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Title – Anti-inflammatory role of a glycan-coated nanoparticle in modulating macrophages and complement in non-exudative AMD.

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Purpose – Age-related macular degeneration (AMD) is a progressive retinal disease which causes irreversible blindness in elderly. Studies indicate a prominent role of inflammation in the pathogenesis of AMD. Both the cellular and non-cellular components of the innate immune system including cytokine production have been extensively studied to understand the pathophysiology of the disease.
We utilize a novel strategy to address severe chronic "non-resolving" inflammation via the body's own self recognition system. Our lead asset is a glycan-coated nanoparticle exhibiting dual function in regulating the immune system. It directly modulates the self-pattern recognition receptors on the immune cells, Siglecs (sialic acid binding immunogloblulin like lectins), by dampening the activity of inflammatory cells and enhancing the activity of complement factor H.

Method – We performed cell-based assays using our proprietary asset in two cell types; THP-1-derived macrophages and PBMC-derived macrophages to characterize the biological activities. Cytokine release as pro-inflammatory markers and complement factor H levels were measured 24 hours post treatment.

Results – Our glycan-coated nanoparticle significantly reduces the production of pro-inflammatory markers (TNF-a) by 2 folds in THP-1-derived macrophages and 2-fold increase in complement factor H levels in PBMC derived M1 macrophages compared to the cells treated with a negative control.

Conclusion – Our glycan coated nanoparticle leads to a significant reduction in pro-inflammatory markers and an increase in CFH levels. Our approach for the treatment of non-exudative AMD is to selectively repolarize the macrophage into a resting state. These preclinical studies provide evidence that our molecule targets both cellular and complement mediated aspects of the innate immune system, which are believed to be involved in the pathogenesis of non-exudative AMD and support the advancement of our glycan coated nanoparticle for further development.