

Developing a digital pathology approach to predicting response to immunotherapy for lung cancer using samples from a large UK phase III clinical study

Supervisor(s):

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Project description:

Our group works on cancer immunology and high dimensional approaches to interrogating this, including digital pathology. Using routine pathology images from patients with lung cancer treated with a drug that activates the immune system, we will apply digital pathology techniques to develop a novel approach to predicting who will benefit from treatment. Samples and clinical data come from the REFINE-Lung study that we are running. Collaborators include Dr. Khalid AbdulJabbar (ICR) and Dr. Shan Raza (Warwick).

Aim 1: Adapt existing computational pipelines for pathology image analysis to lung cancer samples from patients on the REFINE-Lung clinical trial. The steps include - data preprocessing/normalisation, tissue segmentation, cell segmentation and classification. We will adapt existing deep learning approaches including U-Net and HoVer-Net.

Aim 2: To characterise the spatial relationship between immune cells and cancer cells to extract features that may predict patient response and to test this. We will use statistical approaches and concepts from the field of ecology.

Aim 3: To determine whether immune cell morphology can be used to identify cell state as a further predictor of immunotherapy outcome. Typically, immune cells are identified in routine H&E stained images as belonging to one of 3 broad classes (lymphocytes, neutrophils, macrophages). We hypothesise that within these classes, the activation state of the cell can further be identified based on morphological differences. We will approach this by staining the section with antibodies that identify cell states and register these images with the H&E images that reveal morphology in order to train a cell state classifiers.

Timeline (tentative):

Aim 1: aim to complete by Feb 2025

Aim 2: By April 2025

Aim 3: By July 2025

Minimum viable thesis:

A minimal thesis would involve using an existing toolkit (TIAToolbox) to carry out tissue analysis on cancer images followed by extraction of some simple features such as immune cell content to determine whether these are different between patients who response or do not respond to treatment.

Required background & skills:

A background in python programming and ML/DL approaches

Representative References:

<https://www.nature.com/articles/s43856-022-00186-5>

A recently published toolkit for computational pathology analysis.

<https://www.nature.com/articles/s41591-020-0900-x>

A paper on lung cancer digital pathology analysis and features that predict patient outcomes.

[https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045\(23\)00095-5/fulltext](https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(23)00095-5/fulltext)

A paper describing the REFINE-Lung study that provides samples for this analysis.