Rod-derived Cone Viability Factor

Results in Brief

Novel treatments for vision disorders

Retinitis pigmentosa (RP) is a group of hereditary disorders that lead to vision loss. Preserving the function of the degenerating cone photoreceptors was explored as a potential therapeutic intervention in RP patients.

HEALTH

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Affecting over 1 million people worldwide, the genetically heterogeneous RP diseases stem from degeneration of photoreceptors — the specialised neuronal cells in the eye capable of transducing light into a signal to the brain. In RP, rod photoreceptors that are responsible for night vision degenerate first, followed by cones, which mediate central and light-adapted vision.

The rod-derived cone viability factor (RdCVF), a protein expressed and secreted by rod photoreceptors, sustains the viability of cone photoreceptors and has been shown experimentally to correct RP. Given that even 5 % of functional cones provide substantial vision, the EU-funded 'Rod-derived cone viability factor' RDCVF project proposed to administer RdCVF as a therapeutic strategy against the secondary degeneration of cones in RP.

In order to reach clinical applicability, the consortium had to ensure that they were able to produce good manufacturing practices-level functional RdCVF protein in

mammalian cell lines. For this purpose, analytical methods were developed and specific polyclonal antibodies were produced. In addition, partners established a culture system from chick embryos that enabled them to assess the functional outcome of RdCVF protein expression in terms of cone photoreceptor cell viability. Assays for evaluating the impact of RdCVF protein in vivo were also set up, including an automated cone counting system that essentially measured cone density by scanning the retinal surface.

However, the hydrophobic nature of the protein hampered its scalable production and purification using standard method. As a result, researchers explored the Nxnl1 gene for maintaining photoreceptor integrity by responding to oxidative stress.

Pharmacokinetic and toxicology studies into the fate of intravitreal injection of marker proteins revealed that they enter the bloodstream and could potentially induce thrombocyte activation. In order for this administration route to be clinically viable, partners proposed an alternative approach using nanoparticles that ensures stable release of the protein.

RdCVF protein administration as a therapy for RP has enormous potential provided its clinical-grade production overcomes certain technical hurdles. The pharmacological, pharmacokinetics and toxicological studies proposed by the RDCVF study should still pave the way to a protein therapy.

Keywords

Retinitis pigmentosa, rod-derived cone viability factor, Nxnl1 gene, rod photoreceptors, protein therapy

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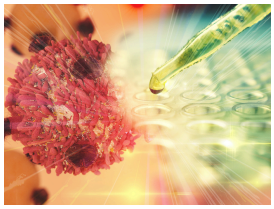

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RDCVF

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