Yale Institute for Nanoscience and Quantum Engineering

Friday- January 16, 2015

12:00 to 1:00 p.m.

BECTON SEMINAR ROOM

Light lunch will be served at 11:45 a.m.

Mark Saltzman

Department of Biomedical, Yale University

"Nanotechnology for delivery of genes and gene-modifying agents"

Site-specific gene modification has the potential to produce permanent changes in genomic DNA to correct genetic defects or to enhance cellular function. But delivery of the molecular tools for site-specific editing in vivo is a major hurdle. In recent years, we have shown that degradable nanoparticles of PLGA can be engineered into surprisingly versatile systems for intracellular delivery of plasmid DNA, siRNA, miRNA, and a variety of synthetic oligonucleotides. Further, we have established several methods for engineering the particle surface to allow for targeting. Now, we have applied this technology to the problem of genome editing, by synthesizing degradable polymer nanoparticles that are loaded with triplex-forming peptide nucleic acids (PNAs) and single-stranded donor DNA molecules. These nanoparticles produce site-specific gene editing of human cells in vivo in hematopoietic stem cell-engrafted NOD-scid IL2rγnull mice. Intravenous injection of particles containing PNA and DNA produced modification of the human CCR5 gene in hematolymphoid cells throughout the mice, including CD4+ T cells in the spleen, CD34+ hematopoietic stem/progenitor cells (HSPCs) in the bone marrow, colony-forming hematopoietic progenitors, and true hematopoietic stem cells capable of engraftment in a secondary recipient mouse. We also induced specific modification of the human β-globin gene using nanoparticles carrying β-globin-specific targeting molecules and the cystic fibrosis gene using CFTR-specific targeting molecules, demonstrating this method's versatility. Direct in vivo gene modification, such as we demonstrate here, eliminates the need for cell harvest, providing a mechanism by which to perform gene therapy in systemic diseases or in cells that cannot be manipulated ex vivo.

Minjoo Larry Lee

Department of Electrical Engineering, Yale University

"Playing the strain game: tensile Ge nanowires embedded in a III-V matrix"

Any mechanical strain that alters the length and angle of atomic bonds in a crystalline semiconductor will change how it interacts with electrons, photons, and phonons. Ge is unique among all semiconductors in that large biaxial tensile strains of 2-4% are predicted to change it from an indirect-gap to a direct-gap semiconductor. However, no conclusive demonstrations of direct-gap Ge have been made, and indirect- to direct-gap conversion remains an outstanding fundamental challenge. In this talk, I will describe a new method to grow nanocomposite layers consisting of a dense array of tensile-strained Ge nanowires (NWs) embedded in an $In_{0.52}Al_{0.48}As$ matrix. The nanocomposites are formed by surface-mediated phase separation that occurs during molecular beam epitaxy (MBE) growth. While the low mutual solubility of Ge and III-V compounds provides the driving force for phase separation, we show that the degree of phase separation is strongly controlled by growth kinetics. The structure and composition of the nanocomposites can also be strongly tuned using growth conditions, allowing the controllable formation of Ge quantum dots, nanowires, and nanobelts.

HOST: Paul Fleury