- Atherosclerosis
- Angiogenesis
- intraplaque hemorrhage

T140

Myeloid PHD2 deficiency stimulates macrophage collagen production and atherosclerotic plaque stability in mice

Theelen, Thomas¹; Marsch, Elke¹; Demandt, Jasper¹; Fallais, Simon¹; Tullemans, Bibian¹; Gijbels, Marion¹; Welting, Tim¹; Mastenbroek, Tom¹; Cosemans, Judith¹; Willems, Brecht¹; Schurgers, Leon J.¹; Biessen, Erik¹; Carmeliet, Peter²; Daemen, Mat³; Sluimer, Judith¹

1. Maastricht University, Maastricht, Netherlands

2. Vesalius Research Center, VIB, Leuven, Belgium

3. Amsterdam Medical Center, Amsterdam, Netherlands

- LysMCre prolyl hydroxylase 2 (PHD2^{-/-}) increased plaque size, collagen and cap thickness in LDLR^{-/-} PHD2^{-/-} m
- PHD2^{-/-} macrophages produce more collagen and SMC plaque content higher explain plaque fibrosis
- Human PHD2 mRNA and protein correlated with CD68 macrophages in human carotid atherosclerosis

T141

TWEAK blockade decreases atherosclerotic lesion size and progression through suppression of STAT signaling in diabetic mice

Sastre, Cristina¹; Sastre, Cristina²; Fernández-Laso, Valvanera²; Egido, Jesús²; Martín-Ventura, José Luis²; Gómez-Guerrero, Carmen²; Blanco-Colio, Luis M.²

1. Massachusetts General Hospital, Boston, MA, USA

2. FIIS-Fundación Jiménez Díaz, Madrid, Spain

- Diabetes-accelerated atherosclerosis
- Tumor necrosis factor-like weak inducer of apoptosis (TWEAK) cytokine
- Inflammation

T142

3D organoid cultures derived from muscle wound healing stem cells create bone tissue. Could heterogeneous calcified atherosclerotic plaques be of monoclonal origin?

Gostjeva, Elena V.

Massachusetts Institute of Technology, Cambridge, MA, USA

- Novel method of calcified diseased enzymatic tissue dissociation was developed to see intact stem cells
- Our observations did not eliminate the possibility that most of vascular lesions derived from a stem cell
- 3D 'Organotypic' spheres grown from muscle wound healing stem cells contained bone tissue

T143

Decreased adiponectin-mediated signalling through the AdipoR2 pathway is associated with carotid plaque instability

Gasbarrino, Karina¹; Zheng, Huaien¹; Hafiane, Anouar¹; Veinot, John P.²; Lai, Ch²; Daskalopoulou, Stella¹

1. McGill University Health Centre, Montreal, PQ, Canada

2. University of Ottawa Heart Institute, Ottawa, Canada

- Unstable carotid plaques express more adiponectin and less overall AdipoR2 than stable plaques

- AdipoR2 signalling through PPAR-a was observed to be significantly impaired in unstable carotid plaques
- In contrast, the AdipoR1 pathway did not appear to play an important role in the context of plaque instability

T144

Loss of PTEN correlates with reduced aSMA expression in dedifferentiated smooth muscle cells of human coronary arteries affected by atherosclerosis or continuous flow left ventricular assist devices

Moulton, Karen S.¹; McClatchey, Penn¹; Li, Marcella¹; Tucker, Rebecca M.¹; Kirkpatrick, Bruce²; Furgeson, Seth¹; Ambardekar, Amrut¹; Weiser-Evans, Mary C.M.¹

1. University of Colorado Denver Anschutz Medical Campus, Aurora, CO, USA

2. University of Colorado Boulder, Boulder, CO, USA

- We have shown nuclear PTEN interacts with SRF to regulate SMC differentiation
- The relationship between PTEN and aSMA was examined in human atherosclerotic coronaries and LVAD patients
- PTEN correlates with aSMA levels and SMC dedifferentiation in vessels with atherosclerosis or LVAD exposure

Endothelial Cells II

T145

Enabling multiplexed single-cell mapping of receptors via quantum dot (QD) nanosensors

Chen, Si; Imoukhuede, Princess

University of Illinois at Urbana-Champaign, Urbana, IL, USA

- Absolute quantification of membrane receptor levels
- Quantifying endothelial cell heterogeneity
- Multiplexing quantification

T146

DNA methylation changes as a consequence of IL-6 induced vascular insulin resistance and its role in vascular diseases

Balakrishnan, Aswath; Satyamoorthy, Kapaettu; B Joshi, Manjunath

School of Life Sciences, Manipal University, Manipal, India

- Chronic IL-6 induced vascular insulin resistance
- DNA methylation changes in vasculature during insulin resistance caused by inflammation
- Examining epigenetic signaling mechanisms under the conditions of vascular insulin resistance

