Dr. Kannan Rangaramanujam is the Arnall Patz Distinguished Professor of Ophthalmology and Co-director of the Center for Nanomedicine at the Wilmer Eye Institute at Johns Hopkins School of Medicine. He has joint/courtesy appointments in Chemical and Biomolecular Engineering, and Materials Science and Engineering at Johns Hopkins. He is also a research scientist at the Kennedy-Krieger Institute. He obtained his PhD in Chemical Engineering from the California Institute of Technology, and followed it with a post-doc from the University of Minnesota. His research interested are in the field of translational nanomedicine, focused on targeted therapies for neuroinflammation, based on a dendrimer platform. He has initiated an interdisciplinary translational research program based on dendrimers, with a specific focus on systemic, targeted drug delivery strategies for treating neuroinflammation, in a variety of central nervous system and ocular disorders. Dr. Kannan is an author of many patents (issued and pending, licensed), more than 85 peer-reviewed publications. He has received recognition for his work, including the NSF CAREER and Unilever awards. His research is primarily funded by the National Institutes of Health (NIH). He is the co-founder and chief technology officer of Ashvattha Therapeutics and Orpheris Inc., which are two spin-off companies involved in translating his team’s patented dendrimer technologies.

Title- Targeted nanotherapies for CNS disorders: from chemistry to clinical translation

Neuroinflammation, caused by activated microglia and astrocytes, plays a key role in the pathogenesis of cerebral palsy (CP), autism, and other debilitating neurodegenerative disorders. Appropriate, targeted manipulation of neuroinflammation can bring novel approaches for treated diseases, increasing the efficacy and decreasing the side effects of drugs. 'Engineering' the functional response of activated glia can be a potent therapeutic strategy. However, targeted delivery of drugs to specific cells in the central nervous system is a challenge. We take advantage of the unique, intrinsic, pathology-dependent, brain uptake of dendrimers (with no targeting moieties) in diseases models of neurodegeneration. For example, upon systemic administration, hydroxyl poly(amidoamine) dendrimers localize selectively in activated microglia and astrocytes in animals with CP. Such selective localization is also seen in multiple brain and retinal injury small and large animal models. Building on these findings, we have designed and synthesized dendrimer-drug conjugates which have shown significant promise for translation. Two examples of this approach of targeting neuroinflammation the brain and the retina (from systemic administration) will be presented. We show that a single intravenous dose of dendrimer-drug conjugate, administered after birth to rabbit kits with CP, results in significant improvement in motor function along with decrease in neuroinflammation and oxidative/neuronal injury, followed by improved myelination, by 5 days of age.1 This improvement is sustained till adulthood, paving way for new approaches to pediatric/neonatal brain injuries. These dendrimer-drug conjugates are undergoing commercialization and clinical translation.