

CRB1 gene therapy coming of age: mechanistic insight and rAAV assays on mouse & human retinal organoid models Buck, T.M.

Citation

Buck, T. M. (2022, September 28). *CRB1 gene therapy coming of age: mechanistic insight and rAAV assays on mouse & human retinal organoid models*. Retrieved from https://hdl.handle.net/1887/3464695

Version:	Publisher's Version
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Downloaded from:	https://hdl.handle.net/1887/3464695

Note: To cite this publication please use the final published version (if applicable).

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