

P035 Image-based screening to characterise cell-signaling networks responsible for retinoblastoma protein activation in response to ionising radiation.

**Elizabeth Runnacles¹, Sibylle Mittnacht¹,
Simon Stockwell¹, Wynne Aherne²**

*¹The Institute of Cancer Research, 237 Fulham Road,
London, SW17 9LN*

*²The Institute of Cancer Research, 15 Cotswold Rd,
Belmont, Sutton, Surrey, SM2 5NG*

In its active, hypophosphorylated state, retinoblastoma protein (Rb) can repress transcription and halt the cell cycle. Current knowledge suggests that stress, such as ionizing radiation (IR), could activate Rb in tumor cells and cause a delay in the cell cycle, promoting the survival of tumor cells. The cell-signaling networks responsible for stress-mediated Rb activation are yet to be accurately identified and the aim of this project is to develop a high-throughput siRNA screen to characterize them.

I have developed and completed an siRNA screen of the Dharmacon human kinome set of 779 kinases, putative kinases, small G-proteins and other signaling proteins, using indirect fluorescence detected by a high-content single cell imaging platform. 41/779 targets scored in the primary screen, eight of which reconfirm using two or more oligonucleotides. Follow-up signaling experiments with these hits suggest the possibility of multiple mechanisms of stress-based Rb regulation.