

2022-2023 POCC Lecture Series

Nov 18, 2022, 7:30 PM **Prof. Donna Huryn** University of Pittsburgh

Development of Allosteric Inhibitors of the ATPase p97 to Interrogate Novel Biology and Fuel Cancer Drug Discovery <u>Women in Chemistry Lecture</u> IN PERSON @:

Carolyn Hoff Lynch Lecture Hall Chemistry Building, University of Pennsylvania

> <u>6:30 Reception in the Nobel Hall</u> Food and drinks to be provided!



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Abstract: Clinical success in targeting the protein degradation pathway using proteasome inhibitors has spurred efforts to evaluate other aspects of this system as approaches to cancer therapy. Among those, the AAA ATPase, p97/ VCP, a master regulator of protein homeostasis, has recently emerged as a promising target. While there is considerable validation that inhibition of p97 will have anti-tumor effects, a number of key question still remain about its potential for therapeutic efficacy, as well as its fundamental biology. Through the auspices of the National Cancer Institute's (NCI's) Chemical Biology Consortium, we discovered and developed novel, potent allosteric inhibitors of p97. We solved the first high-resolution structure of p97 bound to an inhibitor using cryo-electron microscopy, and are using these molecules to decipher the complex biology of p97 and to develop new experimental therapeutics.

Bio: Donna M. Huryn received her undergraduate degree from Cornell University and her Ph.D. in Organic Chemistry at the University of Pennsylvania working in the Smith Group. She began her career as a medicinal chemist in the pharmaceutical industry (Hoffmann-La Roche & Wyeth Research), and contributed to drug discovery efforts for HIV, cancer, asthma, and CNS disorders. In 2004, she joined academia, and is currently Professor at the University of Pennsylvania. She is a Fellow of the American Chemical Society, recipient of the ACS Philadelphia Local Section Award, and has held a number of elected positions within the American Chemical Society and the AAAS. She is Associate Editor of ACS Medicinal Chemistry Letters and co-author of the textbook Medicinal Chemistry.

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