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Early Detection of Pancreatic and Colorectal Cancers via Ultra-Sensitive Circulating Tumor DNA (ctDNA) analysis

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INTRODUCTION

Pancreatic and colorectal cancers are major contributors to cancer-related deaths in the United States, with over 300,000 and 600,000 deaths globally each year, respectively. Both cancers are often diagnosed at advanced stages, leading to high mortality rates despite diagnostic advancements. Screening methods like colonoscopy, though effective, are costly and invasive, and face compliance challenges, underscoring the need for innovative, accessible approaches to early detection.

AIM

To investigate the potential of circulating tumor DNA (ctDNA) as a non-invasive biomarker for the early detection of pancreatic and colorectal cancers, which could enable real-time monitoring and personalized treatment.

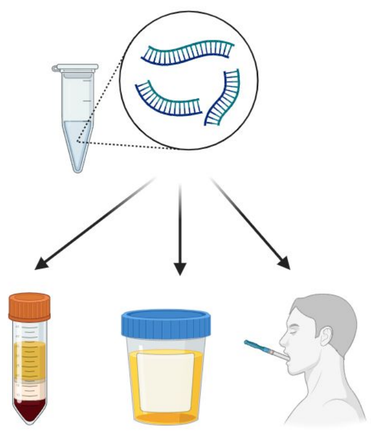
METHOD

A literature review consisting of 46 articles was analyzed and multiple iterations of our project was created based on comments and feedback from all authors.

ctDNA Collection and Analysis: Collection and Extraction

Processing: Centrifugation is used to process the sample, followed by ctDNA extraction via columns or magnetic beads.

Analysis Technique	Description
Targeted Sequencing	Focus on specific mutations , such as KRAS, and TP53 which are common in pancreatic cancer
Next Generation Sequencing (NGS)	Allows a large segment of ctDNA to be analyzing providing comprehensive analysis
Droplet Digital PCR (ddPCR)	Partitions DNA into droplets enabling high sensitivity detection and quantification through PCR amplification
Detecting low frequency mutations	Techniques such as CRISPincette with CRISPR/Cas9 to eliminate abundant wild type DNA, enhancing detection of rare mutations critical for early cancer detection



ctDNA can be collected from plasma, blood, urine, and saliva.Tumor heterogeneity can be captured via ctDNA through different sequencing techniques. Once isolated, ctDNA can be analyzed via various techniques. One of the more common techniques, NGS provides high throughput with a capability of simultaneous sequencing amongst multiple samples. This provides a precise detection of low frequency mutations, allowing treatment options to be tailored to a specific tumor sample.

RESULTS

The use of circulating tumor DNA (ctDNA) in early detection and monitoring of pancreatic and colorectal cancers shows significant promise, particularly in high-risk populations. In a 2020 study, ctDNA detection with methylation markers demonstrated high accuracy for colorectal cancer, achieving sensitivity and specificity rates of 89.7% and 86.8%, respectively.

This could allow for detection of cancerous and precancerous lesions in asymptomatic individuals (Luo et al., 2020). For pancreatic cancer, ctDNA provides a more sensitive alternative to current non-invasive methods like CA19-9, which lacks reliability due to low sensitivity (Yang et al., 2021).

Monitoring ctDNA fluctuations also has clinical applications for assessing tumor progression and treatment efficacy. Its short half-life (2-4 hours) allows real-time tracking of tumor burden, potentially indicating therapeutic response or resistance. A study showed that 77% of patients with post-operative ctDNA detected experienced recurrence, while ctDNA-negative patients had no relapse, underscoring its potential to guide treatment and follow-up strategies (Puccini et al., 2023).

DISCUSSION

While ctDNA shows promise, larger and more diverse studies are necessary to establish it as a universal diagnostic tool. Issues in distinguishing benign from malignant mutations, such as in cases involving clonal hematopoiesis of indeterminate potential (CHIP), must be addressed to reduce false positives (Dasari et al., 2020). Standardizing protocols for ctDNA collection, processing, and analysis is also critical for consistency and reliability (Loft et al., 2023). The potential for ctDNA testing to revolutionize early cancer detection is considerable, but further research is needed to address these limitations and integrate ctDNA effectively into clinical practice.

CONCLUSION

Pancreatic and colorectal cancers are current leading causes of cancer-related death in the US. Modern gold-standard screening methods such as colonoscopy or tissue biopsy are expensive, time consuming, and difficult to access, contributing to the frequent late-stage diagnosis and high mortality rates in these cancers. This matter has become more urgent in recent years, as the diagnosis rates increase, and the age at diagnosis decreases. ctDNA has become an evolutionary tool in cancer care, offering a non-invasive, highly sensitive method for early detection, monitoring, and management of challenging malignancies like pancreatic and colorectal cancer. By providing real-time insights into tumor biology, ctDNA is a valuable alternative to traditional diagnostic methods such as tissue biopsies, imaging, and serum markers.

FUTURE WORK

Future directions in ctDNA research should focus on standardizing detection methods, enhancing sensitivity and specificity, and refining clinical decision-making frameworks. ctDNA has the potential to reform cancer care by offering precise, individualized, and less invasive diagnostic and therapeutic strategies. We propose integrating novel, ultra-sensitive ctDNA detection techniques such as dPCR and Next-Gen Sequencing to provide a high degree of sensitivity and accuracy. With continued advancements, ctDNA-based testing could significantly improve survival rates and quality of life for cancer patients.

REFERENCES