T147

A PPAR gamma-dependent miR-424/503-CD40 axis plays a pivotal role in the regulation of inflammation mediated angiogenesis

Lee, Aram

Sookmyung Women's University, Seoul, Korea

- microRNA
- angiogenesis
- PPAR gamma

T148

Negative regulation of NOD1 mediated angiogenesis by PPARgamma-regulated miR-125a

Park, Youngsook

Sookmyung Women's University, Seoul, Korea

- NOD1
- PPARgamma
- Angiogenesis

T149

Statins and thrombospondin-5 are protective against endothelial cell apoptosis

Helkin, Alex¹; Maier, Kristopher G.²; Gahtan, Vivian²

1. SUNY Upstate Medical Center and Department of Veterans Affairs VA Healthcare Network Upstate New York at Syracuse, Syracuse, NY, Syracuse, NY, USA

2. SUNY Upstate Medical University, Syracuse, NY, USA

- TSP-5 induced gene expression in had an anti-apoptotic pattern and did not induce EC apoptosis
- Fluvastatin greatly affected gene expression by inducing an anti-apoptotic pattern
- Fluvastatin was protective against TSP-1 and TSP-2 induced apoptosis

T150

Endothelial HIF-1alpha Is required for endothelial regeneration and vascular repair following sepsis challenge

Huang, Xiaojia; Zhang, Xiaoming; Zhao, Youyang

University of Illinois at Chicago, Chicago, IL, USA

- Identify the role of endothelial HIF-1 during vascular repair following septic challenge
- Confirm the essential involvement of the transcription factor FoxM1 in endothelial regeneration
- Propose a promising strategy for treatment of inflammatory vascular diseases

T151

7-ketocholesterol induces leukocyte interaction to endothelial cells thorough p38MAPK-dependent pathway

Tani, Mariko; Kamata, Yuko; Deushi, Michiyo; Osaka, Mizuko; Yoshida, Masayuki

Tokyo Medical and Dental University, Tokyo, Japan

- 7-ketocholesterol enhanced leukocyte adhesion to endothelial cells
- The p38MAPK pathway is involved in the up-regulation of adhesion molecules
- 7-ketocholesterol may be the risk factor for developing atherosclerosis

T152

Hypoxic pre-conditioning strengthens adherens junctions (AJs) via HIF-2a signaling

Liu, Menglin; Chen, Jiwang; Rehman, Jalees; Malik, Asrar

University of Illinois College of Medicine, Chicago, IL, USA

- Endothelium
- Adherens Junctions
- Hypoxia

T153

Media with growth factors and serum induces Hes1 and Hey1 expression in lymphatic and vascular endothelial cells in vitro

Defnet, Ann; Bagrodia, Naina; Lec, Bianca; Hernandez, Sonia; Kandel, Jessica J.

University of Chicago, Chicago, IL, USA

- The Notch pathway is frequently investigated in cultured endothelial cells
- Growth factors and serum added to media increase expression of Hes1 and Hey1 in HDLECs and HUVECs
- Not accounting for growth factor and serum addition may cause inaccurate evaluation of Notch status

T154

Investigating the p130Cas interactome

Evans, Ian¹; Paliashvili, Ketevan¹; Kennedy, Susan²; Santra, Tapesh²; Lovering, Ruth¹; Kolch, Walter²; Zachary, Ian¹

1. University College London, London, United Kingdom

2. University College Dublin, Dublin, Ireland

- endothelial motility
- p130Cas interactome
- neuropilin signalling

T155

Neuropilin 1 promotes endothelial function by suppressing TGF β non-canonical signalling

*Raimondi, Claudio*¹; *Lampropoulou, Anastasia*²; *Fantin, Alessandro*¹; *Senatore, Valentina*²; *Denti, Laura*¹; *Chikh, Anissa*³; *Ruhrberg, Christiana*¹

1. University College London, London, United Kingdom

2. UCL Institute of Ophthalmology, London, United Kingdom

3. Queen Mary University of London, London, United Kingdom

- NRP1 deficiency increases TGF β 1 transcription and enhances SMAD-independent TGF β signalling via ERK1/2
- NRP1 has an important role in promoting EC proliferation in vitro and during retinal angiogenesis
- NRP1 suppresses TGF β 1-induced ERK1/2 activation via TGFBR2/ALK1 to prevent anti-proliferative signals in EC

T156

The long noncoding RNA H19 controls endothelial cell ageing and inflammation

Hofmann, Patrick; *Stanicek, Laura*; *Fischer, Ariane*; *Dimmeler, Stefanie*; *Boon, Reinier A.*

