

Institute for Life Sciences Seminar

Prof Julian Downward, Francis Crick Institute

Date: Tuesday 13 October 2015, 16:00

Venue: Building 85, Room 2207



“Mechanisms of transformation by RAS oncogenes: searching for novel therapeutic approaches”

Despite RAS proteins being exceptionally well-validated cancer targets, little progress has been made in targeting them in the clinic. Recently there has been renewed interest in direct targeting of RAS proteins, which were for a long time considered undruggable. I will discuss developing work on this in my laboratory, and also the combination targeting of downstream effectors of RAS, such as RAF protein kinases and type I phosphoinositide 3-kinases (PI3Ks). Another means of targeting this critical oncogene is the identification of unique dependencies of RAS mutant tumor cells through the use of functional genomic screens - a synthetic lethal approach. Several KRAS synthetic lethal screens have been carried out by my group and others, with the one constant feature emerging across multiple screens being the proteasome, suggesting that it would be worth re-examining proteasome inhibition in KRAS mutant tumours. In addition to the above approaches to targeting RAS mutant cancers, there is also increasing interest in how best to combine such therapies with immune checkpoint regulation. I will discuss mechanisms whereby RAS signaling pathways can promote local immune suppression in the tumour, and also the finding that the genetically engineered mouse models used to study RAS mutant cancers are poor models for the interaction of the immune system with the tumour.

All welcome, refreshments available at the start of the seminar