Novel Epigenetic Biomarkers and Targets for Metastatic Colorectal Cancer

RCSI UNIVERSITY OF MEDICINE AND HEALTH SCIENCES

Researchers at RCSI have developed a novel biomarker panel to identify patients with colorectal cancer who are at high risk of developing metastatic disease. The team are seeking industry partners to co-develop this predictive test and also to leverage the extensive epigenetic dataset to identify new drug targets in mCRC. Biomarker-led early intervention with directed therapies may help to improve outcomes for this high-risk group.

BACKGROUND

Colorectal cancer (CRC) accounts for the highest cancer associated deaths globally. While the survival rates of CRC patients with early stage disease is as high as 80%, overall survival for patients where cancer has spread to sites such as liver termed as metastatic colorectal cancer (mCRC) is drastically reduced to 20%. These low survival rates necessitate identification of novel diagnostic and therapeutic strategies that can allow better diagnosis and treatment of these mCRC patients.

Numerous studies in CRC and mCRC have reported that changes in DNA often impact disease progression and thus should be further investigated to establish their potential diagnostic/therapeutic role. One such change in DNA involves a chemical modification called “DNA methylation” which although does not change the structure of the DNA, albeit alters the information that the DNA codes for. This ultimately leads to aberrant switching on/off of genes that accelerate or stop tumour growth and progression.

Using a large cohort of mCRC patients, we for the first time, have identified >300 such sites in DNA extracted from these patients where tumour specific DNA methylation occur and are linked to genes that when turned on lead to disease progression. These sites demonstrate a high potential of predicting disease spread in CRC patients and in parallel can be further investigated as therapeutic targets.

VALUE PROPOSITION

The RCSI DNA methylation-based biomarker panel will be evaluated through clinical trials to develop a CE-IVD marked product for routine clinical use in CRC patients with the intent of identifying those patients most at risk of progression to mCRC. Biomarker-directed early intervention will help to improve outcomes for these high-risk patients.

In parallel, functional CRISPR validation of the genomic loci demonstrating a metastatic potential will enable commercial partners to develop novel therapies for mCRC targeting these specific epigenetic alterations.

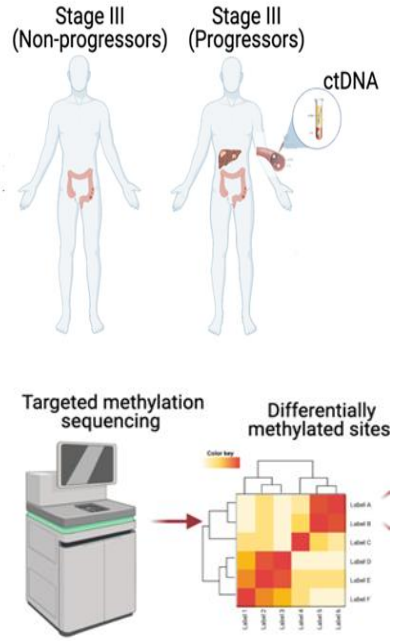

Fig 1. Progressors and non-progressors to mCRC display different epigenetic profiles in their tumour biopsies. Future work will also extend to epigenetic signatures in circulating tumour DNA.

FEATURES	BENEFITS
Novel Biomarker profile for mCRC	Improved patient outcomes with early intervention
Novel epigenetic targets for mCRC	Opportunity for new drug development

APPLICATIONS

- Biomarker Panel for asessing mCRC risk
- Novel drug targets
- Companion diagnostic

TECHNOLOGY READINESS LEVEL

- Patent Filed
- In Vitro proof of Concept

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