University Hospital Frankfurt, Frankfurt am Main, Germany

- Ageing
- long noncoding RNAs
- Senescence

T157

Endothelial IRF-1 regulates LPS-induced VCAM-1 expression independent of NF κ B

Yan, Rui; *van Meurs, Matijs*; *Jongman, Rianne*; *Zwiers, Peter*; *Niemarkt, Anita*; *Kuiper, Timara*; *Kamps, Jan*; *Heeringa, Peter*; *Zijlstra, Jan*; *Molema, Grietje*; *Moser, Jill*

University Medical Center Groningen, Groningen, Netherlands

- Molecular mechanisms of endothelial activation associated with sepsis
- LPS-mediated inflammatory signalling in endothelial cells
- Renal microvascular responses associated with septic acute kidney injury

T158

Development of a novel heterozygous Tie2 knockout mouse to investigate organ specific endotoxemia-induced microvascular endothelial cell responses

Zwiers, Peter J.; *Jongman, Rianne*; *Popa, Eliane*; *Moorlag, Henk*; *van de Sluis, Bart*; *Moser, Jill*; *van Meurs, Matijs*; *Molema, Grietje*

University Medical Center Groningen, Groningen, Netherlands

- Role of Tie2 on endothelial behaviour
- Endothelial cell responses to LPS
- Tie2 heterozygous mice

T159

Convergence of genetic predisposition, bioactive lipid signaling, endothelial metabolism, and miRNA pathway in mechano-transduction mechanisms

*Krause, Matt*¹; *Huang, Ru-Ting*¹; *Wu, David*¹; *Oh, Myung-Jin*¹; *Lusis, Aldons J.*²; *Civelek, Mete*³; *Jo, Hanjoong*⁴; *Gokhan, Mutlu*¹; *Tirrell, Matthew*¹; *Fang, Yun*¹

1. University of Chicago, Chicago, IL, USA

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

3. University of Virginia, Charlottesville, VA, USA

4. Emory University, Atlanta, GA, USA

- Disturbed flow and CAD genetic variation at rs17114036 interact to suppress PPAP2B expression in endothelium
- Disturbed flow increases endothelial glycolysis and reduces mitochondria capacity by activating LPA signaling
- VCAM1-targeted micelles provide better therapeutic efficacy in treating atherosclerosis in Apoe^{-/-} mice

T160

Mechanical regulation of endothelial cell metabolism through HIF-1 α

Wu, David; *Huang, Ru-Ting*; *Hamanaka, Robert*; *Meliton, Angelo*; *Witt, Leah*; *Mutlu, Gokhan*; *Fang, Yun*

University of Chicago, Chicago, IL, USA

- Atheroprone waveform increases glycolysis and depresses mitochondrial function in endothelial cells

- Under atheroprone flow, HIF-1a controls metabolism by regulating pyruvate availability
- Curved regions of pig aortas demonstrate higher levels of HIF-1a than straight regions

T161

Tie1 controls angiopoietin function in vascular remodeling and inflammation

Korhonen, Emilia A.¹; Lampinen, Anita¹; Giri, Hemant³; Anisimov, Andrey¹; Kim, Minah⁴; Allen, Breanna⁴; Fang, Shentong¹; D'Amico, Gabriela¹; Sipila, Tuomas²; Lohela, Marja¹; Strandin, Tomas¹; Vaheri, Antti¹; Yla-Herttuala, Seppo⁵; Koh, Gou Young⁶; McDonald, Donald⁴; Alitalo, Kari⁷; Saharinen, Pipsa^{1,2}

1. *University of Helsinki, Helsinki, Finland*

2. *Wihuri Research Institute, Helsinki, Finland*

3. *Indian Institute of Technology Madras, Chennai, India*

4. *University of California- San Francisco, San Francisco, CA, USA*

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

6. *KAIST, Daejeon, Korea*

7. *Biomedicum Helsinki/Univ Helsinki, Helsinki, Finland*

- The abstract identifies novel signalling interactions of the endothelial Tie1, Tie2 and b1-integrin receptors
- The abstract reveals a novel function for the orphan Tie1 receptor in vascular remodelling and inflammation
- The abstract identifies mechanisms how the context-dependent agonist/antagonist function of Ang2 is regulated

T162

The role of endothelial Kir channels in flow-induced activation of AKT, eNOS and NO release

Ahn, Sang Joon; Fanher, Ibra S.; Phillips, Shane; Levitan, Irena

University of Illinois at Chicago, Chicago, IL, USA

- Role of Kir in flow induced vasodilation is unknown
- Kir mediates shear stress induced eNOS activation via Akt
- Kir regulates flow induced vasodilation by promoting NO generation