AB060. SOH21AS258. The prognostic value of metabolomics with genomic single nucleotide polymorphism cross-talk for colorectal cancer recurrence and 5-year overall survival

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Background: Metabolomic analysis in colorectal cancer (CRC) is an emerging research area. We aimed to examine current evidence and identify prognostic metabolomic signatures for CRC recurrence and overall survival and cross-reference this data with prognostic genomic single nucleotide polymorphisms (SNPs).

Methods: A systematic review of studies utilising metabolomics to identify patients at risk of cancer recurrence and poor survival outcomes in CRC was performed in keeping with PRISMA guidelines. The QUADOMICS tool was used to assess study quality. MetaboAnalyst software, version 4.0 was used to perform metabolic pathway enrichment and identify genomic SNPs associated with CRC prognosis, referencing the following databases: Human Metabolome Database (HMDB), the Small Molecule Pathway Database (SMPDB), PubChem and Kyoto Encyclopaedia of Genes and Genomes (KEGG) Pathway Database. Cohort validation was performed in an Irish population.

Results: Nine studies met the inclusion criteria, reporting on 1,117 patients. Increased metabolic activity in the urea cycle (P=0.002, FDR-0.198) ammonia recycling (P=0.004, FDR =0.359) and glycine and serine metabolism (P=0.004, FDR =0.374) were prognostic of CRC recurrence. Increased activity in aspartate metabolism (P=8.13E-04, FDR =0.079) and ammonia recycling (P=0.004, FDR =0.345) were prognostic of survival. Eight resulting SNPs were prognostic for CRC recurrence (Rs2194980, Rs1392880, Rs2567397, Rs715, Rs169712, Rs2300701, Rs313408, Rs7018169) and three for survival (Rs2194980, Rs169712, RS12106698) of which two overlapped with recurrence (Rs2194980, Rs169712). Poor prognostic metabolomes were further identified on cohort validation, in particular in patients with high visceral fat and or sarcopenia.

Conclusions: Specific metabolites and metabolic pathways are dysregulated in the setting of poor prognostic CRCs and such metabolic signatures are associated with specific genomic SNPs. These findings provide a platform for prognostic biomarker discovery and development in CRC as well as identify potential for therapeutic targeting.

Keywords: Metabolomics; omics; colon cancer; biomarkers

Acknowledgments

Funding: This work was supported by a research fellowship funded by the European Association for Cancer Research.

Footnote

Conflicts of Interest: DPO serves as an unpaid editorial board member of *Mesentery and Peritoneum*. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

doi: 10.21037/map-21-ab060

Cite this abstract as: Fleming C, Mohan H, O'Leary DP, Kirwan J, Redmond H. The prognostic value of metabolomics with genomic single nucleotide polymorphism cross-talk for colorectal cancer recurrence and 5-year overall survival. Mesentery Peritoneum 2021;5:AB060.

