Topics cfNA (Circulating free nucleic acid)
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Abstract;

NEW APPROACH TO SCREENING COLORECTAL CANCER PATIENTS BY LIQUID BIOPSY; DIFFERENTIAL PRESENCE OF EXONS (PDE).

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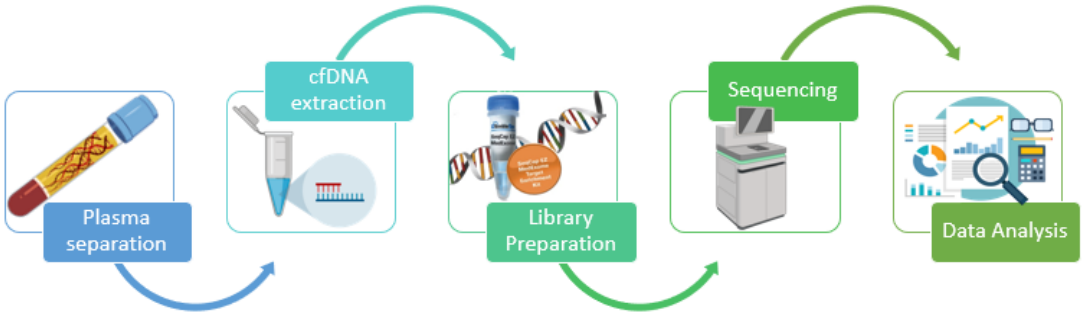
Current biomarkers of colorectal cancer (CRC) and screening tests for its detection have limited diagnostic accuracy and are subject to the risk of overdiagnosis. Therefore, there is a real need to develop new genomic tools to help us identify patients with colorectal cancer.

Measurement of differential presence of exons (DPE) of circulating free DNA (cfDNA) derived from patients' plasma could address these challenges, the aim of this study being to identify and demonstrate the diagnostic utility of DPE in CRC identification.

Plasma samples were collected from 97 CRC patients from the Hospital Fundación Jiménez Díaz and 63 healthy controls from the biobank of the same hospital. Extraction of cfDNA from plasma was performed using the DSP-Circulating-DNA kit (QIAGEN) using the QIASymphony platform, library preparation was performed using the Twist-Human-Core-Exome Kit (Twist Bioscience). To date, 31 CRC patients and 32 healthy controls have been sequenced on the NovaSeq-6000™ platform (Illumina) at a depth of 100x.

Samples were aligned to the GRCh38 human reference genome using Bowtie-2 software and the count table for each exon was obtained using HT-Seq. Data analyses were processed using an internal pipeline, removing those exons belonging to sex chromosomes to avoid sex bias.



In the discovery phase, 25,214 differentially present exons were identified using DESeq2 with a p.value adjusted by Bonferroni correction of 0.001. These exons belong to 9,790 genes and the results using these exons were highly significant and with high ability to discriminate between patients and controls, the results were observed in dendograms and principal component analyses.

Next, another package was used for "differential expression" and 3,727 differentially present exons were identified using the limma package with a False Discovery Rate p.value-adjusted of 0.001 and with a log-fold-change cutoff value of 2, relevant differences between patients and controls were shown. We are currently improving the analysis and sequencing those patients that we have not yet sequenced, this will help us to confirm our findings of DPE involved in cancer.

The DPE analysis approach could serve as a diagnostic biomarker in CRC patients, leading to a minimally invasive blood-based screening test for CRC detection and prevention.