The role of c-Met endosomal signalling in cancer

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The receptor tyrosine kinase c-Met is overexpressed in 20-80% of cancers with the level of expression correlating with metastasis and poor prognosis. We have shown that upon activation, c-Met rapidly internalizes. However c-Met continues to signal inside the cells on endosomes. Moreover c-Met endocytosis is an important aspect of its oncogenic properties. Thus we reported that c-Met mutants found in cancer patients are oncogenic not only because they are highly activated but also because they signal on endosomes. We have shown that c-Met signalling from a late endosome triggers breast cancer cell migration. We discovered that beta1-integrin and c-Met co-traffic through a novel "Autophagy Related Endomembrane (ARE)". From there, the integrin plays the non-adhesive role of a scaffold to sustain c-Met signalling. This leads to cell survival in anoikis and metastasis. Thus we hypothesise that c-Met intracellular localisation and signalling play major roles in cancer progression. A better understanding of the molecular biology of intracellular c-Met may lead to improved cancer treatment as well as improved biomarker to select the patients who would respond to c-Met targeted therapy.

Speaker Biography

Stephanie Kermorgant completed her PhD with Thérèse Lehy at the French National Institute of Health and Medicine (INSERM) and Paris VII University, France, in 1999. Between 2000 and 2005, She performed postdoctoral studies with Professor Peter J Parker at the Cancer Research UK London Research Institute. She joined the Centre for Tumour Biology at the Barts Cancer Institute in May 2005, as a Lecturer. Thanks to a "Medical Research Council New Investigator Award" and funding from the "Barts and the London Charitable Foundation", she set up her research group "Spatial Signalling", which is investigating the role of growth factor receptor signalling and trafficking in tumour metastasis.

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