PhD Project Proposal

Funder details	
Studentship funded by:	Cancer Research UK Convergence Science Centre

Project details	
Project title:	Morphological phenotyping of the ccRCC TME using Deep Learning and Morphometrics

Supervisory team	
Primary Supervisor:	Prof. Samra Turajilic
Associate Supervisor(s):	Prof. James Larkin
Secondary Supervisor:	Dr. Guang Yang

Divisional affiliation	
Primary Division:	Division of Clinical Studies
Primary Team:	Melanoma and Kidney Cancer Team
Primary Location:	Sutton

Project background

Histopathology is the foundation of cancer diagnostics and histopathologists are tasked with diagnosing various histological tumour subtypes by examining haematoxylin & eosin (H&E) stained tissue sections, relying on morphology to accurately classify cells within the tumour microenvironment (TME). In clear cell renal cell carcinoma (ccRCC), the most common and aggressive form of kidney cancer, the histological features are profoundly varied between and within tumours. Despite this complexity, clinical decision-making in ccRCC is based on limited features including tumour grade and the presence of necrosis, neglecting numerous other features where prognostic significance has been suggested. One such prognostic histological feature is the composition of cell types within the TME which to date can only be achieved by using costly techniques such as multiplexed fluorescence microscopy which can cost more than £1000 per slice. Coupled with the advances in deep learning we hope to leverage foundational computer vision models to automate this process by analysing morphological and textural features of individual cells to determine their phenotype.

Project aims

- Create a computational pipeline that can accurately phenotype cells in ccRCC tissue sections at single-cell resolution using both textural and morphological features extracted from H&E whole slide images (WSIs).
- Define a set of descriptors that encapsulate the unique characteristics of each cell type by combining textural and morphological features, enabling more accurate cell classification and phenotyping.
- Deploy this pipeline in the TRACERx Renal cohort to understand the morphological features and TME composition associated with ccRCC aggressive disease behaviour and acquisition of metastatic competence.

- Explore the link between histological features and genomic data, allowing for a deeper understanding of the tissue phenotype associated with genetic features at a single-cell level.

Research proposal

The major aim of the PhD will be to develop a pipeline to accurately phenotype cells in situ at single-cell resolution using only H&E biopsy slides. To achieve this a foundational computer vision model will be used to extract the textural features of each cell whilst a morphometric algorithm will be used for the extraction of morphological features. By concatenating textural and morphological features a set of descriptors will be defined that encapsulate the unique characteristics of each cell type. A machine learning model will subsequently be trained to phenotype each cell based on the concatenated textural and morphological features. This model will then be applied to the TRACERx Renal cohort, comprising of 1600 tumour regions from 100 ex-vivo sampled ccRCC tumours with H&E WSIs demonstrating the largest spatially resolved single-cell analysis of any cancer type to date. With each H&E WSI we have paired specially resolved histopathological annotations including tumour grade, architecture and cytology, understanding the morphological and textural features associated with each of these categories would facilitate interpretability of the pipeline whilst also creating a description of features associated with tumour grade thus forming the basis of an automated grading system.

The timeline of the project will be as follows:

- Year 1: Refinement of morphometric algorithm and cell texture foundation model for extraction of cell features.
- Year 2: Creation of an algorithm for the accurate classification of cells based on morphological and textural cell features of each cell.
- Year 3: Translation of collective morphological and textural features with coupled single-cell classifications to whole slide image biomarkers to correlate with disease progression.
  Year 4: Creation of user interface which takes as input a H&E WSI and outputs statistics on disease progression and thesis writeup.

Literature references

1. Valentyna Zinchenko, Johannes Hugger, Virginie Uhlmann, Detlev Arendt, Anna Kreshuk (2023) MorphoFeatures for unsupervised exploration of cell types, tissues, and organs in volume electron microscopy eLife 12:e80918
2. Alexey Dosovitskiy, Lucas Beyer, Alexander Kolesnikov, Dirk Weissenborn, Xiaohua Zhai, Thomas Unterthiner, Mostafa Dehghani, Matthias Minderer, Georg Heigold, Sylvain Gelly, Jakob Uszkoreit, and Neil Houlsby. (2021). An Image is Worth 16x16 Words: Transformers for Image Recognition at Scale.
3. Mathilde Caron, Hugo Touvron, Ishan Misra, Hervé Jégou, Julien Mairal, Piotr Bojanowski, and Armand Joulin. (2021). Emerging Properties in Self-Supervised Vision Transformers.
4. Chen, R.J. et al. (2022) 'Scaling vision transformers to gigapixel images via hierarchical self-supervised learning', 2022 IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR) [Preprint]. doi:10.1109/cvpr52688.2022.01567.

Candidate profile

Note: the ICR's standard minimum entry requirement is a relevant undergraduate Honours degree (First or 2:1).

Pre-requisite qualifications of applicants:

B.Sc. in computer science or mathematics
Experience in data and image analysis

Intended learning outcomes:

- Foundational understanding of cancer biology.
- Understanding of histopathology and the key role it plays in cancer diagnostics.

- Proficiency in computational pathology and its use within clinic.
  Confidence in the use of machine learning and artificial intelligence for biomedical image analysis.

Advertising details

Project suitable for a student with a background in:

- ☐ Biological Sciences
- ☐ Physics or Engineering
- ☐ Chemistry
- ☒ Maths, Statistics or Epidemiology
- ☒ Computer Science