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A nanostrategy for characterizing the phenotypic evolution of circulating tumor cells during therapy

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Targeted therapies have been proved to be effective in cancer treatment but are limited by the rapid acquisition of drug resistance (within months). A rapid and non-invasive method to monitor drug response would promote precision medicine and improve treatment efficacy. Circulating tumour cell (CTC) analysis has emerged as a useful monitoring tool, but its routine usage is restricted by either limited multiplexing capability or sensitivity. Here we demonstrate the use of antibody-conjugated and Raman reporter-coated gold nanoparticles for simultaneous labelling and monitoring of multiple CTC surface markers (named as "cell signature"), without the need for isolating individual CTCs. Our nanostrategy is capable of detecting 10 tumor cells in 10 mL of blood. We also observe cell heterogeneity and phenotypic changes of melanoma tumor cells during molecular targeted treatment. Furthermore, we follow the CTC phenotypic changes of 10 stage-IV melanoma patients receiving immunological or molecular targeted therapies. Our technique maps the phenotypic evolution of patient CTCs and shows drug-resistant clones having different CTC signatures of potential clinical value. We believe our proposed method is of general interest in the CTC relevant research and translation fields.

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