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Research Paper

The transcriptional and mutational landscapes of lipid metabolism-related genes in colon cancer

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ABSTRACT

Metabolic alterations encountered in tumors are well recognized and considered as a hallmark of cancer. In addition to Warburg Effect, epidemiological and experimental studies support the crucial role of lipid metabolism in colorectal cancer (CRC). The overexpression of four lipid metabolism-related genes (*ABCA1, ACSL1, AGPAT1* and *SCD* genes) has been proposed as prognostic marker of stage II CRC (ColoLipidGene signature).

In order to explore in depth the transcriptomic and genomic scenarios of *ABCA1*, *ACSL1*, *AGPAT1* and *SCD* genes, we performed a transcriptomic meta-analysis in more than one thousand CRC individuals. Additionally we analyzed their genomic coding sequence in 95 patients, to find variants that could orchestrate CRC prognosis.

We found that genetic variant rs3071, located on *SCD* gene, defines a 9.77% of stage II CRC patients with high risk of death. Moreover, individuals with upregulation of *ABCA1* and *AGPAT1* expression have an increased risk of CRC recurrence, independently of tumor stage.

***ABCA1* emerges as one of the main contributors to signature's prognostic effect. Indeed, both high *ABCA1* expression and presence of tumoral genetic variants located in *ABCA1* coding region, seem to be associated with CRC risk of death. In addition the non-synonymous polymorphism rs2230808, located on *ABCA1*, is associated with gene expression. Patients carrying at least one copy of minor allele showed higher levels of *ABCA1* expression than patients carrying homozygous major allele.**

This study broaden the prognostic value of *ABCA1, ACSL1, AGPAT1* and *SCD* genes, independently of CRC tumor stage, leading to future precision medicine approaches and "omics"-guided therapies.