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Distinguished Seminar

Wednesday, January 29, 2020
Seminar Presentation: 11:00am – 12:00pm
SME room 248

"Turning Immunity On and Off"

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Abstract: The immune system exists in a delicate balance of mounting active, effector responses to fight infection from invading pathogens and to kill mutated cells, while existing in an active state of tolerance to the non-self contents of the gut and on the skin and to self proteins throughout the body. Dysfunction can lead to susceptibility to infection and cancer on the one hand, and to allergy and autoimmunity on the other. Immunotherapies are being developed to tip this balance one way or the other – for example to engineer cytokines to create an immune response against mutated self, or engineer antigen delivery to inverse vaccinate against an autoimmune disease to re-establish immunological tolerance to self.

With regard to turning immunity on, vaccinologists frequently employ molecular signals of danger to enhance immune responses to pathogen or mutated self antigens, termed adjuvants. We are developing adjuvant systems that employ both physical and molecular mechanisms of action. Adaptive immune responses are triggered particularly powerfully in the lymph nodes and in the lymphoid tissues associated with mucosae. We are developing nanomaterials and soluble polymers to exploit interstitial flow from the site of administration to the lymph nodes, using the material vectors to carry both antigen and associated adjuvant biomolecules. We build these material carriers to include biomolecular features of pathogens to enhance targeting of precise cell populations in the lymph nodes, dendritic cells, for example employing the sugar residue mannose. Thus, materials conjugated to signals for cellular targeting and uptake, to signals of danger for activation of those target cells, and of antigen, to which the effector immune response is intended, are being developed as multifunctional vaccines. We are interested in these materials to turn immunity on to pathogens such as malaria, for which there is no highly effective vaccine, and to cancer.

Immunity to tumors is particularly complex. Normal tissues display regulatory biomolecules that attenuate potential immune responses to prevent autoimmunity; cancers exploit these mechanisms to actively resist killing by the immune system once mutated proteins in the tumor have been detected. These regulatory biomolecules, referred to as checkpoints, are promising targets for cancer immunotherapy, to block these inhibitors of anti-cancer immunity. Moreover, immune regulatory biomolecules, cytokines and chemokines, are also promising candidates to develop anti-cancer immunity. The difficulty with these drugs and potential drugs is their frequently high toxicity, since they tip the delicate balance described above and can causes anti-self responses. We are exploring means by which to target these powerful immunotherapeutics to tumors, to enhance their efficacy and reduce their toxicity.

In addition to usual vaccines to induce protection to a pathogen, so-called inverse vaccination to induce antigen-specific tolerance is of high interest. We are exploring biological approaches to deliver protein antigens in a tolerogenic manner, including targeting antigen to particular cell subsets in the liver. We have shown the ability to induce antigen-specific anergy as well as T regulatory responses, working in models of autoimmunity and of immune response to protein drugs.

Biosketch: Jeffrey Hubbell is Professor in the Institute for Molecular Engineering of the University of Chicago. Previous to moving to Chicago, he was on the faculty of the Swiss Federal Institute of Technology Lausanne (EPFL, where he served as Director of the Institute of Bioengineering and Dean of the School of Life Sciences), the Swiss Federal Institute of Technology Zurich and University of Zurich, the California Institute of Technology, and the University of Texas in Austin. He holds a BS from Kansas State University and a PhD from Rice University, both degrees being in chemical engineering. He was elected to the US National Academy of Engineering in 2010, the National Academy of Inventors in 2014, and the National Academy of Medicine in 2019.

Hubbell uses biomaterials and protein engineering approaches to investigate topics in regenerative medicine and immunotherapeutics. In regenerative medicine, he focuses on biomaterial matrices that mimic the extracellular matrix and on growth factor - extracellular matrix interactions, working in a variety of animal models of regenerative medicine. In immunotherapeutics, he focuses on nanomaterials in vaccines that target lymphoid-resident antigen presenting cells and on protein engineering approaches to deliver antigen to the spleen and liver for inverse vaccines to induce tolerance to protein drugs and in autoimmunity. His interests are both basic and translational, having founded or co-founded six biomedical companies based on his technology, namely Focal, in Boston, acquired by Genzyme; Kuros Biosciences, in Zurich, in the domain of regenerative medicine; Anokion and Kanyos Bio, in Boston, both in the domain of immunological tolerance; Clostra Bio, in Chicago, in the domain of food allergy, founded together in with Prof. Cathryn Nagler at the University of Chicago; and Arrow Immune, in the domain of cancer immunotherapy, founded together with Prof. Melody Swartz at the University of Chicago.