

Study on detection of circulating tumor DNA in breast cancer

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BACKGROUND: Circulating tumor DNA (ctDNA) carrying tumor-specific sequence alterations is found in the cell-free fraction of blood, representing a variable and generally small fraction of the total circulating cell-free DNA (cfDNA). Detection of ctDNA promises to provide new avenues for cancer diagnosis and monitoring.

HYPOTHESIS: the positive detection rate of ctDNA was low due to the limited number of genes or loci analyzed in the previous study. This might restrict the feasibility of applying ctDNA analysis. To explore the potential application of ctDNA, we conducted the present research study.

METHODS: In this study, matched DNA was extracted from the tumor tissues, plasma and peripheral blood cells of 11 invasive breast cancer patients. The primers were designed against the exons of PIK3CA, TP53, EGFR, AKT1 and PTEN. Next, the amplicon-based method for whole-exon sequencing was performed. The association between the ctDNA mutant frequency and cancer DNA mutant frequency as well as that between the ctDNA concentration and clinical data were analyzed.

RESULTS: A strong linear relationship was observed between the ctDNA concentration and tumor volume in basal-like breast cancer, but not in other subtypes. The mutation frequency exhibited the smallest difference between ctDNA and tissue DNA in basal-like breast cancer. ctDNA retained the constituent ratio of gene mutation found in the corresponding tumor tissue. We demonstrated that the ctDNA detection rate depended on the mutation frequency in tumor tissue. The mutant locus, which showed a mutation frequency greater than 30% in tissues, presented a detection rate greater than 40% in plasma. The locus with a mutation frequency of less than 10% in tissues was associated with a detection rate of no more than 1% in the plasma. ctDNA, which retained the constituent ratio of gene mutation in tumor tissue, could therefore reflect the mutations observed in cancer. Therefore, compared with other subtypes, ctDNA is a highly sensitive biomarker for the assessment of mutation and cancer burden in basal-like breast cancer.