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Association of mitochondrial DNA copy number and telomere length with colorectal cancer patient outcomes

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The dysfunction of mitochondria is one of the cancer hallmarks. Mitochondria evince a limited DNA repair capacity and compensate for damage by increasing the mitochondrial DNA copy number (mtDNA-CN). Current studies on the mtDNA-CN in cancer have reported ambiguous results; most were based on a case-control design and were inconsistent for various cancer types. Telomere shortening has a dual role in tumorigenesis. It promotes cancer initiation by inducing chromosomal instability, while telomere length (TL) maintenance characterized by telomerase expression is required for cancer cell proliferation and tumour growth. Similar to mtDNA-CN, the reports on TL as a biomarker for cancer risk, patient therapy response and/or survival are contradictory. MtDNA-CN and TL are highly variable across cell types but maintained within a constant range according to the specific tissue type. It has been demonstrated that mitochondrial biogenesis and energy production were decreased in telomerase-deficient mice with severe telomere dysfunction. It thus has been hypothesized that telomere alteration affects not only oxidative defence mechanisms but also mitochondrial functions. The deregulation of the telomere-mitochondria axis, as caused by ageing or other physiological factors, triggers carcinogenesis. We, therefore, investigated mitochondria and telomere changes in colorectal cancer (CRC), one of the leading causes of cancer-related deaths. Our study particularly aimed to look closely at mtDNA-CN, mtDNA damage, TL, and the expression of mitochondrial transcription factor A and telomerase reverse transcriptase in association with CRC patient outcomes. Our cohort included deep-frozen tumour tissue, adjacent non-tumour tissue, and blood from 163 untreated sporadic CRC patients. We isolated DNA and RNA from these samples and measured particular molecular biomarkers using a quantitative-polymerase chain reaction assay. Currently, the experiments are running and after collecting the experimental data, comprehensive statistical analysis using patient clinical and follow-up data will be performed.

The results will be presented during the conference and we believe that they may aid improvements in the current understanding of CRC, by identifying the role of mtDNA-CN and TL in CRC pathogenesis. This study was financially supported by the Ministry of Health of the Czech Republic (NU22J-03-00033); and by the Grant Agency of the Czech Republic (21-04607X).

Keywords:
Mitochondrial DNA; telomere length; DNA damage; colorectal cancer; patient outcomes.