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(54) Title: METHODS FOR FRAGMENTOME PROFILING OF CELL-FREE NUCLEIC ACIDS

$$\text{cfDNA} = \sum_{\substack{\text{tissue} \\ \text{(including blood)}}} \begin{bmatrix} \text{benign systemic response} \\ \text{tumor systemic response} \\ \text{tumor microenvironment} \\ \text{tumor} \end{bmatrix}$$

FIG. 1A

(57) Abstract: The present disclosure contemplates various uses of cell-free DNA. Methods provided herein may use sequence information in a macroscale and global manner, with or without somatic variant information, to assess a fragmentome profile that can be representative of a tissue of origin, disease, progression, etc. In an aspect, disclosed herein is a method for determining a presence or absence of a genetic aberration in deoxyribonucleic acid (DNA) fragments from cell-free DNA obtained from a subject, the method comprising: (a) constructing a multi-parametric distribution of the DNA fragments over a plurality of base positions in a genome; and (b) without taking into account a base identity of each base position in a first locus, using the multi-parametric distribution to determine the presence or absence of the genetic aberration in the first locus in the subject.

