KIM Dae EOI 2022 - ICR

Project title: Understanding Role of Tumour Heterogeneity and Evolution in treatment resistance in Aggressive Thyroid Cancers: utility of circulating free tumour DNA (ctDNA).

Project Summary:

Medullary (MTC) and Anaplastic thyroid carcinomas (ATC) are uncommon but aggressive forms of thyroid cancer which usually present with locally advanced and metastatic disease, with few treatment options. Metastatic disease is the major cause of mortality. Response to systemic treatment is highly variable within and between patients, and overall poor. Intra-Tumour heterogeneity (ITH) provides the substrate for tumour evolution and is increasingly recognised as a major cause of treatment resistance and hurdle to improvements in therapeutic outcome. With the ever-increasing number of new therapy options, a better understanding of the critical genetic changes will enable 'ultra-precision' personalised treatment in MTC & ATC by guiding both the optimal timing and sequencing of these agents.

Research Aims:

1. Through multi-region tumour sampling and NGS, we aim to define the genomic landscape and the impact of ITH upon therapeutic and survival outcome. Clonal/subclonal mapping (using mathematical machine-learning modelling) may help stratify for optimal drug choice (Primary resistance). Deep-sequencing of matched serial & blood tumour samples will assess temporal dynamics of cancer subclones that emerge during treatment may reveal basis of secondary resistance development.
2. We will evaluate the utility of ctDNA in blood, as a non-invasive method, in demonstrating the tumour genetic profile, its heterogeneity and as a rapid biomarker of treatment response. Further, there is a need for a method to genotype metastatic disease and overcome difficulty in serial-sampling multiple tumour deposits, often at inaccessible sites. ctDNA offers means to profile all sites simultaneously and monitor their individual response to treatment.
3. We aim to develop an organoid biobank of aggressive thyroid cancers to accelerate drug discovery and novel 3-D cancer models (tumour slice clusters and xenographs) to study tumour evolution during therapy. These activities will form the foundation for a co-clinical trial using patient 'avatars' to deliver personalized therapeutics in MTC/ATC.

Supervisory Team:

- Prof Dae Kim, Institute of Cancer Research and Royal Marsden
- Dr Kate Newbold, Institute of Cancer Research and Royal Marsden
- Dr Rob Hynds, Francis Crick Institute
- Prof Kevin Harrington, Institute of Cancer Research

Clinical Specialities: Oncology & Otolaryngology