University of Cyprus
Department of Biological Sciences

Seminar Series: Fall 2023/24

Deregulated Signaling in Disease: Protein Kinase C Unbalanced

Dr. Alexandra Newton

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Wednesday 1 of November 2023, 17:00-19:00

Building CTF 01, **Room 110**.

The seminars are open to the public.

Abstract: Protein kinase C (PKC) isozymes that transduce signals from lipid hydrolysis have historically been considered oncoproteins. This stems in large part from the discovery in the early 1980s that PKC is directly activated by tumor-promoting phorbol esters. Yet three decades of clinical trials using PKC inhibitors in cancer therapies not only failed, but in some cases worsened patient outcome. Why has targeting PKC in cancer eluded successful therapies? Our recent findings reframe PKC isozymes as generally having tumor suppressive function and suggest that therapeutic strategies should focus on restoring, rather than inhibiting, PKC activity in cancer. In striking contrast, enhanced activity of PKC is associated with degenerative diseases, with gain-of-function variants in PKCalpha identified in Alzheimer's disease and PKCgamma in cerebellar Ataxia Type 14, suggesting that inhibitors for PKC could be repurposed for neurodegenerative diseases. Understanding the molecular mechanisms that control PKC, including by upstream regulators such as mTORC2 and the phosphatase PHLPP, inform on how to effectively target this ubiquitous family of kinases in disease.

Biography: Dr. Alexandra Newton received her PhD in Chemistry from Stanford University and postdoctoral training in the lab of Daniel E. Koshland, Jr., at the University of California, Berkeley. She joined the Chemistry Department at Indiana University in 1988 and was recruited to the Department of Pharmacology at UCSD in 1995, where she is currently Distinguished Professor. Dr. Newton is a passionate mentor and has trained 30 PhD students; she serves on numerous national and international committees, is founding Director of Cell Signaling San Diego and is currently President of the International Union of Biochemistry and Molecular Biology (IUBMB). Dr. Newton's research focuses on understanding of the structure, function, and regulation of a key signaling molecule in cells, protein kinase C, and how its function is altered in disease. Her work exemplifies how detailed dissection of the mechanisms of allosteric regulation of enzyme function provides the necessary biochemical understanding to drive effective therapeutic strategies.