Targeting redox homeostasis in cancer.

Dr Stewart Martin, Associate Professor and Reader in Cancer and Radiation Biology

The efficacy of a variety of cancer therapies is primarily mediated via the production of reactive oxygen species (ROS) and free radicals, that leads to increased oxidative stress, lipid and protein peroxidation, DNA damage and cell death. Redox buffering systems are often deregulated in cancer cells and can interfere with the effectiveness of ROS generated by conventional therapies. A number of studies have shown, in vitro, that modulation of redox homeostasis can alter the response of cancer cells to radiation and chemotherapy. The regulation of redox homeostasis is complex with a number of pathways being interlinked. We have an established track history of examining the role of redox proteins in cancer and have focussed our attention on members of the thioredoxin (Trx) and Glutathione (GSH) family of proteins. We have developed expertise using novel in vitro 3D systems to A) model phenotypic differences in breast cancer, B) develop models that replicate redox patterns observed in clinical specimens, and C) modulate redox protein expression to observe how this affects radio- and chemo-response.

This project will seek to address our hypothesis that Trx family protein expression regulates radiation and chemotherapy response in breast cancer, that levels of different members vary between different breast cancer phenotypes and that this contributes to the different response rates observed clinically. We further hypothesize that the radioresponse of different breast cancer phenotypes can be differentially modulated using agents that modulate the Trx and GSH expression and/or activity. Experiments using novel redox homeostasis modulators, provided via collaborations with researchers based in the School of Chemistry, will be expanded to investigate efficacy in Pancreatic cancer models (single agent and drug-radiation interactions). A variety of histopathology, cell and molecular biology and biochemical assays will be used through the course of the PhD.

Please **email a CV with a covering letter** to Dr Stewart Martin (stewart.martin@nottingham.ac.uk), who can also supply more information to interested parties.