Overview ongoing research 'Microcirculation' Research Program ACS – October 2018

PI	UMC	Dept	Mission	Expertise
Peter Hordijk*	VUmc	Physiology	Molecular mechanisms underlying endothelial and vascular permeability and perfusion	• Cell biology & Biochemistry of RhoGTPases; • Medium throughput siRNA screens in human primary EC; • Endothelial integrity and barrier function; • Advanced (live-cell) imaging (protein dynamics and traffic); • Protein stability and ubiquitylation; • Endothelial monolayers and flow • Hypoxia (ism PK) • Zebrafish injections and imaging
Jan Piek*	AMC	Cardiology / AMC Heart Center	Improvement of diagnosis and treatment of coronary syndromes	Intracoronary hemodynamics • Diagnosis during cardiac catheterization • Evaluation effect of PCI • Prognosis/Gender differences in coronary syndromes Reperfusion injury AMI • Translational research on role of monocytes following myocardial infarction • Exaggeration of • Ischemic injury • Loss of viable myocardium • Development of chronic heart failure Coronary collateral circulation • Quantification of arteriogenesis using intracoronary hemodynamics and MRI
Charissa van den Brom	VUmc	Anesthesiology	Targeting microvascular leakage to prevent/restore microcirculatory perfusion disturbances in critical illness to prevent organ failure	*Preclinical* • Animal models: cardiopulmonary bypass (rat), hemorrhagic shock (rat, mouse), Tie2 knockdown mouse line • Intubation, mechanical ventilation, venous and arterial lines (continuous registration MAP, CVP, HR and temperature) • Intravital microscopy of cremaster (rat, mouse) • Contrast enhanced ultrasonography of heart and kidney (rat, mouse) • Two-photon microscopy for renal perfusion/leakage (rat, mouse)

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				• Evans blue dye leakage • In vitro endothelial barrier measurements in human endothelial cells *Clinical* • Patients undergoing cardiac surgery or following hemorrhagic shock • Side-stream Dark Field imaging (sublingual capillary bed) • Contrast enhanced ultrasonography (heart, kidney) • Near-infrared spectroscopy (brain) • Hyperspectral imaging (kidney)
Reinier Schlingemann/ Ingeborg Klaassen	AMC	Ophthalmology	To understand molecular mechanisms of ocular angiogenesis, vascular leakage and wound healing, and to translate these insights to the clinical management of eye disease	<u>In vitro models:</u> • Model for blood-retinal and blood-brain Barrier: *Permeability, TEER* • Endothelial tip cells: *FACS, IF-staining, lentiviral transfection* • Spheroid based angiogenesis model: S*prouting, live-cell imaging* <u>In vivo models:</u> • Oxygen induced retinopathy model: *Angiogenesis, vascular permeability, siRNA* • Developing mouse retina: *Whole mount staining* <u>Other:</u> • High-throughput analysis of proteins: *Antibody arrays, ELISA*
Pieter Koolwijk/ Victor van Hinsbergh	VUmc	Physiology	To investigate the interaction of endothelial cells and tissue cells in de 3D microvessel flow system at physiological conditions	• Vascular aspects of Tissue Engineering - Human microvascular endothelial cells - Angiogenesis models (in vitro) - 3D in vitro microvessel flow model • (longterm) Hypoxia/normoxia/hyperoxia and metabolism • Interaction cardiac MVEC and cardiomyocytes
Ed van Bavel/Erik Bakker	AMC	Biomedical Engineering and Physics	To understand the control of arterial structure and function in relation to tissue (mal)perfusion • Biomechanics and mechanobiology • Focus on resistance arteries and vascular networks • Focus on brain	• Vascular biomechanics, mechanobiology, physiology • In vivo/in vitro/in silico

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			• Experimental / clinical imaging / modeling	
Kakkhee Yeung	VUmc	Vascular Surgery	Unravel the pathophysiology of aortic aneurysms and dissections	• PARELSNOER AAA, biobank • Transdifferentiation of SMC of skin fibroblast • Functional tests for genes • Live aortic tissue handling for stimulation tests • Contraction studies of SMC with ECIS and microscopy • 3D-bio engineering of vessels • Live aortic models • qPCR for quantification of RNA or DNA • Studies on periaortic fat tissue • Anatomy studies, flow MRI • WES • Metformin, glucose studies (Stanford)
Jaap van Buul	Sanquin Research. Landsteiner Laboratory Dept at AMC.	Molecular Cell Biology lab	Understanding the molecular mechanism that regulate leukocyte transendothelial migration.	Molecular mechanisms of leukocyte transendothelial migration • In vitro TEM-under-flow assays. • Combined Permeability and TEM assays. • Permeability / Electrical Resistance measurements. • Functional Imaging: FRET / FRAP / Photo-activatable probes / Light-induced dimerization probes.
Elga de Vries	VUmc	Molecular Cell Biology and Immunology	Dedicated to investigating the role of alterations of the neurovascular unit in neurological disorders in order to better understand their pathophysiology and enable novel diagnostic and therapeutic applications	• Understanding function of CNS barrier endothelial / epithelial cells (miRNA, integrity, transmigration) • CNS cell – cell interactions (primary CNS cells human / rodent: endothelium, astrocytes, microglia, neurons, pericytes: iPSC) • Animal models: marmoset & cortical, EAE, transgenic AD models, MCAO (stroke model) • Biological samples: MS & AD brain tissue/CSF/blood
Stephan Huveneers	AMC	Medical Biochemistry	• Investigating vascular integrity in inflammation and cardiovascular disease. • Understanding how vascular stiffening controls endothelial adhesions.	• Mechanobiology (integrins/cadherins) • Vascular cell biology and advanced live cell imaging

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			• Establishing the importance of cell-cell junctions forcollective cell behaviour in angiogenesis. • Elucidating the endothelial role in Sturge-Weber syndrome.	
Arjan Griffioen/ Else Huijbers	VUmc	Medical Oncology	To unravel the fundamental processes and mechanisms underlying angiogenesis and vascular development. The major aim is to use new knowledge and technology for the development of new treatment modalities in the clinic.	• Target finding in the tumor vasculature • Vaccine & antibody development • In vitro/in vivo angiogenesis assays • Mouse tumor models

* Research Program leaders