

GERLINGER Marco EOI 2022 – ICR

Project title: T-cell phenotypes and dynamics in gastro-oesophageal cancer immunotherapy

Project Summary:

Immunotherapy with checkpoint inhibitors is revolutionising the treatment of gastro-oesophageal adenocarcinomas (GOA). Recognition and killing of cancer cells by CD8 T-cells is the main effector mechanism triggered by checkpoint inhibitors. Despite clinical successes, it remains unknown what tumour antigens are recognized by T-cells and how the presence of tumour specific T-cells can be detected in patients. As a consequence, predictive biomarkers are lacking.

This PhD project will build on our unique biobank of patient-derived cancer organoid cultures and T-cells from PD-L1 checkpoint inhibitor trials in GOA to define the frequency of tumour specific T-cell, their phenotypes and antigen specificities. Autologous T-cells will be analysed by FACS, in organoid recognition assays and by T-cell receptor sequencing. MHC presented neoantigens will be identified by mass spectrometry immunopeptidomics in cancer organoids. Integrating these data with radiological response and survival information will define how T-cell phenotypes and their dynamics during treatment can predict responses and support the development of biomarkers for immunotherapy stratification. Defining the neoantigen landscape of GOAs and how these impact checkpoint-inhibitor responses will inform novel immunotherapy strategies, for example with neoantigen vaccines.

We are looking for enthusiastic individuals with a strong interest in immuno-oncology. The host laboratory is led by Dr Gerlinger who is a Medical Oncologist and Clinician Scientist. It employs biologists, immunologists, oncologists, pathologists and bioinformaticians focusing to understand mechanisms of immunotherapy response and resistance in GI cancers in order to develop the next generation of immunotherapies.

Supervisory Team:

- Dr Marco Gerlinger, Molecular Pathology, Institute of Cancer Research
- Prof Jyoti Choudhary, Institute of Cancer Research

Clinical Specialities: Medical or Clinical Oncology and pathology