

Shaomeng Wang Drug Discovery Distinguished Lecture Series

Hosted by the
Department of Medicinal Chemistry

Turning Problems into Opportunities via Small Molecule Design

Presented by Brian Blagg, Ph.D.

October 29, 2026 | 11:00 AM
Forum Hall, Palmer Commons



Brian Blagg, Ph.D.

The Hsp90 protein folding machine is a powerful modulator of proteostasis. It's role in the maturation of signaling proteins and mutant proteins is well-documented and supports tumor initiation, progression and metastasis. Such studies led to the clinical evaluation of more than 20 investigational new drugs (IND) for the treatment of various cancers. Unfortunately, those studies led to the failure of most candidates due to dose-escalating toxicities that led to cardio- and ocular toxicities amongst other adverse events. Since Hsp90 exists as four isoforms that share greater than 85% identity within the ligand binding site, those IND's led to pan inhibition of all four isoforms, which was the cause for most failures. While researchers stated that isoform-selective inhibition of Hsp90 was impossible, we discovered methods to inhibit each isoform with excellent selectivity. These new isoform-selective inhibitors provide significant advantages over the pan-Hsp90 inhibitors and exhibit the ability to treat cancer, glaucoma, neurological and/or metabolic disorders. The design of such inhibitors and their translational development will be described in this presentation.