

Project Title

Development of a deep learning-based approach to characterize the immune landscape in liver cancer

About This PhD Project

Institute of Cancer Research

Supervised by Dr Nadia Guerra, Dr Yinyin Yuan and Dr David Pinato

The student will be registered at Imperial College, leading to the award of a PhD from Imperial College, London

Project Description

Liver cancer, worldwide, is the third leading cause of cancer mortality. Most of the primary liver cancers are hepatocellular carcinoma (HCC). In the past 10 years, increased prevalence of obesity and type II diabetes led to an acceleration of HCC in the UK which is projected to rise by 38% in the next 20 years¹. Advanced stage HCC are aggressive with a poor long-term prognosis - up to 70% of patients relapse within 5-year post surgery mainly due to persistent inflammation. While recent studies have provided an in-depth characterization of the immune landscape in lung and colorectal cancer, HCC is understudied and the role of human natural killer (NK) cells – particularly abundant in the liver tissue where they represent 30-50% of resident lymphocytes- is not fully understood.

NK cells are innate immune cells increasingly recognized for their potent anti-tumour function and multiple advantages as immunotherapeutic tool. However, several preclinical studies have evidenced that bona fide anti-tumour effectors such as NK cells and also NKT and CD8+T cells can promote tumour growth in causing tissue damage that drives tumorigenesis in this type of cancer. This paradoxical role highlights our lack of mechanistic understanding of this typical model of cancer driven by chronic inflammation, delaying the testing of a panel of IO approaches currently trialled against other types of cancer.

Thus far, we are limited by current approaches to study the relationship between inflammation, tumour molecular alterations and progression in human tumours in general and HCC in particular. It is becoming increasingly evident that we need to develop novel, spatially explicit computational and experimental approaches to study the complex cancer-immune interactions.

The aim of this project is to apply deep learning methods to analyse digital pathological images, map the spatial distribution of key effector cells and infer spatial patterns in both the tumour microenvironment (TME) and NTME; and integrate such spatial phenotypic data with transcriptomics data in HCC. This will be done using datasets from both human and translational mouse models of HCC in the following 3 steps:

1. Characterise the spatial organisation of NK and T cells in preclinical models of HCC on the immune landscape.
2. Relate the lymphocyte spatial patterns from mouse model to those in human HCC
3. Test how image-based lymphocyte spatial patterns are associated with the expression of key receptor/ligands pathways with HCC patient's overall survival

This is a highly multidisciplinary project linking cancer immunology with bioinformatics through the integration of digital pathology, genomics and machine learning.

Keywords /Subject Areas

Tumour Immunology
Deep learning
Mouse models
Nk cells and T effector cells
Bioinformatics
Liver cancer

Candidate profile

Candidates must have a first class or upper second class honours BSc Honours/MSc in Life Science, Chemistry, Computer Science, Mathematics, Physics or a degree relevant to the post.

How to apply

Full details about these studentship projects, and the online application form, are available on our website, at: www.icr.ac.uk/phds Applications for all projects should be made online <https://apply.icr.ac.uk/> . Please ensure that you read and follow the application instructions carefully.