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(54) **Title:** FRAGMENTATION FOR MEASURING METHYLATION AND DISEASE

(57) **Abstract:** Fragmentation of cell-free DNA molecules is measured and used for various purposes, including determining methylation, e.g., at a particular site of a DNA molecule, at a particular genomic site in a reference genome for a biological sample (e.g., plasma, serum, urine, saliva) of cell-free DNA of a subject, or for a particular region in the reference genome for the biological sample (also just referred to as a sample). Various types of fragmentation measurements can be used, e.g., end motifs and cleavage profiles. Another purpose is determining a fractional concentration of DNA of a particular tissue type (e.g., clinically-relevant DNA). Another purpose is determining a pathology of a subject using a biological sample including cell-free DNA. The cell-free DNA can be of the subject or of a pathogen (e.g., a virus) in the subject's sample. Sites/regions that are hypermethylated, hypomethylated, 5hmC-enriched, and 5hmC-depleted for a particular tissue type can be used.