

The Institute of Cancer Research  
Clinical Fellowship Studentship Project Proposal 2011/12

<b>PROJECT PROPOSAL</b>	
Project Title:	<b>Analysis of how chemo- and radiotherapy affects cancer associated fibroblasts: implications for recurrence and resistance</b>
<b>SUPERVISORY TEAM</b>	
Primary Supervisor 1:	Kevin Harrington – ICR
Primary Supervisor 2:	Erik Sahai - LRI
Contact person for the project:	Kevin Harrington – ICR, Erik Sahai - LRI
<b>DIVISION/TEAM DETAILS</b>	
Division 1:	ICR Division of Radiotherapy and Imaging
Team 1:	<b>Targeted Therapy Team</b>
Division 2:	London Research Institute
Team 2:	Tumour Cell Biology Team
<b>PRE-REQUISITE QUALIFICATIONS OF APPLICANTS</b>	Applicants must have General Medical Council registration, or be eligible for GMC registration. They should have completed general professional training (and have MRCP or equivalent). Candidates should have acquired some experience in Oncology and normally should not be more than 10 years from the date of their first medical qualification.

<b>SUMMARY OF PROPOSED PROJECT</b>	
<p>It is now appreciated that tumours contain many cell types in addition to cancer cells. These stromal cells can profoundly affect disease outcomes. This project will build on extensive functional and genomic analyses of cancer associated fibroblasts from mouse models. These analyses have revealed two findings of significant potential clinical relevance. First, genomic analysis suggests that radiation therapy may increase the pro-tumorigenic capacity of CAFs. Thus, although the treatment may kill the cancer cells it could simultaneously be generating a more tumorigenic environment for cancer cells that are not effectively killed. Second, many of the genes expressed by CAFs have been implicated in resistance to chemotherapy. Thus, CAFs may represent a source of chemo-resistance.</p> <p>Biopsies of oral SCC will be collected before and after chemo- radiotherapy. Cancer-associated fibroblasts will be isolated and tested for their ability to promote cancer cell invasion, proliferation, survival and drug resistance. In particular, we will</p>	

investigate whether the properties of cancer associated fibroblast change as a result of therapy. These analyses will be combined testing novel targeted therapies (mainly kinase inhibitors) for their ability to modulate cancer associated fibroblast function. We believe that insights into both of these issues will translate into improve treatment possibilities in the long term.