

Hunter College of the City University of New York  
Department of Biological Sciences  
Fall 2025 Inga Richter Seminar Series

**Urko del Castillo, PhD**  
**Department of Pharmacology**  
**Weill Cornell Medicine**



**Unconventional Strategies to Inactivate Oncogenic Receptor  
Tyrosine Kinase Fusions**

**Research Summary:** My research focuses on developing innovative therapeutic strategies to overcome drug resistance in receptor tyrosine kinase (RTK) fusion-driven cancers, which represent critical oncogenic drivers across multiple malignancies. By targeting the oligomerization domains of fusion proteins, which are essential structural elements that enable constitutive RTK activation through protein clustering, rather than the kinase domains where resistance mutations typically accumulate, we have demonstrated selective oncogenic inhibition. Our multidisciplinary approach integrates structural biology, protein engineering, and cancer therapeutics to systematically identify minimal peptide sequences that effectively interfere with the oligomerization of fusion proteins. This novel strategy addresses the clinical challenge faced by thousands of patients who develop resistance to conventional kinase inhibitors, offering new options for durable responses in ALK, RET, ROS1, and NTRK fusion-positive cancers.

**12:30pm, Monday, Sept. 15, 2025**  
**Hunter College 926HN**  
**Host: Andy Wolfe**