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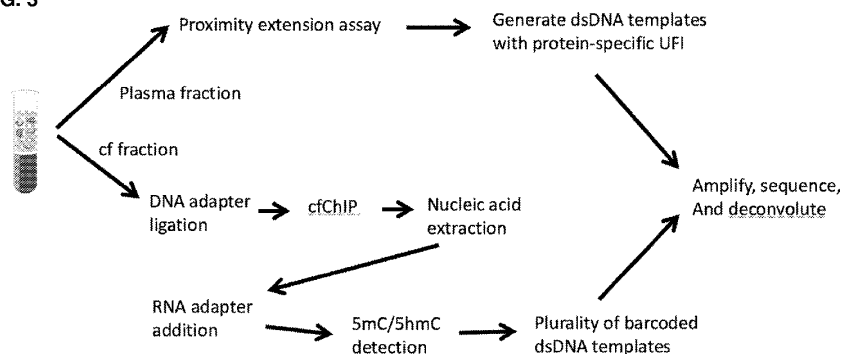
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(54) Title: SIMULTANEOUS, SEQUENCING-BASED ANALYSIS OF PROTEINS, NUCLEOSOMES, AND CELL-FREE NUCLEIC ACIDS FROM A SINGLE BIOLOGICAL SAMPLE

FIG. 3



In a comprehensive combined workflow, sequencing is used to measure the following biomolecules:

- Targeted plasma proteins
- cfDNA histone modifications
- cfDNA 5mC/5hmC (including sequence)
- cfRNA

(57) Abstract: The invention provides a method for the analysis of a biological sample to determine multiple types of information therefrom in a streamlined, combined workflow, where all information is obtained in a sequencing-based analysis. The information includes the presence and concentration of specific plasma proteins in a blood sample; the number, location, and types of histone modifications associated with cell-free DNA obtained from the same sample; the sequence of cfRNA and cfDNA in the cell-free DNA sample; and epigenetic information pertaining to the cell-free DNA, such as hydroxymethylation and methylation profiles, i.e., the distribution of 5-hydroxymethylcytosine (5hmC) and 5-methylcytosine (5mC) residues, respectively. The invention additionally pertains to a classical sequencing-based method for analyzing a biological sample to determine one or more non-classical sequence features of the sample. Compositions, kits, and related methods are also provided, including an embodiment in which truncated sequencing adapters are used in conjunction with barcoded PCR primers.

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