**Titel des Projekts**

Role of lipid mediators in corneal nerve regeneration

Ein Antrag im Rahmen des Potentialbereichs Pathomechanismen der zellulären Differenzierung und Kommunikation bei selteneren Erkrankungen: Chancen zur Regeneration

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**Zusammenfassung des Projekts**

Neurotrophic keratopathy (NK) is a progressive, rare eye disease which results from decreased innervation of the cornea due to injuries of the *N. trigeminus*. The loss of sensory innervation leads to decreased tear secretion and reduction in the regeneration potential of the corneal epithelium. This can lead to persistent epithelial defects, corneal perforations and graft loss. To date, only one curative treatment exists. Therefore, the research of new therapeutic approaches is clinically important. Our group recently established new 3D *in vitro* models of the cornea using tissue engineered materials, which can be used to investigate regeneration-associated factors and underlying pathways in an *in vivo*-like manner. Additionally, our group established an *in vivo* mouse model for analyzing nerve regeneration. Using these new methods, the Rho Kinase (ROCK) inhibitor was identified as a factor for corneal nerve regeneration *in vitro* and *in vivo*. Interestingly, it has been shown that the ROCK pathway can be regulated upstream by bioactive lipids, such as lysophosphatidic acid (LPA). LPA, a small bioactive phospholipid that acts as an extracellular signaling molecule, has been suggested to be an important player in both de- and regeneration processes in the CNS and PNS. Recent publications revealed a connection of the LPA and ROCK pathway in different cell types. This led to our hypothesis that the inhibition of LPA signaling might lead to an inhibition of ROCK during nerve injury and therefore to an enhancement in corneal nerve regeneration. The aim of this project is to investigate the effect of LPA/ROCK on the regeneration potential of corneal nerves to reveal a possible new therapeutic drug, as an inhibition of an signaling pathway by blocking receptors is more promising concerning the effectivity of eye drops than blocking downstream factors in the cells. Therefore, the effects of ROCK inhibition in combination with LPA receptor inhibition will be investigated in our 2D and 3D models. Furthermore, the effects of LPA/ROCK during corneal nerve injury will be analyzed. In a third part, promising combination of LPA/ROCK inhibition will be investigated in our *in vivo* model. The results of the project could reveal new substances that can restore the innervation of the cornea and thus represent a new curative therapy approach for NK.