

## Poster

## Characterization of retinal cells derived from iPSCs of a patient with PRPF31 associated retinitis pigmentosa



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### ABSTRACT

**Motivation:** Retinitis pigmentosa (RP) is a group of hereditary retinal dystrophies caused by mutations in different genes with a prevalence of 1 in 4000. It is an untreatable disease with a variable clinical evolution in which patients develop severe visual impairment or total blindness. Mutations in pre-mRNA splicing PRPF31 gene have been described as the second most common cause of autosomal dominant RP. Previous studies relate mutations in PRPF31 with dysfunction and degeneration of the retinal pigment epithelium (RPE). Thanks to the ability to obtain and differentiate induced pluripotent stem cells (iPSC), retinal models can be generated to study the disease mechanism and to evaluate new therapies. This work is based on a personalized cellular model obtained by differentiating RPE from iPSCs of a patient with PRPF31 c.165G mutation, which will be used to study the mechanism of the disease.

**Methods:** iPSCs and previously differentiated RPE cells have been cultured and imaged. The characterization of the RNA level expression of specific genes of both cell types has been performed by RT-PCR. Expression at the protein level has been analyzed by Western blot. At the physiological level, the ability of the cellular model to establish an epithelial barrier has been evaluated by transepithelial electrical resistance (TER).

**Results:** Phase contrast images showed a characteristic and distinctive morphology of iPSC and RPE cells. RT-PCR showed the silencing of pluripotency genes such as NANOG in RPE cells, as well as the exclusive expression of specific genes such as CRALBP and RPE65 in RPE. In the comparative study of the cellular models of patient and healthy control, it was observed a variation in the expression levels of the PRPF31 and RPE65 genes. In Western blot, the PRPF31 protein detected in the patient's RPE showed a different band pattern compared with healthy control and iPSCs. Finally, TER showed a similar maturation of the two cell models compared, indicating that PRPF31 c.165G mutation does not affect the cells adhesions.

**Conclusions:** The cellular model of RPE with PRPF31 c.165G mutation has been correctly differentiated, allowing the study of the consequences at the cellular level of this genetic defect. The decrease found in RPE65 gene expression suggests that this could be the mechanism by which PRPF31 c.165G mutation causes RP, because RPE65 insufficiency is a known cause of blindness.

### REFERENCES

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