NSF NANOSCALE SCIENCE AND ENGINEERING GRANTEES CONFERENCE: NANOBIOLOGY
DECEMBER 7-8, 2023

FUNCTIONAL INTERACTION OF NANOMATERIALS WITH CELLULAR CLEARANCE AND STRESS RESPONSE PATHWAYS

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Abstract: Due to their nanoscale size, nanomaterials interact with biological components and systems, many of which also operate at the nanoscale level. Progress in the field of nanotechnology has led to a rapid growth in the number of engineered nanomaterials currently being produced and introduced into the marketplace, increasing organismal and cellular exposure to these specially designed highly reactive materials. Emerging cell engineering technologies have also enabled cell-based manufacturing and self-assembly of nanosized materials. A sophisticated quality control system has evolved in mammalian cells to prevent accumulation of aberrant materials, such as proteinaceous aggregates, through the activation of stress response and degradative pathways. Nano-sized materials are likely to be perceived as foreign or toxic and may stimulate activation of these cellular stress and clearance mechanisms. For instance, nanomaterials of different size and composition have been shown to elicit activation of the autophagy system, the main catabolic pathway that mediates degradation of bulk intracellular material. While activation of autophagy can lead to enhanced clearance, it may also be associated with activation of cell death programs. Moreover, nanomaterials that activate autophagy may also cause impairment of cellular components that mediate degradation, ultimately leading to blockage of autophagic flux. This talk will analyze the cellular response to nanomaterials for applications related to the design of cells for nanomaufacturing as well as to address concerns related to the environmental health and safety of nanomaterials.

Bio: Laura Segatori is a Professor in Bioengineering at Rice University. She received a Laurea in Industrial Biotechnology from the University of Bologna in Italy in 2000 and a PhD in Chemical Engineering from the University of Texas at Austin in 2005. She completed her postdoctoral work at The Scripps Research Institute in La Jolla, CA, and joined the faculty at Rice University in 2007 where she holds joint appointments in the departments of Chemical & Biomolecular Engineering and Biosciences.

Drawing on her interdisciplinary training, she combines principles and tools from engineering and science to elucidate, manipulate, and control biological systems. Her research group applies cell and protein engineering tools, synthetic biology strategies, and classical biochemistry and molecular biology methods to understand and manipulate cellular quality control mechanisms to create synthetic cells for applications ranging from the design of cell-based therapeutic modalities to improved methods for biomanufacturing. Specifically, she pioneered the development of cell engineering approaches for (i) sensing highly dynamic environments with exquisite sensitivity and dynamic resolution, (ii) modulating protein quality control in cells (*i.e.,* ensuring that newly synthesized proteins are properly folded and have the requisite post-translational modification) and (ii) directing the elimination of misfolded proteins via targeted intracellular proteolysis. These approaches are relevant for a diverse range of applications. Preventing the accumulation of misfolded proteins is of key significance for numerous disease states, especially in neurodegeneration and inflammation. Engineering cells with control systems that regulate protein biogenesis also provide a transformative set of technologies for the development of smart cellular therapies with spatial and temporal control of drug delivery as well as well as improved cell factories for biomanufacturing.