

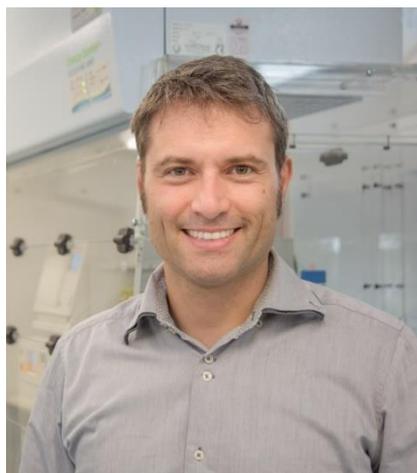
Lecture Title:

Targeted protein degradation with small molecules: How PROTACs work

Speaker:

Prof. Alessio Ciulli (University of Dundee, United Kingdom)

Abstract: Proteolysis-targeting chimeras (PROTACs) are a new class of chemical tools and drugs that target disease-causing proteins for degradation. PROTACs are designed to harness the cell's natural disposal system (the ubiquitin-proteasome) to specifically remove proteins. A PROTAC is a two-headed (i.e. bifunctional) molecule where one end binds an enzyme (an E3 ubiquitin ligase) and the other binds the target protein, bringing the two proteins into close proximity as a ternary complex. The ligase is then able to label the target protein for ubiquitination and so degradation by the cell's disposal system. Whereas conventional drugs only inhibit disease proteins by binding and locking up their most important functional parts for the duration of the drug's action, PROTACs can bind at any positions and rapidly cause the disease protein's permanent and long-lasting destruction. Due to this revolutionary mode of action, PROTACs can attack targets previously thought 'undruggable'. In this lecture, I will outline some key discoveries from my laboratory that have advanced the chemistry and structural biology of PROTACs, and are providing fundamental insights into our understanding of their mechanism of action and design.



Alessio Ciulli holds the Personal Chair of Chemical and Structural Biology at the School of Life Sciences, University of Dundee. His laboratory focuses on developing small molecules inducing protein degradation and targeting protein-protein interactions (PPIs). His group's significant discoveries jump-started the PROTAC field and led to significant commercial impact across academia and biopharma worldwide. He is the scientific founder of Amphista therapeutics, a company that develops new protein degradation platforms. Alessio graduated in Chemistry from his hometown Florence, Italy (2002) and obtained a PhD in Chemical Biology from Cambridge, UK (2006). Following post-doctoral research at Cambridge, and a brief visit at Yale University, he returned to Cambridge in 2009 to start his independent career. In 2013 Alessio moved his

laboratory to Dundee and was promoted to Full Professor in 2016. He is a Fellow of the Royal Society of Chemistry and recipient of several prestigious awards.