**POCC Seminar**
March 29, 2007
Dr. Timothy Macdonald
University of Virginia
Title: Molecular mechanisms of adverse drug reactions
8:00 p.m.
Carolyn Hoff Lynch Lecture Hall
University of  Pennsylvania

**Dr. Timothy Macdonald** received his B.S. degree from UCLA and his Ph. D. at Columbia University under Gilbert Stork.  He has been at the University of Virginia since 1982 where he is a Professor of Chemistry and Pharmacology and the past Chair of Chemistry. The unifying theme of his research program is the application of organic chemical theory and technique to the investigation of problems in biology. Long standing interests have been directed at elucidating the molecular interactions and mechanisms of small molecule-protein interactions and current efforts are focused on several rather broad areas: elucidation of the molecular pharmacology of ligand-receptor interactions, particularly of lipid signaling molecules; identification of the molecular processes underlying idiosyncratic drug reactions; and characterization of the mechanisms underlying the modification of proteins and other biomolecules by reactive oxygen and nitrogen species.

**Abstract:** Adverse drug reactions have been estimated to be responsible for 15% of all hospital admissions, 100,000 deaths and $136B costs to the health care system annually.  Idiosyncratic drug reactions, although only ~15% of all adverse reactions, constitute a significant share of this burden and are often responsible for the withdrawal or restriction of a drug.  This presentation will discuss idiosyncratic drug reactions and focus on felbamate, an antiepileptic drug that exhibits a unique profile of activity and therapeutic benefits.  Within a year of its widespread release, felbamate was shown to cause idiosyncratic aplastic anemia and hepatotoxicity and its use was severely restricted.  The mechanisms of drug bioactivation and covalent association with proteins will be presented and the roles of these processes in the idiosyncratic toxicities discussed.