Proteome analyses in colorectal carcinoma reveal major protein alterations upon cancer development and metastasis

Qiujin Shen, Naveen Reddy Muppani, Alireza Azimi, Eva Freyhult, Ulf Landegren, Masood Kamali-Moghaddam
Uppsala University, Uppsala, Sweden

Facts & Figures

Start date:	01/01/2011
End date:	31/12/2016
Contributions	
IMI funding:	16 757 282€
EFPIA in kind:	10 976 557€
Other:	3 346 480€
Total Cost:	31 080 319€
Project website:	www.oncotrack.eu

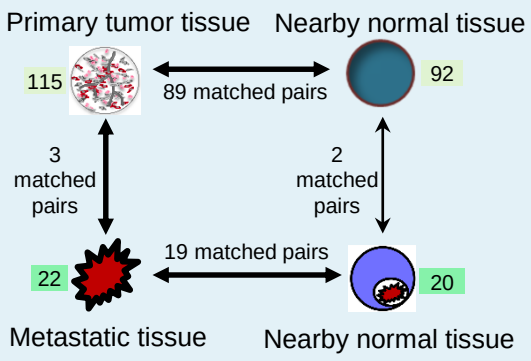
Challenge

Despite significant advances in standard of care therapy, the survival rate of colorectal carcinoma (CRC) remains relatively poor. CRC is a highly heterogeneous cancer where patients respond to the same drug in different way.

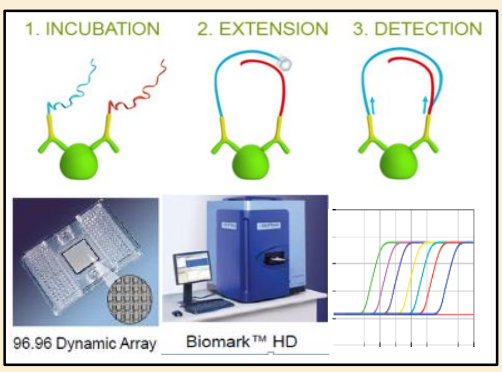
The OncoTrack IMI project has provided a basis to collect and extensively analyze tumor samples from over 100 CRC patients at different disease stages and having undergone different treatments. The purpose of the present substudy was to reveal fingerprints from high-throughput protein analyses during CRC development and metastasis, and to identify the most important proteins correlating with CRC biology and the heterogeneity between patients and also within a malignancy.

Approach & Methodology

Tissue samples



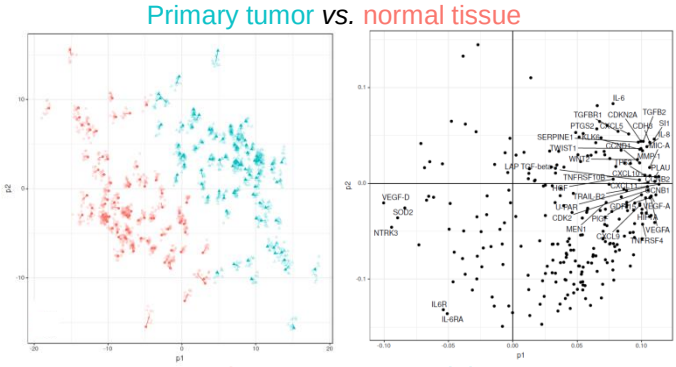
Method: Olink™ Multiplex proximity extension assay (PEA) 275 proteins



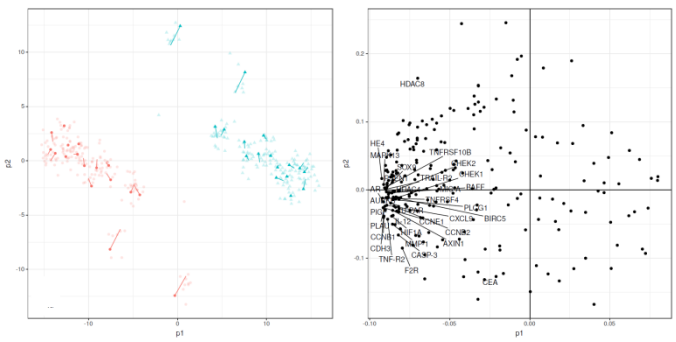
Results

Multilevel Partial Least Square-Discriminant Analysis (PLS-DA)

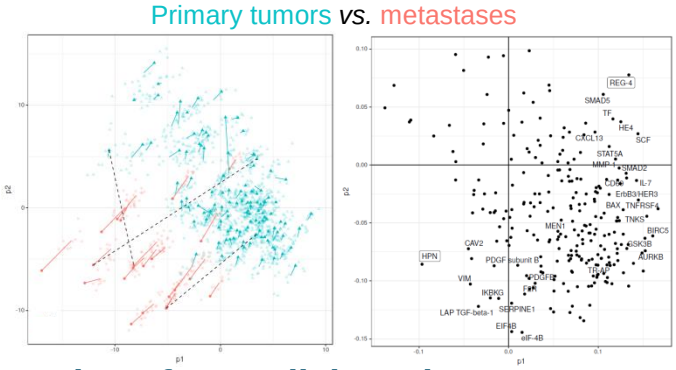
Primary tumor *vs.* normal tissue



Metastatic tumor *vs.* normal tissue



Primary tumors *vs.* metastases



Value of IMI collaboration

The OncoTrack project brought together leading academic, clinical and industrial scientist, allowing multidimensional molecular analyses of colorectal cancer patient samples, collected in a comprehensive database that also includes extensive clinical data with follow-up. This valuable resource provides a background for specific analyses, such as the PEA studies presented herein. We next aim to relate our protein data to DNA and RNA sequencing and other data accumulated in the OncoTrack project for a more comprehensive understanding of the disease.

Impact & take home message

By applying the highly sensitive and specific multiplex PEA technology, we compared alterations of protein profiles between primary and metastatic tumor tissues as well as their corresponding surrounding normal tissues, and identified the most significantly changed proteins. These findings increase the understanding of CRC biology and pave the way to identify promising diagnostic and prognostic protein markers for CRC.

This work has received support from the EU/EFPIA/[Associated Partner] Innovative Medicines Initiative