

Focus of research group (I)

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Size of research group: 2 PhD students, 1 technician

Current mission, vision and aims

To understand molecular mechanisms of ocular angiogenesis, vascular leakage and wound healing, and to translate these insights to the clinical management of eye disease

Research lines:

- 1) Mechanisms of inner **Blood-Retinal Barrier** loss in (diabetic) macular edema

*Focus on the **transcellular** mechanism of barrier breakdown; Development of PLVAP, a marker of increased vascular permeability, as a target for therapy*

- 2) Molecular regulation of angiogenic **tip cells**

CD34 is a marker for tip cells in vitro and allows studies into new mechanisms of tip cell regulation and angiogenesis which may identify new targets for anti-angiogenesis therapy

- 3) Mechanisms involved in the angio-fibrotic switch in proliferative diabetic retinopathy

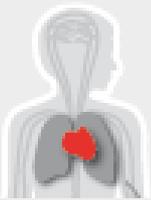
A change in the balance between VEGF and CTGF causes the angio-fibrotic switch; Identification of proteins that cause formation of fibrovascular membranes

- 4) Diagnostic and predictive biomarkers in (diabetic) macular edema

Proteins, mRNA, miRNA, EVs

- 5) VEGF inhibitors in retinal disease

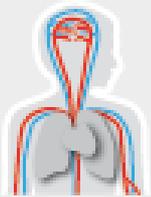
RCT programme for cost-effective implementation of VEGF inhibitors in ophthalmology



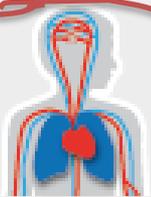
Heart Failure & Arrhythmias



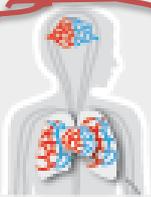
Pulmonary Hypertension & Thrombosis



Atherosclerosis & Ischemic Syndromes



Diabetes & Metabolism



Microcirculation

Focus of research group (II)

Current expertise

In vitro models:

- Model for blood-retinal and blood-brain Barrier
- Endothelial tip cells
- Spheroid based angiogenesis model

*Permeability, TEER
FACS, IF-staining, lentiviral
transfection
Sprouting, live-cell
imaging*

In vivo models:

- Oxygen induced retinopathy model
- Developing mouse retina

*Angiogenesis, vascular
permeability, siRNA
Whole mount staining*

Other:

- High-throughput analysis of proteins

Antibody arrays and ELISA

Current funding

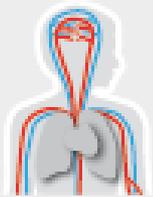
1. Dutch Eye Funds (10-100K/yr)
2. Dutch Diabetes Fund (€250K)
3. Bayer Global Ophthalmology Award - I. Klaassen (\$50K)
4. EFSD/Boehringer Ingelheim European Research Programme in Microvascular Complications of Diabetes (€100K)
5. Private Fund (€500K)



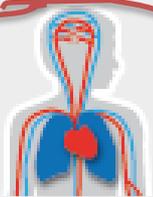
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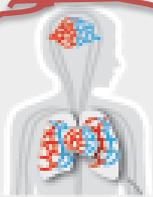
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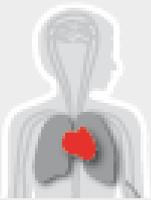
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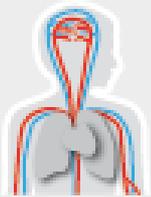
Microcirculation



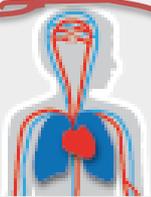
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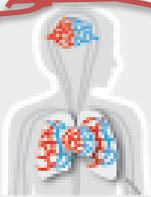
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Microcirculation

Future plans

Short term (1-2 year) plan

- Preclinical intervention targeting Plvap in mouse DME model
- Characterize novel genes involved in tip cell formation and angiogenesis

Necessary infrastructure:

ML-II and DM-II laboratories, CLSM, EM, live cell imaging

Long term (>2 year) plan

- Develop tools for transcellular EC transport mechanisms
- Develop 3D tools for angiogenesis
- Validate novel targets for anti-angiogenesis therapy in vivo

Necessary infrastructure:

- Idem + access to zebrafish facility

Collaborations in ACS

Pieter Koolwijk, Elga de Vries, Riekelt Houtkooper, Peter Hordijk, Ed van Bavel, Stephan Huvneers