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

Lara P. Fernández¹, Ricardo Ramos-Ruiz², Jesús Herranz³, Roberto Martín-Hernández², Teodoro Vargas¹, Marta Mendiola⁴,⁵,⁶, Laura Guerra⁷, Guillermo Reglero¹, Jaime Feliu⁶,⁸,⁹ and Ana Ramírez de Molina¹

¹Molecular Oncology Group, IMDEA Food Institute, CEI UAM + CSIC, Madrid, Spain
²Genomics Unit, Parque Científico de Madrid, Madrid, Spain
³Biostatistics and Bioinformatics Unit, IMDEA-Food Institute, CEI UAM+CSIC, Madrid, Spain
⁴Molecular Pathology Section, Institute of Medical and Molecular Genetics (INGEMM) La Paz University Hospital, Madrid, Spain
⁵Molecular Pathology and Therapeutic Targets Lab, IdiPAZ, La Paz University Hospital, Madrid, Spain
⁶CIBERONC CB16/12/00398, La Paz University Hospital, Madrid, Spain
⁷Pathology Department, IdiPAZ, La Paz University Hospital, Madrid, Spain
⁸Clinical Oncology Department, La Paz University Hospital, Madrid, Spain
⁹Translational Oncology Lab, IdiPAZ, La Paz University Hospital, Madrid, Spain

Correspondence to: Ana Ramírez de Molina, email: ana.ramirez@imdea.org

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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.