UF College of Pharmacy
Department of Medicinal Chemistry
UNIVERSITY of FLORIDA

"Controlling Human Sulfuryl-Transfer Biology"

Thomas S. Leyh, Ph.D.

Professor, Microbiology and Immunology

Albert Einstein College of Medicine, New York

Human cytosolic sulfotransferases (SULTs) transfer the sulfuryl-moiety (-SO_3) from PAPS (3-phosphoadenosine 5'-phosphosulfate) to the hydroxyls and amines of hundreds, perhaps thousands of metabolites, including many drugs and signaling small molecules… estrogens, androgens, thyroid hormones, hydroxysterols, catecholamine neurotransmitters — the target interactions of these metabolites are altered dramatically *via* sulfonation, which, when imbalanced, leads to disease. Thirteen SULT isoforms are encoded in the human genome. Each isoform operates in a separate metabolic domain and offers a unique means of controlling the domain-linked biological processes. Our structural and dynamics descriptions of SULT molecular behavior are revealing, for the first time, how these catalysts can be controlled *in vivo.* New isoform-specific allosteric-binding pockets are bringing to light a deeper metabolic dialogue, and the pocket structures are providing templates for the design of novel first-generation therapeutics, which we are synthesizing and testing *in vivo*. Finally, our studies of SULT ligand-recognition principles reveal how molecules/drugs can be designed to escape sulfonation without affecting their target interactions or inhibiting SULTs — a strategy which we have used to enhance the *in vivo* efficacy of dopamine and nuclear-receptor agonists 10^2- to 10^5-fold.

Wednesday, November 15, 2017 at 3:00 PM

Communicore Building, Room C1-15