Research Project 3 [1]

PCBs and Hydroxysteroid (Alcohol) Sulfotransferases

Polychlorinated biphenyls (PCBs) continue to persist in our environment and are linked to multiple threats to human health. Of most recent concern is the ongoing contamination by PCBs in older buildings (e.g., public school buildings) and in the air of these and other indoor and outdoor environments.

Those PCBs with lower numbers of chlorine atoms (i.e., semi-volatile PCBs in air) are metabolized in humans and other mammals to hydroxylated derivatives (OH-PCBs), and these metabolites are important in their toxicities. OH-PCB-mediated inhibition of mammalian cytosolic sulfotransferases (SULTs) that are important in endocrine hormone function has been the subject of increasing attention, however, relatively little is known about the formation, disposition, and biological activities of the sulfated metabolites of OH-PCBs (i.e., PCB sulfates).

Project 3 has made substantial progress in studies on the potential for hydroxylated and sulfated metabolites of polychlorinated biphenyls (PCBs) to have biological effects that result in human toxic responses such as altered thyroid hormone status and changes in localized steroid hormone concentrations.

The long-term goal of Project 3 is to understand the relationships between human SULTs and toxic responses to the lower chlorinated PCBs present in air.

- **Project Leader: Michael W. Duffel, PhD**
  Dr. Duffel is responsible for overall direction of the project, including the planning and design of all experiments, data collection, analysis and interpretation of results, preparation of manuscripts, and progress reports. In addition to experimental design of all phases of Project 3, he will coordinate joint studies with Project 1 [2] of the isrp, and interact directly with both the Synthesis Core [3] and the Analytical Core [4] for preparation of OHPCBs and the analysis of peptide disulfides, respectively.

- **Larry W. Robertson, PhD, MPH**
  Dr. Robertson will be directly involved in the design and interpretation of the results of all in
vivo studies on the effects of PCBs and OHPCBs in rats. Dr. Robertson and Dr. Duffel will coordinate all aspects of the treatment and acquisition of tissues from rats treated with these agents.

- **Hans J. Lehmler, PhD**
  Dr. Lehmler will provide expertise in those portions of the studies that relate to crystal structure- and computationally-based analysis of torsion angles in PCBs and OHPCBs. The *Synthesis Core* [3], directed by Dr. Lehmler, will provide synthesis of PCBs and OHPCBs to Project 3. He will also guide conformational analyses of torsion angles compounds for Project 3.