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Dendrimer-based targeted nanotherapeutics for ocular inflammation

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Retinal neuroinflammation, mediated by activated microglia, plays a key role in the pathogenesis of photoreceptor and retinal pigment epithelial cell loss in age-related macular degeneration and retinitis pigmentosa. Targeted, sustained attenuation of activated microglia may be a powerful strategy to arrest retinal degeneration. Nanomedicine approaches are being explored for targeted drug therapy for attenuation of neuroinflammation in the retina was explored using hydroxyl-terminated polyamidoamine (PAMAM) dendrimer-drug conjugate nanodevices.

We show that, upon intravitreal administration, PAMAM dendrimers selectively localize in activated microglia in the retina in multiple animal models of retinal degeneration, but not in the retina of healthy controls. This pathology-dependent biodistribution was exploited for drug delivery, by covalently conjugating anti-inflammatory drugs to the dendrimer. For example, a dendrimer-fluocinolone acetonide conjugate was prepared, and was released the drug in a sustained manner over 90 days. One intravitreal injection of 1 μ g of FA conjugated to 7 μ g of the dendrimer was able to arrest retinal degeneration, preserve photoreceptor outer nuclear cell counts, and attenuate activated microglia, for an entire month. These studies suggest that PAMAM dendrimers (with no targeting ligands) have an intrinsic ability to selectively localize in activated microglia, and can deliver drugs inside these cells for a sustained period for the treatment of retinal neuroinflammation. The talk will highlight the role of nanomedicine, especially dendrimers, in addressing ocular inflammation.

Biography

Kannan Rangaramanujam is a Professor of ophthalmology and the center for nanomedicine at the Wilmer Eye Institute in Johns Hopkins School of Medicine. He obtained his Ph.D. from the California Institute of Technology (1994) in Chemical Engineering, and performed post-doctoral research at the University of Minnesota. His primary research interests are in the field of dendrimer-based targeted therapeutic platforms for neuroinflammation in CNS diseases, with a focus on retinal degeneration, cerebral palsy, and traumatic brain injury. Kannan and his team have discovered ways to target neuroinflammation using dendrimers. Kannan is an author of four patents, more than 75 peer-reviewed publications. He has won several recognitions, including the NSF CAREER award, Unilever award, and is on the editorial board of Nanomedicine: nanotechnology, biology and medicine.

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