

Recent discoveries in the characteristics and clinical significance of cell-free DNA in plasma

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There is a global interest in the use of cell-free DNA in plasma for non-invasive prenatal testing and cancer. Cell-free DNA in plasma consists mostly of short fragments of DNA. Recently, there is appreciation that the fragmentation of such DNA molecules is non-random. The study of the biology and diagnostic application of such fragmentation is called fragmentomics. Fragmentomic biomarkers include the size of cell-free DNA, the end sequences (called end motifs) and the jaggedness of such molecules. We have also demonstrated that the fragmentation is related to the DNA methylation status of DNA molecules. Through the use of single molecule sequencing, we have also demonstrated that there is a subset of cell-free DNA in plasma that is longer than 500 bp, with some molecules being of kilobase sizes. Because of the length of such long cell-free DNA molecules, they carry an increased amounts of genetic and epigenetic information, and can provide useful information for molecular diagnostics. Hence, the study of the biology of cell-free DNA has enhanced our ability to use such materials for novel diagnostic applications.