**Terry McGuire, PhD**
**Res. Assist. Professor**
**Dept. of Pharm. Sciences**
**Biology Group Leader, PSP**
**Sci. Admin., CCGS Center**

**PSP Course Lecture:**
***Computational ADME(T)***

**Current Student Mentoring:**
**1 PhD Students**
**2 MS Students**

**Research Interests**
**CB2/p62 aberrant signaling pathways in cancer, neurodegenerative disease, & addiction; Discovery of small molecules targeting CB2/p62 that can regulate aberrant signaling.**

# Research Areas

## I. Cannabinoid Receptor 2 (CB2) Allosteric Modulators.

Development of allosteric modulators (AMs) to G protein-coupled receptors (GPCRs) is at the forefront of Drug Discovery. We work very closely with the Computational and Medicinal Chemistry groups to use cutting-edge algorithms and powerful biophysical approaches (CryoEM and X-ray diffraction of CB2 crystals) to:

(i) Elucidate the high resolution 3-D structure of CB2 bound to either positive or negative AMs (PAMs or NAMs). Site-directed mutagenesis is used to confirm the involvement of specific CB2 amino acid residues in the binding of AMs.

(ii) Use the high-resolution CB2 structural data to develop novel CB2 PAMs and NAMs that can be developed into drug lead molecules for treatment of CB2-associated diseases, such as inflammatory/immune-related diseases and drug addiction.

## II. P62 ZZ Domain Modulators for Cancer and Neurodegenerative Diseases.

We are the first group to develop compounds that selectively bind to the ZZ domain of P62/SQSTM-1, a cytosolic multi-domain protein that mediates several important signaling pathways often deregulated in cancer and and neurodegenerative diseases. More specifically, our p62 ZZ domain modulators (p62ZZMs) have been shown to inhibit pathogenic signaling (TNF$\alpha$-NF$\kappa$B pathway) in multiple myeloma (MM), strongly blocking the growth of MM tumor cells and reversing pathogenic bone loss at sites of MM bone lesions. P62ZZMs also induce autophagic signaling, a protein degradation pathway used to maintain cell survival. In engineered cells, P62ZZMs induce clearance of aggregated over-expressed mutant Huntingtin protein.