



SEMINARS IN CHEMICAL AND BIOMOLECULAR ENGINEERING



Friday, May 17, 2019

10:00am - 11:00am

Boelter Hall 3400

Paula Hammond

David H. Koch Professor in Engineering

Department of Chemical Engineering

Massachusetts Institute of Technology

"Electrostatic assembly for nanoparticle targeting of cells and tissues"

Nanomaterials of many types have been applied to address biomedical challenges, particularly in the delivery of drug to targeted regions of the body. One of the most powerful interactions that can regulate tissue transport and nanomaterial trafficking is electrostatic charge. In our lab, we have used electrostatic assembly methods in conjunction with well-defined charged macromolecules to enable delivery of drug to specific tissues or organs based on a combination of multivalent charge interactions coupled with other secondary non-specific or specific binding interactions. These systems vary from highly designed synthetic vectors that can deliver mRNA and even gene editing systems to electrostatically assembled complexes that can be generated with a great deal of control. The generation of such systems requires, in each case, a tuning of the ratio of charged species, and an ability to direct responsive behavior that enables release in such systems. In one approach, a layer-by-layer (LbL) technique toward construction of nanostructured nanoparticles provides multiple advantages for chemotherapy. We have generated LbL outer layers that provide effective stealth properties, with long systemic plasma blood half lives and higher tumor accumulation over time. We have demonstrated efficacy in genetically induced non-small cell lung cancer mouse models in which key siRNA targets have been selected with chemotherapy drug in the same nanoparticle system, and are now examining new siRNA and drug combinations in ovarian cancer. By staging release of different drug components via the adaptation of the nanoparticle structure, we can achieve highly synergistic release behavior in these systems. We have found that certain LbL nanoparticle formulations traffic differently in cells based on the negatively charged polypeptide, and are exploring ways to utilize these differences in affinity for more selective tumor cell binding and deliver within cells. Ongoing work that includes new ovarian cancer and lymphoma efforts utilizing siRNA and combination drug therapies will be discussed, including new work involving the delivery of cytokines for activation of the immune system against cancer. Finally, we have also begun investigating the use of these LbL nanoparticle systems as a means of targeting nanoparticles across the blood-brain-barrier using conjugated peptides, followed by targeting of glioma cells based on affinity of the particle outer layer for tumor cells. Recent developments in this area will also be presented.

Professor Paula T. Hammond is the David H. Koch Chair Professor of Engineering at the Massachusetts Institute of Technology, and the Head of the Department of Chemical Engineering. She is a member of MIT's Koch Institute for Integrative Cancer Research, the MIT Energy Initiative, and a founding member of the MIT Institute for Soldier Nanotechnology. The core of her work is the use of electrostatics and other complementary interactions to generate functional materials with highly controlled architecture. Her research in nanomedicine encompasses the development of new biomaterials to enable drug delivery from surfaces with spatio-temporal control. She also investigates novel responsive polymer architectures for targeted nanoparticle drug and gene delivery, and has developed self-assembled materials systems for electrochemical energy devices. Professor Paula Hammond was elected into the National Academy of Engineering in 2017. She was elected into the National Academy of Medicine in 2016, and into the 2013 Class of the American Academy of Arts and Sciences. She won the ACS Award in Applied Polymer Science in 2018, and she is also the recipient of the 2013 AIChE Charles M. A. Stine Award, which is bestowed annually to a leading researcher in recognition of outstanding contributions to the field of materials science and engineering, and the 2014 AIChE Alpha Chi Sigma Award for Chemical Engineering Research. She was selected to receive the Department of Defense Ovarian Cancer Teal Innovator Award in 2013, which supports a single visionary individual from any field principally outside of ovarian cancer to focus his/her creativity, innovation, and leadership on ovarian cancer research. By developing degradable electrostatically assembled layer-by-layer (LbL) thin films that enable temporal and even sequential controlled release from surfaces, Paula Hammond pioneered a new and rapidly growing area of multicomponent surface delivery of therapeutics that impacts biomedical implants, tissue engineering and nanomedicine. A key contribution is her ability to introduce not only controlled release of sensitive biologics, but her recent advances in actually staging the release of these drugs to attain synergistically timed combination therapies. She has designed multilayered nanoparticles to deliver a synergistic combination of siRNA or inhibitors with chemotherapy drugs in a staged manner to tumors, leading to significant decreases in tumor growth and a great lowering of toxicity. The newest developments from her lab offer a promising approach to messenger RNA (mRNA) delivery, in which she creates pre-complexes of mRNA with its capping protein and synthesized optimized cationic polypeptides structures for the co-complexation and stabilization of the nucleic acid-protein system to gain up to 80-fold increases in mRNA translation efficiency, opening potential for vaccines and immunotherapies. Professor Hammond has published over 320 papers, and over 20 patent applications. She is the co-founder and member of the Scientific Advisory Board of LayerBio, Inc. and a member of the Scientific Advisory Board of Moderna Therapeutics.