A Game-Changing Idea for Rapid Cancer Screening: Detection of Circulating Tumor DNA on the Surface of Red Blood Cells

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Nowadays, liquid biopsies based on detecting cell-free DNA (cfDNA) by Real-Time PCR have gained momentum in cancer diagnosis owing to their painlessness to patients. However, detecting cancer by this technique is inefficient as the concentration and lifespan of circulating tumor DNA (ctDNA) in plasma are low and short respectively, due to nuclease digestion. This work demonstrated a challenging approach to detect ctDNA on the surface of red blood cells instead of plasma. The concentration of cell surface-bound DNA (csbDNA) was expected to be increased via a DNA binding property of Toll-like receptor (TLR) presenting on red blood cell surfaces. As chicken TLR21 is a homolog to human TLR9, it likely binds ctDNA. This assumption together with the safety issue let us select food-grade chicken blood as a representative model. Cell-free DNA circulation in blood was mimicked by mixing cancer DNA (amplified HER2 gene) from SKBR3 and MDA-MB-231 (triple-negative cell), and blood cells. Real-Time PCR was used to quantitate csbDNA and determine the ratio between the cycle threshold (Ct) of HER2 and EIF5B (internal control) genes, compared to those of the original cells. The ratio between the Ct of both genes from MDA-MB-231 is close to 1:1 and from SKBR3 is approximately 4:1, which matches the ratio from the original cells. This can be concluded that our proposed strategy could enhance the concentration and stability of csbDNA, which in turn boost real-time PCR sensitivity for earlier-stage detection of cancer. The positive outcome of this research is a game-changing idea for rapid cancer screening that potentially prevents millions of cancer deaths worldwide. Keywords: Toll-like receptor (TLR), circulating tumor DNA (ctDNA), Liquid biopsy, HER2, cell surface-bound DNA (csbDNA)