EACR 2023 Abstract

Title: Sequence homology of bacterial and mitochondrial genes implicated in cancer pathogenesis

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Introduction

Bacteria have been implicated in the pathogenesis of various cancers. While the precise mechanisms remain unclear, it has been suggested that epigenetic reprogramming, immune evasion, and dysregulated mitochondrial function could play a role. Given the bacterial origins of mitochondria, we explore the overlap between mitochondrial genes implicated in cancer pathogenesis and genes from bacterial species.

Material and method

Using the BioCorteX CarbonMirror™ platform, we examine the nucleotide sequences of key mitochondrial genes implicated in cancer pathogenesis (ATP6, ATP8, CO1, CYB, ND3, ND4, ND5, TL1). We examine for sequence homology against a subset of 8,570 bacterial species and 63,000 strains with thresholds of 70% in sequence homology and 80% in length similarity. The platform includes a deterministic engine based upon first principles - note it did not include any *a priori* bacteria-cancer connections.

Results and discussion

Within the subset of 6026 strains processed, 5290 strains contain at least one of the eight mitochondrial genes at the required threshold. Four mitochondrial genes in total had bacterial overlap: ATP8, CO1, ND3 and TL1.

The mitochondrial gene ATP8 was present in 18 out of 6026 strains investigated. 10 of these were *Helicobacter pylori* strains, and both this species and the ATP8 gene have established causative links with gastric cancer through gene mutation. All 18 strains were further identified within the tumour microbiome of gastric cancer specimens.

Similarly, the mitochondrial gene ND3 was found in 2 bacterial strains of the species *Campylobacter jejuni*, a common cause of diarrhoea. Again, both this bacterial species and ND3 mutations have been implicated in colorectal tumorigenesis. These strains are further found in the tumour microbiome of colorectal cancer specimens too.

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Conclusion

The BioCorteX engines have rediscovered the mechanisms underlying two key bacteria and cancer pathogenesis from first principles: *Helicobacter pylori* and gastric cancer through the ATP8 mitochondrial pathway, and *Campylobacter jejuni* and colorectal cancer through the ND3 mitochondrial pathway. Out of over 500,000 known bacterial strains, the chances of finding those that are specifically found within the tumour microbiome are miniscule: 2e-30 to be exact. The engines have successfully identified these strains, using the mitochondrial mechanism illustrated, validating this mechanism of interaction. With the application of a more extensive list of oncogenes and bacterial strains, the BioCorteX CarbonMirror™ platform can be further leveraged to discover thousands of mechanistic actionable insights into the microbiome's role in cancer pathogenesis, opening a novel field for cancer therapeutics.

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