THE ROLE OF THE VEGF-ISOFORMS IN PATHOLOGICAL CHOROIDAL/RETINAL ANGIOGENESIS

VAN DE VEIRE S., VAN BERGEN T., VANDEWALLE E., CARMELIET P., MOONS L., STALMANS I.

Affiliation Institution: K.U.Leuven/ U.Z.Leuven

Promotor of the Project: STALMANS I., MD, PhD

BACKGROUND AND AIM OF THE PROJECT

This study investigates the specific role of the VEGF-isoforms in pathological choroidal/retinal angiogenesis, as their role in physiological angiogenesis was already described (1,2). VEGF-isoform specific mice (VEGF $^{120/+}$, VEGF $^{164/164}$ and VEGF$^{188/188}$ mice) were bred to study the role of the VEGF isoforms in pathological angiogenesis. In these mice, two established models of pathological angiogenesis were induced, laser-induced choroidal neovascularisation (CV) (3) and retinopathy of prematurity (ROP) (4). The amount of the newly formed blood vessels was determined on wholemounted retinas/choroids.

DEVELOPMENT OF THE PROJECT

Previous findings showed the *in vitro* effect of adding VEGF 121, 164 or 189 in endothelial and fibroblast cultures. The data show that VEGF121 and VEGF165 isoforms significantly inhibit the amount of angiogenesis, whereas VEGF121 and VEGF189 isoforms play a more important role in fibrosis.

In vivo, the VEGF-isoform specific mice were backcrossed into a C75Bl/6 background. CNV was then induced (100 μm spot size, 0.05 sec spot duration and 400 mW power) around the optic nerve. Results from one small experiment showed that the area of neovascularization in the VEGF$^{120/+}$ and VEGF$^{164/164}$ mice was comparable to the wild type mice, whereas an inhibition in neovascularization was present in the VEGF$^{188/188}$ isoform specific mice.

Future aims are firstly to enlarge the mice colonies to repeat CNV experiments. In a second step, these mice will be intercrossed to obtain double transgenic mice (VEGF$^{120/164}$, VEGF$^{164/188}$ and VEGF$^{120/188}$ mice). Finally, pathological retinal angiogenesis will then be induced using the ROP model. This study already sheds new light on the differential role and inhibition of the VEGF-isoforms in CNV formation during AMD.

REFERENCES

(1) Carmeliet P, Ferreira V, Breier G, et al. – Abnormal blood vessel development and lethality in embryos lacking a single VEGF allele. Nature 1996; 380,435-39.

(2) Stalmans I, Lambrechts D, De Smet F, et al. – VEGF: a modifier of the del22q11 (DiGeorge) syndrome? Nat Med 2003; 9(2): 173-82.

(3) Kwak N, Okamoto N, Wood JM, Campochiaro PA – VEGF is a major stimulator of choroidal neovascularization. Invest Ophthalmol Vis Sci. 2000 Sep; 41(10): 3158-64.

(4) Smith LE, Wesolowski E, McLellan A, et al – Oxygen-induced retinopathy in the mouse. Invest Ophthalmol Vis Sci. 1994; 35(1):101-11.