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New T Cell Subset Associated With Survival In Non-Small Cell Lung Cancer Identified with Hi-Plex Spatial Proteomics

Claire Marceaux[1,2,4], Kenta Yokote[1], Ilariya Tarasova[3,5], Daniel Batey[1], Reema Jain[1,4], Velimir Gayevskiy[1], Marina Leiwe[1,4], Laurie Choux[1], Lucy Riley[1], Nina Tubau Ribera[2], Jack Hywood[7], Michael Christie[7], Phillip Antippa[6,7], Terence P Speed[3,5], Kelly L. Rogers[2,4], Belinda Phipson[3,5], and Marie-Liesse Asselin-Labat[1,4*]

[1] Personalised Oncology Division, The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia
[2] Advanced Technology and Biology Division, The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia
[3] Bioinformatics Division, The Walter and Eliza Hall Institute of Medical Research, Parkville, Australia
[4] Department of Medical Biology, The University of Melbourne, Parkville, Australia
[5] School of Mathematics and Statistics, The University of Melbourne, Parkville, Australia
[6] Department of Surgery, The University of Melbourne, Parkville, Australia
[7] The Royal Melbourne Hospital, Parkville, Australia
*** Corresponding author: labat@wehi.edu.au**

Claire Marceaux ORCID iD's - https://orcid.org/0000-0002-9107-8772

Lung cancer remains the leading cause of cancer-related deaths worldwide. Surgical resection is the most suitable treatment for early-stage non-small cell lung cancer (NSCLC). However, recurrence is common [1,2]. Understanding the composition and spatial organization of the tumour immune microenvironment (TME) is crucial to explaining the diverse prognoses of lung cancer patients [3,4].

This study aims to correlate spatial characteristics of the immune microenvironment with patient outcomes to identify predictive biomarkers and suggest therapeutic strategies. We apply emerging methodologies on paraffin-embedded tissues: imaging-based single-cell spatial proteomics with the MIBI-TOF (Multiplexed Ion Beam Imaging) platform [5], which enables high-resolution, multiplex imaging of single-cells using heavy metal-conjugated antibodies detected by mass spectrometry; and whole transcriptome analysis of tumour cells using the Nanostring GeoMx Digital Spatial Profiling (DSP) technology [6].

Our 38-antibody MIBI panel explores immune cell infiltration in 94 NSCLC tissues with survival and smoking status data. Initial results reveal distinct TMEs between LUAD and LUSC, the two main NSCLC subtypes. Notably, neutrophil-enriched tumours are associated with worse survival. We also identified a new T cell subset, when accumulating in the tumour core, correlates with patient outcomes. We validated this subset using complementary techniques and are exploring its functional role through in vitro assays.

By integrating multi-omic approaches, we have characterized a novel T cell population associated with patient survival, offering new avenues for biomarker discovery and therapeutic intervention in NSCLC.

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