

Seminar

Monday 27th February 2012

11:00 to 12:00 pm - Room 531

Professor Jean Chmielewski

Chemistry & Biomedical Engineering Purdue University, USA

Next Generation Therapies: Multidrug Resistance & Regenerative Medicine

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Multidrug Resistance & Regenerative Medicine

Jean Chmielewski, AW Kramer Distinguished Professor of Chemistry & Biomedical Engineering, Purdue University

This seminar will focus on two areas of interest: inhibition of the multi-drug resistance transporter P-glycoprotein with designed dimeric prodrugs, and the development of collagen peptide building blocks that can be assembled using metal ion/ligand interactions to generate unique micron-scaled structures, such as fibers, spheres, meshes and disks.

P-glycoprotein (P-gp) is an ATP-dependent pump that reduces accumulation of drugs within cells and is a member of a superfamily of membrane transporters. P-gp is over-expressed on the surface of cancer cells and plays a major role in multi-drug resistance in cancer. P-gp is also present on apical side of the luminal membrane of brain capillary endothelial cells (the blood brain barrier), and precludes access of a number of therapies to the brain. By taking advantage of the multiple substrate binding sites within the transporter domain of P-gp, we have developed novel dimeric prodrug inhibitors of P-gp based on the therapeutic agents themselves. Inhibition of P-gp transport with these agents will be discussed.

Collagen is one of the major structural proteins of the extracellular matrix and is found associated with skin, bone, tendons, ligaments, and blood vessels. As such, there is great interest in using collagen for applications in regenerative medicine and tissue engineering. Natural collagen has limitations, however, for these applications due to difficulties in precisely controlling the protein's structure at the nano- and micro-scale and a limited ability to modify its chemical structure. These difficulties could be overcome by using synthetic fragments of collagen (peptides) as building blocks for larger, functional biomaterials. To this end, we have designed collagen peptide building blocks that can be assembled using metal ion/ligand interactions to generate unique micron-scaled structures, such as fibers, spheres, meshes and disks.