Project title: Delineating Immune Signalling in Solid Tumours via Integrative Data Science

Project reference: DT4H_09_2024

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Aim of the Project

Comprehensive computational modelling and data integration pipelines to delineate immune features in tumours such as the skin cancer, melanoma, are lacking. Despite the success of immunotherapy, immune responses vary, and no prognostic or predictive tools are available. This project aims to dissect the immune cell types, cell dynamics, signalling profiles and cellular interactions in the tumour microenvironment and are indicative of patient prognosis and response to therapy. Through assembling a large collection of transcriptomics data at single-cell resolution and integrating with resources on signalling pathways and ex vivo cultures of immune cells from patients with cancer, we will develop models of molecular signatures and signalling pathways involved in immune cell activation and differentiation in the cancer context. The nature of this project will be multidisciplinary, drawing from advanced ML/AI methods for data representation and predictive inference, as well as addressing the data domain relevant to cancer immunology and immunotherapy.

Project Description

Understanding of mechanisms underlying disease and discovery of remedial treatments are dependent on efficient computational data representation and accurate data-driven inference. The recent availability of molecular profiling at single-cell and spatial resolution is revolutionising data mining approaches in cancer and allows dissection of complex immune responses. However, challenges still exist in successful integration and representation of diverse datasets, as well as accurate predictive modelling of disease state or individualised treatment.

Novel computational modelling pipelines to delineate immune features are urgently required in the study of solid tumours such as melanoma, the 5th most common cancer in the UK and the most aggressive skin cancer (>16,700 cases each year, 2,500 UK deaths/year). The incidence of melanoma has increased by 140% since the 1990s and is projected to rise to ~26,500 cases in 2038-2040. Despite representing the archetypal immunogenic tumour, the immune responses and pathways stimulated in patients with melanoma highly vary. Alongside, the rate of cancer progression and spread varies widely between patients, but approximately half of those with stage III disease experience distant metastases, associated with poor 5-year survival (ranging from 5-20%). Presently there are no predictive tools for patient outcomes. Furthermore, there is insufficient understanding of how clinical course is linked to immune features in melanoma. The development of AI/computational tools to understand disease course and develop accurate data-driven inference prediction algorithms are required and can significantly improve monitoring and clinical management of this aggressive disease.

Immunotherapy in the form of checkpoint inhibitor (CPI) antibodies designed to activate T cell functions, have revolutionised treatment. Yet, despite their clinical success, more than half patients do not derive long term benefit from these drugs. There is therefore an unmet need to identify immune cellular, molecular and signalling pathway signatures which can be employed to predict and monitor therapy and treatment response.

This project aims to leverage data representation and inference related to digital twin concepts to delineate immune cell responses and signalling pathways in patients with solid tumours. The outcome of the project will be enhanced understanding of the contribution of specific immune cell types, immune cell interactions in cancer progression, treatment response including response to immunotherapy, and will be directly applicable to the development of novel therapies.

Requirements:

The student will be expected to have a computational background in Computer Science or related discipline. S/he will be trained in multidisciplinary science, including advanced topics of Data Science and AI/ML, as well as cancer immunology.

Suggested reading:

Amiri Souri et al., Br J Cancer. 2021, PMID: 34131308; Chauhan et al., Nat Commun. 2023, PMID: 37291228; Harris et al., Cancer Res, 2021, PMID: 34224371.