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Sensoresponsive Nanoelements to Detect Individual Cancer Cells

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The main cause of cancer-related death is due to cancer cell spreading and formation of secondary tumors in distant organs, the so-called metastases. Metastatic cancer cells are detectable in the blood of cancer patients as circulating tumor cells (CTC) and may be exploited for prognostic and monitoring purposes, including in breast cancer. Due to their very low frequency, however, their quantitative detection remains a challenge in clinical practice. To develope a simple, highly sensitive, specific and robust test to detect and quantify rare CTCs in patients'blood or complex biological environments, by inspiration from Nature, two innovative approaches have been investigated based on the design and generation of sensoresponsive, self-assembling gold nanoparticles and DNA amplification cascades.

The first approach focused on design, characterization and establishment of multifunctional gold nanoparticles with enhanced anti-biofouling and targeting properties to detect $HER2^+$ breast cancer cells. These engineered gold nanoparticles exhibited excellent physicochemical stability, strong affinity and high specificity for $HER2^+$ cells, while showing stealth-like behaviour toward $HER2^-$ cells.

In the second approach, a novel activatable theranostic strategy was pursued to detect individual cancer cells, based on a signal amplification cascade using a programmable DNA hybridization chain reaction (HCR) circuit. This approach was applied to detect $HER2^+$ cancer cells using the anti-HER2 antibody (trastuzumab) coupled to initiator DNA eliciting a HCR cascade that leads to a fluorescent signal at the cell surface. The HCR detection scheme resulted in highly efficient, specific and sensitive signal amplification of the DNA hairpins specifically on the membrane of the $HER2^+$ cells in a background of $HER2^-$ cells and peripheral blood leukocytes, which remained almost non-fluorescent. This proposed system can be deployed for sensitive detection of CTCs in vitro diagnostic test.

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