Focus of research group (I)

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UD Dr. I. Klaassen
Department, UMC Ophthalmology
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
Focus of research group (II)

**Current expertise**

**In vitro models:**
- Model for blood-retinal and blood-brain Barrier Permeability, TEER
- Endothelial tip cells FACS, IF-staining, lentiviral transfection
- Spheroid based angiogenesis model Sprouting, live-cell imaging

**In vivo models:**
- Oxygen induced retinopathy model Angiogenesis, vascular permeability, siRNA
- Developing mouse retina 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)
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 Huveneers