6. Summary

Glaucoma is a multifactorial disease, which leads to irreversible RGC loss and optic nerve degeneration. Patients suffer from gradual visual field loss. Although an elevated IOP is still the main risk factor, other mechanisms are also involved in the cell loss. Besides oxidative stress, ischemia, or an enhanced glutamate level, immunological processes are discussed in the pathogenesis. Altered antibody levels could be detected in the sera of glaucoma patients. Additionally, autoantibodies in the retinas of glaucoma patients and in animal models were found. These autoantibodies were identified as IgG and IgM antibodies, which revealed the possibility that the complement system could be involved in the glaucoma pathogenesis. Therefore, we analyzed complement components in an IOP-independent EAG-model as well as in an OHT-model. In the EAG-model, we noted significantly more C3 and MAC 7 days after ONA immunization and before any RGC loss or optic nerve degeneration occurred. Interestingly, the activation of the complement system was triggered through the lectin pathway, namely MASP2. On the other hand, no changes were noted regarding to the classical pathway component C1q. The activation of the complement system was observed simultaneously in the retinas and optic nerves and seems to be an early response, which then triggers degeneration.

After a slight IOP increase in the OHT-model, significantly fewer RGCs, but no signs of gliosis were observed. However, an increase of C3 and the terminal pathway MAC was shown in these retinas. In contrast to the EAG-model, the activation of the complement system was not initiated via the lectin pathway. In the OHT-model, the other pathways seem to be the activator of the complement.

These results indicate a crucial role of the complement system in the pathogenesis of glaucoma. New therapy strategies could be based on these findings.

It is known that alterations in the ECM components are involved in RGC loss and optic nerve degeneration. However, most studies deal with an elevated IOP. Here, we wanted to analyze the contribution of ECM proteins in an IOP-independent model. It could be demonstrated that the glycoprotein tenascin-C and its interaction partner phosphacan, a member of the RPTPβ/ζ family, are significantly increased after immunization with ONA and S100. This remodeling occurred in the retinas as well as in the optic nerves before any degenerative processes were noted. Interestingly, we did not note any signs of alterations in the astrocyte or in Müller cell expression.
However, phosphacan levels in Müller glia and astrocytes increased before reactive gliosis was detectable. Therefore, we assume that both ECM molecules represent early indicators in glaucoma disease. It seems likely that tenascin-C tries to restrict neuronal damage and that phosphacan acts as an early marker of gliosis.

In summary, these studies revealed an involvement of the complement system and ECM components in early stages of glaucoma disease. In regard to the complement activation, further experiments should analyze, if an inhibition of complement components leads to a rescue of RGCs. Knock-out studies of ECM molecules should reveal the precise function of the remodeling in degenerative processes.