Investigating signal transduction with Multicolour Single Particle Tracking

The Epidermal Growth Factor Receptor (EGFR) family of cell surface receptors transduce a signal across the plasma membrane in response to binding of small peptide signalling molecules. Depending on the family members involved and the cellular context, signalling leads to diverse outcomes ranging from differentiation and growth to programmed cell death. Aberrant signalling by the four EGFR family members has been implicated in the development of many solid human cancers and they are the target of numerous novel cancer therapies. Unfortunately these therapies often lose their effectiveness within months of treatment commencing as the complicated interplay between the four receptors adapts to bypass the targeted family member and aberrant signalling resumes.

Challenge

The signalling mechanism of the four receptors has been previously studied individually or in pairs and a large emphasis has been placed on biochemical and high-resolution structural studies of soluble and crystallised receptors. Information about the dynamic interactions between the different types of receptor on the surface of a live cancer cell under normal conditions or when dosed with anti-cancer drugs is required to begin to understand how treatments can be improved.

Solution

Researchers from a consortium of institutions (STFC, King's College London, University of Cambridge and the University of Oxford) used Multicolour Single Particle Tracking of fluorescently labelled EGFR family members to build up a picture of receptor behaviour in a model cell line before determining the changes introduced by small molecule inhibitors of the receptors.