

Age-Related Macular Degeneration

Polyphosphate (polyP) for the treatment of complement-associated disorders

Advantages:

- Potent against wet AMD *in vivo*
- Highly water-soluble and stable
- Suitable for intravitreal injections
- polyP is a natural blood component
- Inexpensive and easy to produce

Principal Inventor(s):

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Publications:

- [1] *Circ. Res.* 2016 (118) 1392-1408.
[2] *Blood* 2014 (123) 768-776.
[3] *Blood* 2016, in review.

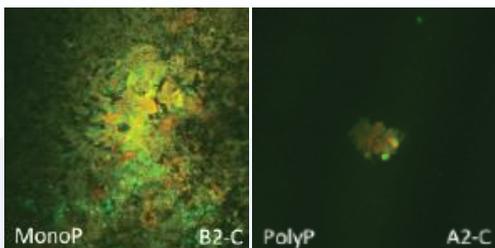
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PolyP suppresses 'wet' AMD in rat model.

Technology Details:

Age-related macular degeneration (AMD) is a major cause of blindness in people over the age of 50 and expected to exceed 50 million worldwide by the year 2020. Loss of vision is a catastrophic event for the affected individuals and their families. In addition, AMD amounts to a major socio-economic cost to global healthcare exceeding \$340 billion.

Two forms of AMD are known: exudative or 'wet' and atrophic or 'dry'. Currently, there are no treatment options for dry AMD available, which constitutes ~90% of cases. The wet form features excess blood vessel growth and bleeding in the retina. Treatments for wet AMD are principally designed to suppress vessel growth by interfering with vascular endothelial growth factor (VEGF)-related pathways. Lifelong once per month, these VEGF pathway inhibitors need to be injected into the eye leading to arrested progression in ~90% and improved vision in ~30% of patients; however, these injection treatments have detrimental effects on the retinal vasculature and widespread atrophy of the retinal pigment epithelial cells (RPE), while diminished vision is still common. The pathogenesis of AMD is complex and not fully understood. Coagulation and complement are evolutionarily related with several well-described mechanisms of cross-talk [1]. Excess complement activation in the retina of the eye appears to be a major contributing factor to the pathogenesis of AMD.

Researchers at The University of British Columbia have shown that polyphosphate (polyP) is a potent negative regulator of the terminal pathway and membrane attack complex (MAC) formation [2]. PolyP, a linear polymer of orthophosphate linked by phosphoanhydride bonds, dampens the innate immune response by suppressing complement [3], therewith attenuating choroid neovascularization and MAC deposition in the retina of AMD patients.

Development Stage:

The therapeutic potential for AMD has been confirmed *in vitro* and *in vivo*. *In vivo* studies were conducted in rodent models for wet AMD, which are considered highly predictive for human therapies. Further pharmacokinetic studies, such as dose-response studies, are ongoing.

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