**Precision medicine for melanoma: are we there yet?**

Richard Marais PhD, Cancer Research UK Manchester Institute, The University of Manchester, UK

There have been remarkable advances in the treatment of malignant melanoma over the last 5-10 years, driven by increased knowledge of the biology of melanoma cells and improved understanding the immune system. Immune checkpoint inhibitors activate the patient’s own immune system to kill cancer cells, revolutionary drugs that mediate remarkable responses in 40-60% of patients, and in some even achieving cures. However, not all patients respond to these drugs and we still do not know how to select patients for specific immune checkpoint drugs. In parallel, drugs that target the BRAF-MEK signalling pathway are very effective in the ~50% of melanoma patients whose tumours carry mutations in BRAF. However, most patients eventually develop resistance to these drugs and fail treatment after a relatively short period of disease control. Thus, although there has been a paradigm shift in the treatment of malignant melanoma over the last decade, most patients still die of their disease and several clinical challenges remain. We do not know how to select patients for immunotherapies, or which specific immunotherapies will be most effective in individual patients. We also do not know how to combine or schedule targeted and immunotherapies, and our knowledge of when to switch patients from one treatment modality to another is still rudimentary. For many patients, effective second and third-line treatments are still largely lacking. Our group is developing new protocols for melanoma precision medicine driven by close interactions between basic scientists and clinicians. We use next generation sequencing to reveal the genetic landscape of tumours and identify actionable target in individual tumours. Patient-derived xenografts (PDX) are used to validate hypothesis-driven treatments and to inform clinical trial development. Moreover, to monitor patient responses to specific treatments and to reveal the emergence of resistance we are developing circulating cell-free tumour DNA (ctDNA) as a minimally-invasive biomarker. We are also developing this technology to direct decisions about when to switch patients from one treatment to another. In essence, we aim to use our basic research discoveries to guide clinical decisions, and conversely we use our experience of patient responses to ensure that our basic science addresses the most pressing clinical question and challenges, with the ultimate aim of improving outcomes for patients.