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Facile Production of Multifunctional Nanoparticles for Difficult to Deliver Therapeutics: hydrophobic drugs, peptides, and siRNA

ABSTRACT

Several classes of therapeutics are Nanoparticle formulations of hydrophobic drugs present unique opportunities for treatment of solid tumor cancers, for delivery of drugs by aerosol administration, and as a route to novel vaccine adjuvants. The common requirements of these applications are precise control of particle size and surface functionality. For cancer therapy particles in the size range of 100-200 nm passively pass through defects in the vasculature in tumors and deposit by “enhanced permeation retention”. In addition to delivery, the ability to monitor the fate of the nanoparticles is also of important since anti-cancer agents are invariably toxic to healthy tissue. Our process --Flash NanoPrecipitation – a controlled precipitation process that produces stable nanoparticles at high concentrations using amphiphilic diblock copolymers to direct self-assembly enables the production of composite nanoparticles that enable simultaneous imaging and delivery. The engineering science involved in the fluid mechanics and self assembly of these nanoparticles will be to focus of the talk. The key to the process is the control of time scales for micromixing, polymer self-assembly, and particle nucleation and growth. The PEG protective layer creates long-circulating particles and the inclusion of PEG chains with terminal ligands allows drug targeting. The incorporation of gold nanoparticles, magnetic nanoparticles, or fluorophores into the composite particle enables imaging by x-ray, MRI, or confocal microscopy, respectively. The use of hydrolytically unstable linkers enables the controlled release of single and multiple drugs from nanoparticles to enable “drug cocktails” in a way that has not been possible previously.

BIOGRAPHY

Robert K. Prud'homme is a professor in the Department of Chemical and Biological Engineering at Princeton University and Director of the Engineering Biology Program at Princeton. He received his BS at Stanford University and his PhD from the University of Wisconsin at Madison under Professor Bob Bird. He has served on the executive committees of the American Institute of Chemical Engineers Materials Science Division and the U.S. Society of Rheology and was the President of the U.S. Society of Rheology. He served as the chair of the Technical Advisory Board for Material Science Research for Dow Chemical Company, which directs Dow’s materials research programs, and he was on the Board of Directors of Rheometric Scientific Inc., the leading manufacturer of rheological instrumentation. He also served on the Nanotechnology Scientific Advisory Committee for BASF, which provided guidance for future trends in nanotechnology for the company. His awards include the NSF Presidential Young Investigator Award, Princeton School of Engineering and Applied Science Outstanding Teaching Award, the Sydney Ross Lectureship at RPI, the Bird,Stewart and Lightfoot Lecturer at the University of Wisconsin, the Dinesh Shah lectureship at the University of Florida, and the Midland Macromolecular Institute Visiting Professor in Midland Michigan. He has been the organizer and Chair of the Gordon Conference on Ion Containing Polymers, and the Society of Petroleum Engineers Forum on Stimulation Fluid Rheology, in addition to organizing numerous sessions at AIChE, ACS, and SOR meetings. He directed the Princeton-University of Minnesota-Iowa State NSF NIRT Center on nanoparticle formation. His research interests include rheology and self-assembly of complex fluids. Systems of interest are biopolymer solutions and gels, surfactant mesophases, and polymer/surfactant mixtures. The goals of the studies are to understand how weak molecular-level interactions can be used to tune macroscopic bulk properties and phase behavior. Application of the work is directed at nanoparticle formation for the drug delivery.