CANCER RESEARCH UK CLINICAL ACADEMIC TRAINING PROGRAMME

ICR The Institute of Cancer Research | Imperial College London

KUMAR Sacheen EOI 2022 – ICR

Project title: Investigation of Immune and Microbiome Disruption as drivers of mutagenic pathways in Oesophago-Gastric Cancer

Project Summary:

Background: Oesophago-gastric (OG) cancer represents one of the cancers with the fastest rising incidence in Western populations with 5-year overall survival of 15.1%. Endoscopy-based screening programmes are not justified in the UK given low incidence of significant pathology and associated healthcare costs. Hence, there is a critical need to develop novel diagnostic techniques and improve our understanding of the underlying mutagenic mechanisms in OG adenocarcinoma. OG cancer is characterized by early breakdown of local protective barriers, immune disruption and consequent alterations in mucin composition and the microbiome.

Hypothesis: Mucosal disruption in early OG cancer induces perturbations in immune pathways leading to alterations in mucus profile and the upper GI microbiota. Characterization of these components will reveal novel early diagnostic biomarkers for early detection of potentially curative disease.

Experimental approach: This project will utilize biological samples from subjects with biopsy-confirmed OG cancer in comparison to subjects with benign disease to allow a detailed evaluation of the immune/microbial changes that drive the neoplastic process. We will initially use unbiased approaches to evaluate the transcriptome, proteome and microbiome in these samples with bioinformatic multi-modal systems biology methods to study interactions between these datasets and elucidate aberrant pathways. Pathways of interest will then be interrogated using established assays to quantify immune mediators (qPCR/ELISA/Western blot), commensal bacteria (genus/phylum-specific qPCR), and mucins (ELISA/mass spectrometry).

The project will combine cutting-edge techniques in immunology, cancer biology and molecular microbiology with access to unique longitudinal human disease samples and thus provide comprehensive research training. The long-term translational aim of this research programme is to develop a non-invasive diagnostic test to allow for risk-stratification of patients with non-specific Upper GI symptoms and increase the pickup rate for OG cancer.

Supervisory Team:

- Mr. Sacheen Kumar, Division of Radiotherapy & Imaging, Institute of Cancer Research
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Clinical Specialities: RMH GI Unit