CRB1 gene therapy coming of age: mechanistic insight and rAAV assays on mouse & human retinal organoid models

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Stellingen behorende bij het proefschrift:

CRB1 gene therapy coming of age: Mechanistic insight and rAAV assays on mouse & human retinal organoid models

1. The less CRB protein at the outer limiting membrane (OLM), the more OLM breaks and misplaced cellular nuclei. (This thesis)

2. A *CRB1*-like mouse model can be protected against OLM damage by rAAV-h*CRB1*co or rAAV-h*CRB2*co delivery to Müller glial cells. (This thesis)

3. The *CRB1*-associated retinitis pigmentosa can be modelled in mouse studies and human retinal organoid studies. (This thesis)

4. rAAV5 and the rAAV6-variant ShH10^{Y445F} can efficiently infect human photoreceptors and Müller glial cells. (This thesis)

5. *CRB1*-associated retinitis pigmentosa organoids repress early endosome maturation and increase the number of endosomal degradative compartments. (This thesis)

6. Design-of-Experiments (DoE) should preferably be implemented on finding optimal rAAV vectors and dose-finding studies, also in an academic stetting.

7. No perfect model exists for testing gene therapy candidates, only the sum of the results of orthogonal methods provides a calm mind for the preparation of clinical studies.

8. Every existing viral vector batch is unique having its own infectious and impurity profile.

9. Personalized medicine will increase human lifespan but not necessarily the quality-of-life.

10. We live in a time where the (academic) freedom of inquiry is gradually replaced by industry sponsor agendas, internal university rating systems, and publish-or-perish business.

11. Er was geen goede (*) stelling (**) zonder *CRB1* (*neuroretinale; ** in deze thesis). (This thesis)