Sensoresponsive nanomaterials to detect individual circulating tumor cells

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Breast cancer accounts for about one quarter of women cancers and is a leading cause of cancer-related mortality in developed countries.[1] Over one third of all breast cancer patients succumb to the disease due to metastasis formation. Circulating tumor cells (CTCs) in blood play a critical role in initiating metastases. CTCs are indicative of the presence of a disseminated cancer and their determination has been proposed for detection and monitoring of cancers, including breast cancer.[2]

In this project we aim to develop an *in vitro* diagnostic (IVD) test for one-step detection and characterization of CTCs in blood samples with sensoresponsive nanomaterials. Currently, CTCs detection is a multi-step procedure involving antibody-based immunomagnetic enrichment, followed by immunostaining for additional markers and imaging-based enumeration.[3] Developing a single step test to enumerate and characterize CTCs is a challenge putting us at the forefront of IVD test research.[4]

As a first step toward the development of such IVD, we engineered gold nanoparticles (NP1) to target CTCs. Trastuzumab, a humanized anti-HER2 IgG1, was chosen as targeting molecule because it has been proven to be an essential tool in the immunotherapy of beast carcinoma. We have established an *in vitro* cellular model consisting of HER2 positive and negative cell lines and non-cancerous primary cells (fibroblasts and endothelial cells). Different variants of NP1 have been synthesized and their physicochemical behavior under *in vitro* conditions has been fully characterized. In addition, their ability to specifically target HER2 expressing cancer cells have been characterized by FACS, inductively coupled plasma optical emission spectrometry (ICP-OES), dark filed optical microscopy with high resolution hyperspectral imaging (DF-HIS) and laser scanning microscopy (LSM). We demonstrated that the conjugation of 5 Trastuzumab molecules per NP1 is sufficient to identify and target HER2 expressing cancer cells. Toxicity study on non-cancerous and cancerous cells demonstrated excellent biocompatibility of all NP developed. We have also shown the importance of applying a set of different methods (such as ICP-OES and DF-HSI) to study and evaluate the targeted NPs-cell interactions.

References

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