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The Retinal Crumbs Complex: from animal models and retinal organoids to therapy

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STELLINGEN BEHORENDE BIJ HET PROEFSCHRIFT:

The Retinal Crumbs Complex: From Animal Models and Retinal Organoids to Therapy

1. CRB2 in the retinal progenitor cells, photoreceptors and Müller glial cells is a modulating factor of the *Crb1* phenotype; this may be one factor which explains the phenotypic diversity observed in patients with *CRB1* retinal dystrophies. (this thesis)

2. There is an overlap of function for CRB1 and CRB2 proteins in mouse Müller glial cells; this compensatory mechanism may also be present in non-human primate Müller glial cells and perhaps also photoreceptors. (this thesis)

3. Retinal phenotypic spread either superiorly/inferiorly or centrally/peripherally may be due to cell type-specific gradients of CRB proteins. (this thesis)

4. *CRB* gene supplementation rescuing CRB protein levels in photoreceptors and Müller glial cells is a promising therapeutic strategy for *CRB1* retinitis pigmentosa patients. (this thesis)

5. In very early retinal development CRB2 is the predominant CRB member and CRB1 becomes involved during the maturation of the retina. (this thesis)

6. The presence of photoreceptor segments may be crucial for the uptake of various serotypes of AAV; this should be taken into consideration during the timing and administering of AAV mediated therapeutics. (this thesis)

7. Despite the relative immaturity of retinal organoids, patient-derived or genome engineered human retinal organoids will provide valuable insight into disease mechanisms and will be a platform for personalised therapeutics. (field)

8. The current transient benefits of retinal gene therapeutics should not deter scientists about the positive impact these benefits have on a patient's quality of life. (field)

9. Homophilic and perhaps heterophilic extracellular domain CRB-CRB interactions and how these may affect epithelial polarity, signalling and adhesion is a vastly under-researched area in mammals which demands more of our attention. (field)

10. Reassessment about the impact of previous cell transplantation studies is required, however, material transfer from transplanted retinal cell types to host cells represents a novel area of research that will open up new therapeutic avenues. (field)

11. The hours you put into something will not always equal what you get out, but that is not the point in the first place.

12. Observation's, no matter how tantalising, should not distract from applying the scientific method thoroughly and rigorously.