**Saliva Cell-Free DNA as a Biomarker for Early Detection of Gastric Cancer**

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Gastric cancer (GC) is one of the leading causes of cancer death annually and due to its disease heterogeneity, it is difficult to detect during early stages. The tumor microenvironment (TME) includes various molecular components, such as immune cells, that favor tumor progression. Previous studies have utilized salivary cell-free DNA (cfDNA) as a non-invasive means to guide early cancer detection. This project explores non-mutational analyses of cfDNA and considers the TME of GC to investigate the underlying genetic differences between healthy and cancer patients. We employed a low-coverage single-stranded library NGS pipeline on saliva samples of the two cohorts to study cfDNA characteristics including fragmentomics, G-quadruplex prevalence, and end-motif profiles. Our analysis showed a significant difference between the two cohorts for both saliva cfDNA characteristics and TME-specific biomarkers. These discoveries could potentially improve the application of cfDNA analysis in clinical settings for both early disease detection and monitoring its progression.