



ENGINEERING THERAPEUTIC NANOSCALE HYDROGELS



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ABSTRACT

Various nanoscale hydrogels or “nanogels” have been fabricated for drug delivery. However, relative to lipid nanoparticles and other nanomedicines, little is known about how their characteristics (i.e., composition, diameter) affect biodistribution or direct immunological fate. To address this knowledge gap, my lab asked several key questions (1) How do systemically dosed nanogels distribute at the organ, tissue, and cellular levels? (2) To what extent do nanogels intrinsically shift the phenotype of immune cells? And finally (3) Can purposefully engineered active nanoscale hydrogel resolve inflammatory disease in live animals? To test these questions, we have synthesized ~100 distinct nanoscale hydrogels (80–250 nm diameter), starting from pure monomers, and have evaluated their immunological performance in various model systems (i.e., cell lines, primary cells, and live C57/BL6 mice). In this lecture, I will show how nanogel composition predicts immunological performance based on cellular analysis and genomics studies. I will also describe two case studies based on bioconjugation of recombinant cytokines to a nearly inert nanogel substrate (P(AAm-co-MAA). In the first, we demonstrated proof-of-concept that systemically dosed, active nanogels can modulate macrophage phenotype. In the second, we show for the first time that systemically dosed nanogels can be delivered to the placenta in pregnant mice, a potential strategy for mitigating developmental consequences of maternal health and pregnancy-related diseases to offspring. Together, our studies both establish fundamental understanding and illustrate emerging application of rationally designed therapeutic nanogels.

BIO

Dr. John R. Clegg is an Assistant Professor of Biomedical Engineering at the University of Oklahoma, Associate of the Materials Science & Engineering Graduate Program and member of the Harrold Hamm Diabetes Center and Stephenson Cancer Center at OU-Health Sciences Center. Dr. Clegg obtained his PhD from the University of Texas, Austin and conducted postdoctoral training at Harvard University. His lab studies hydrogel delivery systems (including nanoscale hydrogels and injectable hydrogel biomaterials), as well as combination products involving hydrogels and adoptively transferred immune cells, for a range of inflammatory diseases. His translational research has additionally led to biomaterial treatments for neurotrauma and metastatic brain tumors.