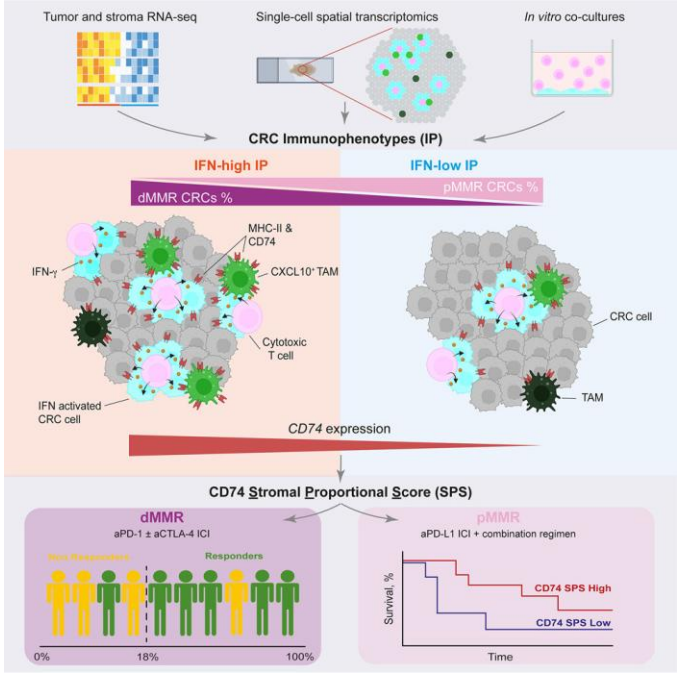
CD74 as a biomarker for responsiveness to cancer immunotherapy

Technology: An assay measuring CD74 (a chaperone protein that regulates class II antigen presentation to activate immune response) levels to predict whether someone with bowel cancer will respond to immunotherapy.



Colorectal cancers (CRCs) can be classified as interferon-high (IFN-high) or interferon-low (IFN-low) based on gene signatures. IFN-high CRCs, marked by T cell-induced CD74 expression in tumour-associated macrophages (TAMs) and cancer cells, are more responsive to immune checkpoint inhibition (ICI) therapy. CD74 levels predict clinical benefit in both deficient and proficient mismatch repair CRCs.

Unmet clinical need:

Anticancer therapy based on immune checkpoint inhibition (ICI) is one of main treatments for mismatch repair deficient (dMMR) metastatic colorectal cancer (mCRC).

Currently, tumour mutational burden (TMB) and programmed cell death ligand 1 (PD-L1) protein expression are used in the clinic as biomarkers of response to anti-PD1 ICI. However, approximately half of patients with high TMB dMMR mCRCs show no durable benefit and PD-L1 is not a marker of response in CRC. The unmet need is lack of effective biomarkers to stratify patients who will respond to ICI before initiating treatment.

Solution:

A biomarker assay based on CD74, which is expressed at high levels not only in dMMR CRCs responsive to ICI but also in a group of mismatch repair proficient (pMMR) CRCs responsive to ICI in combination with other agents.

Unique value:

The assay is both TBM and PD-L1 agnostic and is based on immunohistochemistry of a surface protein (CD74) expressed by cells in the tumour stroma. Thus, it shows high sensitivity, fast turnaround and low experimental complexity. Immunohistochemistry-based assays are routinely done in the pathology labs of any hospital with a variety of proteins with diagnostic or prognostic values.

Stage of development:

The data has been validated in both dMMR and pMMR bowel cancers from several international clinical trials demonstrating that patients who responded to ICI alone or in combination treatments had significantly higher levels of CD74 than those who did not respond. The work has been published on Cancer Cell in Jan 2025.

Clinical impact:

Approximately 85% of CRCs show proficient DNA mismatch repair. Immunotherapy has shown efficacy in only dMMR CRC patients and it is currently not used in the treatment of pMMR CRCs, although several trials are ongoing. Measuring CD74 levels could predict whether someone with bowel cancer will respond to ICI, independent of which type of CRC they have. Crucially, this means that some people with the proficient subtype, who are currently ineligible for immunotherapy, might benefit from this treatment.

Intellectual Property status:

Patent protecting the methodology and quantification of CD74 for predicting response to ICI is pending. PCT filed on 29 January 2025 (PCT/EP2025/052256): BIOMARKERS FOR IMMUNOTHERAPY RESPONSIVENESS IN COLORECTAL CANCER.

Commercial Strategy:

We look for potential commercial partners for co-development and/or licensing to translate this technology into a clinical assay.

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