Medical Xpress

Genetics research could revolutionize how bowel cancer is treated

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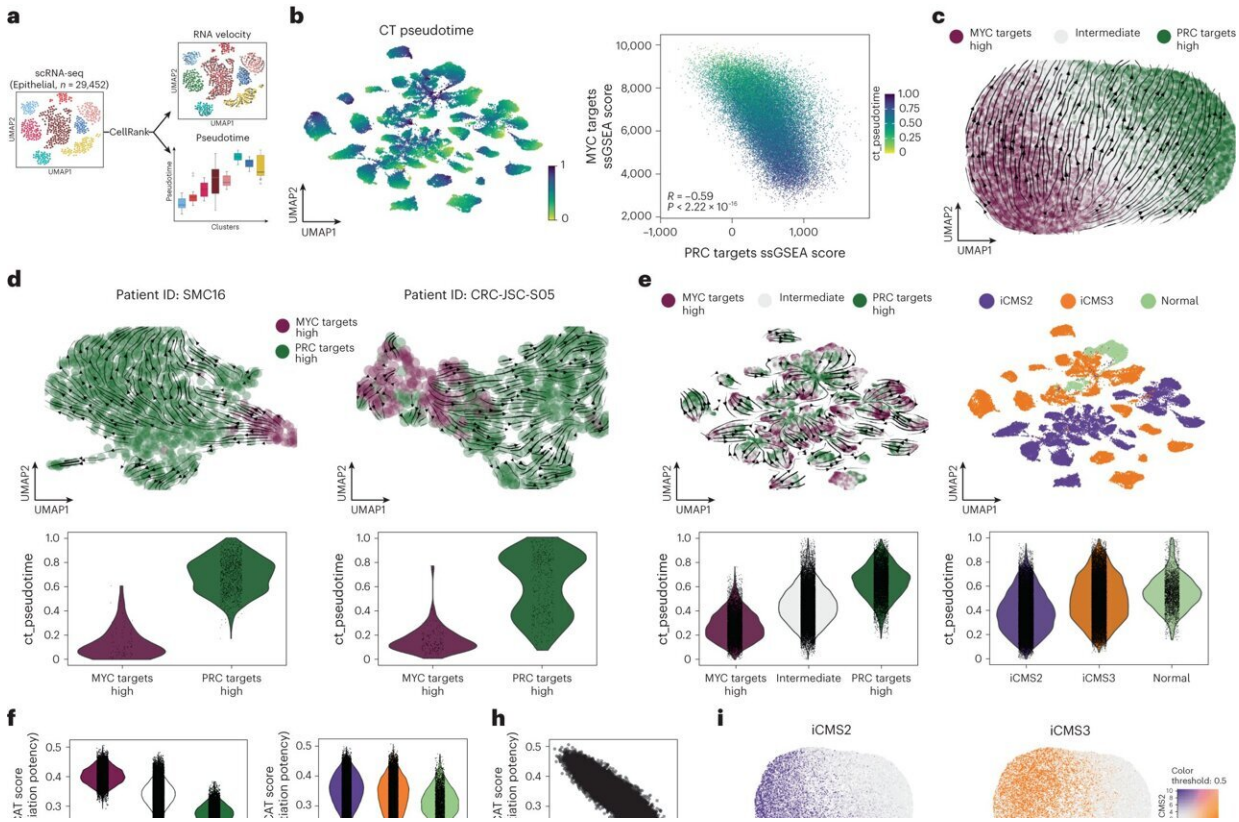

PDS3 differentiation-like trait relates to tumor biology unexplained by single-cell-derived iCMS. Credit: *Nature Genetics* (2024). DOI:10.1038/s41588-024-01654-5

New research led by a team of scientists from Queen's University Belfast and the Cancer Research UK (CRUK) Scotland Institute in Glasgow

have made a series of groundbreaking discoveries into tumor biology that may be used to deliver a more effective personalized medicine approach for patients with bowel (colorectal) cancer.

Bowel cancer is the fourth most common cancer in the UK, with around 42,900 new bowel cancer cases and around 16,600 bowel cancer deaths in the UK every year, a statistic that highlights the need for new ways to treat patients with this aggressive disease.

The new study published in *Nature Genetics*, used a unique and innovative approach developed in Belfast, to identify a set of previously unseen molecular patterns in tumor tissue that provides new information related to treatment response and risk of disease progression.

These remarkable results mean that clinicians and scientists can now draw more information from a patient's tumor tissue which may lead to better treatment options.

Previously, the most common approach for identifying groups of tumors based on their biological signaling, known as molecular subtyping, used information about how active individual genes are within tumor tissue.

The subtypes identified using this method have shaped understanding of cancer development, progression and response to therapy over the last decade and served as the basis for numerous clinical trials and pre-clinical studies.

Dr. Philip Dunne, Reader in Molecular Pathology from the Patrick G Johnston Center for Cancer Research at Queen's University Belfast and senior author of the study explains, "While looking at patterns across individual genes has revealed remarkable insights into cancer signaling, advances in laboratory research over the last decade have shown that assessing activity in groups of closely related genes in combination can

provide new understanding that isn't apparent when using the traditional single gene approaches."

Given the potential value of this new pathway approach, researchers from Queen's University Belfast, the CRUK Scotland Institute, University of Zurich, University of Oxford alongside a multinational collaborative group proposed a new data-driven method for reclassification of bowel cancer, which has been published in this new groundbreaking study.

By assembling genes into biological pathways prior to the development of molecular subtypes, the team rearranged tumors into a series of new groups, based on activity across a complex network of cancer-related signaling; all of which appears to be critical in predicting how well a tumor will respond to different treatments such as chemotherapy and radiotherapy.

To ensure that scientists and clinicians around the world can immediately access these data and test this new subtyping approach, the team have released a freely available classification tool that allows the Belfast-developed approach to be used on tumor samples in any research lab.

Dr. Sudhir Malla, Postdoctoral Research Fellow from the Patrick G Johnston Center for Cancer Research at Queen's University Belfast and first author of the study said, "By developing an unrestricted classification tool for the cancer research community, it means that researchers from around the world can reproduce our finding on data emerging from their own collections of tumor samples, to identify biological pathways that cancer cells switch on or off to control their movement, growth and response to their environment."

Professor Owen Sansom, Director of the Cancer Research UK Scotland Institute in Glasgow, who co-authored the study said, "The research

presented today in *Nature Genetics* exemplifies the value of collaborative research between scientists and clinicians. Studies such as this are essential to enable us to understand the complexities of a patient's tumor and will be used in our pre-clinical laboratories to identify novel treatments specifically targeting the biological patterns we have identified."

Dr. Sam Godfrey, Research Information Lead at Cancer Research UK, said, "Cancer is perhaps the most complex disease we face, and no single treatment will ever beat it."

"Research like this could lead to better and more precise treatments for the thousands of people diagnosed with bowel cancer every year in Scotland."

The team is now applying their new subtyping approach on tumor samples derived from clinical trials run in the UK, to build the essential clinical evidence needed before the new method can be used to make clinical decisions about which treatments a patient should be offered.

More information: Sudhir B. Malla et al, Pathway level subtyping identifies a slow-cycling biological phenotype associated with poor clinical outcomes in colorectal cancer, *Nature Genetics* (2024). DOI: 10.1038/s41588-024-01654-5

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