

 FULL TITLE	Restoring Mueller glia cell – photoreceptor interactions with Crumbs
ACRONYM	CRUMBS IN SIGHT
COORDINATOR	Dr. J. Wijnholds (Netherlands Institute for Neuroscience, Amsterdam, The Netherlands)
CONTRACT NUMBER	Project Number: 200234
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FUNDING INSTRUMENT	EC: FP7 HEALTH Collaborative Project
KEY WORDS	Mueller glia cell, neuron, photoreceptor, interactions, retina, disorganization, degeneration, blindness, Crumbs.
SUMMARY	<p>Mutations in the Crumbs homologue 1 (CRB1) gene cause photoreceptor degeneration resulting in progressive retinitis pigmentosa (RP) or Leber congenital amaurosis (LCA), which both currently are untreatable blinding diseases. CRB1 is localized in Mueller glia cells at a subapical region (SAR) adjacent to adherens junctions between Mueller glia cells and photoreceptors. Loss of CRB1 function results in loss of adhesion between Mueller glia cells and photoreceptors. This ultimately results in the death of photoreceptors and other retinal neurons with loss of vision at birth (LCA) or before the age of 20 years (progressive RP). Using fruitfly and mouse genetics we will analyze the biochemical, cellular, developmental and physiological functions of CRB1, its family member CRB3, and CRB1-interacting-proteins PALS1, PATJ and MUPP1, in function of the SAR and its role in cell-cell interactions. We will analyze the effect of loss of interaction between Mueller glia cells and photoreceptors and subsequent retinal degeneration in retinas lacking both CRB1 and CRB3, or lacking the CRB1-interacting protein PALS1. To further understand the role of these proteins in neural-glia interactions in general, we will also assess what role these molecules play during development. To develop a cure restoring the impaired interaction between glial cells and photoreceptors, we will explore the efficacy of Mueller glia progenitor cell transplantation in mouse retinas. In collaboration with a small enterprise we will also deliver clinical grade adeno-associated viral (AAV) gene therapy vectors to transfer and express human CRB1 specifically in Mueller glia cells lacking CRB1 function. At the end of the project we will develop a demonstration project using these vectors in clinical phase I/II tests</p>
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BUDGET	3 000 000 €
PROJECT WEB-SITE	***