Surfactant Functionalization Induces Robust, Differential Adhesion of Tumor Cells and Blood Cells to Charged Nanotube-Coated Biomaterials Under Flow

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Statement of Purpose: The separation of circulating tumor cells (CTCs) in large numbers and at high purity levels from patient blood could lead to the development of effective personalized medicine regimens for those with metastatic cancer. Our lab has recently developed microscale flow devices containing nanostructured surfaces of halloysite nanotubes (HNT) and recombinant human E-selectin (ES) to both isolate CTCs from patient blood. Improvement of current CTC isolation purity levels is challenged by the fact that both CTCs and leukocytes possess ligands for ES. Here, a straightforward technique to functionalize and alter the charge of naturally occurring nanotubes using surfactants is reported to induce robust, differential adhesion of tumor cells and blood cells to nanotube-coated biomaterial surfaces under flow.

Methods: HNT were functionalized with surfactants and immobilized on biomaterial surfaces, followed by incubation with ES. HNT were characterized using dynamic light scattering, AFM, and SEM. Tumor cells, human neutrophils, and blood samples from cancer patients were perfused over surfaces at physiologically relevant shear stresses. Micrographs and videos were acquired to quantify adhesion phenomena.

Results: Adsorption of sodium dodecanoate (NaL) surfactant into the HNT inner lumen increased the net negative HNT charge, which enhanced the electrostatic repulsion and thus the colloidal stability of the HNT solution. NaL treatment altered the HNT average negative zeta potential from -25.1 to -103.4 mV (Fig. 1A), compared to the average negative zeta potential for untreated HNTs. Conversely, the HNT average negative zeta potential was reduced to -4.0 mV upon treatment with decyltrimethylammonium bromide (DTAB). The number of cancer cells captured from flow increased on surfaces coated with NaL-functionalized HNTs and ES (Fig. 1B). Interestingly, the number of leukocytes captured from flow decreased on identical surfaces (Fig. 1B). Cancer cell capture significantly increased on HNT surfaces of increasing net negative charge, while leukocyte capture significantly decreased (Fig. 1C).

Conclusions: This work reveals that charged nanomaterials can differentially control tumor cell and leukocyte adhesion, enabling new approaches to increase the number and purity of CTCs separated from patient blood for the development of effective personalized cancer therapies.

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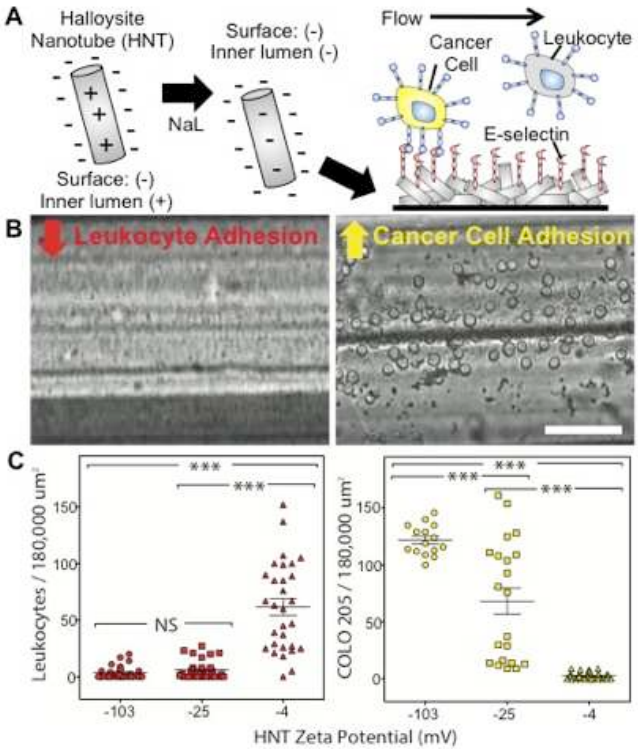

Fig. 1: (A) Schematic of HNT functionalization immobilization, and blood cell perfusion within a microscale flow device. (B) Reduced adhesion of leukocytes and enhanced adhesion of cancer cells from flow using a microscale flow device coated with NaL-functionalized HNT and ES. Scale bar:150 µm. (C) Leukocytes and tumor cells captured from flow per 180,000 µm2 using functionalized HNT surfaces coated with ES. ***P<0.001. NS: not significant.