Project title: Analysis and modulation of RNA splicing in retinal dystrophy

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Abstract: Mutations in several RNA splicing factors affect specific cells in the retina and lead to hereditary retinal degeneration - retinitis pigmentosa (RP). In addition, numerous mutations in retina-specific genes that also cause RP are found in introns and have potential negative effects on the splicing of these genes (e.g. RHO). Thus, splicing defects are key factors in the development of RP. Despite intensive research, the molecular mechanisms of cell-specific susceptibility to these mutations remain unclear. In this project, we plan to use relevant biomodels to study defects caused by RP mutations in splicing factors in target cell types. We will analyze the effect of RP mutations in different genes on in vitro generated human retinal organoids and retinal pigment epithelium. We will examine defects in RNA splicing and tissue-specific RNA production and identify genes with aberrant splicing that we will subsequently correct. We will also test the hypothesis that cellular sensitivity to RP mutations correlates with reduced expression of splicing factors. The results will allow us to identify potential treatments for RP. This project is part of Marie Skłodowska-Curie Training Doctoral Network focused on retinal dystrophies (ProgRET), which includes eight European academic teams and four industrial partners, which are leaders in retinal dystrophy research. Eligibility - M.Sc. or equivalent education in molecular biology, developmental biology or biochemistry obtained outside the Czech Republic.

Image of in vitro differentiated human retinal organoids