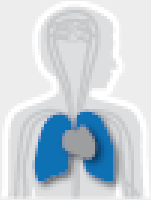
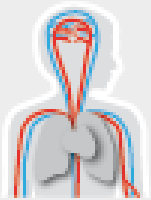


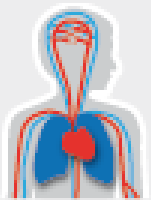
Heart Failure & Arrhythmias



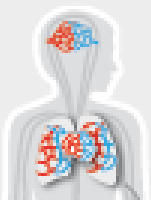
Pulmonary Hypertension
& Thrombosis



Atherosclerosis
& Ischemic Syndromes



Diabetes & Metabolism



Microcirculation

Focus of research group (I)

Name PI: Peter Hordijk

Department, UMC: Physiology, VUmc

Size of research group: 3-6

(associated PhD students from clinical depts)

Current mission, vision and aims

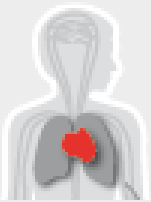
Research topic: Molecular mechanisms underlying endothelial and vascular permeability and perfusion

Approaches:

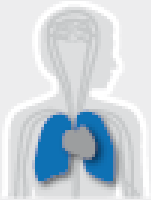
- in vitro analyses of endothelial barrier function: leakage ; transendothelial electrical resistance; confocal imaging
- In vivo: leakage in mice / zebrafish embryo's
- Mechanistic focus on RhoGTPases: expression and localized (in)activation of RhoGTPases; regulation of the actin cytoskeleton

(future) Aims:

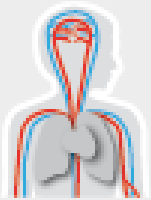
- To establish novel signaling towards loss and gain of cell-cell contact in endothelial cells ; under normoxia/hypoxia
- To define protein regulation by (de)ubiquitylation in the control of endothelial integrity in 2D and 3D



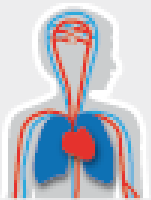
Heart Failure & Arrhythmias



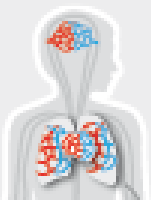
Pulmonary Hypertension
& Thrombosis



Atherosclerosis
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Diabetes & Metabolism



Microcirculation

Focus of research group (II)

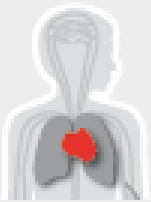
Current expertise

- **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**

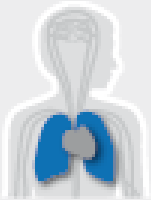
Current funding

ACS, Vumc, LSBR

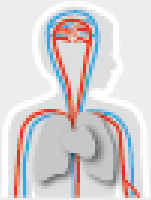
CVON-Phaedra (afd Longziekten, Vumc)



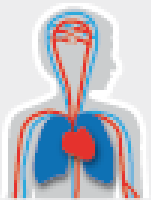
Heart Failure & Arrhythmias



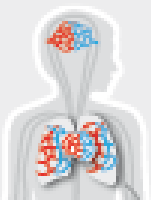
Pulmonary Hypertension
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Diabetes & Metabolism



Microcirculation

Future plans

Short term (1-2 year) plan

- further establish the role of ubiquitin-based modification in endothelial signaling towards barrier function
- Focus on RhoB and Rac1 (ubi-mediated) activity, traffic and functional relationships in control of EC integrity
- Towards 3D analysis of endothelial networks

Necessary infrastructure:

3D vascular models need to be further developed; in house or commercial (e.g. Aimbiotech)

Long term (>2 year) plan

towards an ex vivo model to study microvascular permeability and tissue perfusion – inclusion of mural cells and use of patient derived ECFCs or e.g. SMC

Necessary infrastructure: 3D model for vascular perfusion

Collaboration in ACS Stephan H; Ed vB, Erik B; Noam Z; Marc V; Charissa vdB; Harm Jan B; Kakkhee Y;