THE HARTWELL FOUNDATION

2015 Individual Biomedical Research Award

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Microchip Diagnostic for the Rapid Isolation and Identification of Human Plasma-Derived Exosomes

A central problem in pediatric cancer is that even at diagnosis many patients may have unrecognized metastasis (transference to other areas of the body). Given that approximately 20% of children in the U.S. diagnosed with cancer will not survive even after rigorous and often painful therapy, it would be preferable to detect metastasis early and respond to it rapidly, rather than wait for its appearance. In the last several years, nano-scale lipid vesicles that originate from most living cells and circulate in blood have been discovered to contain a wealth of proteomic and genetic information useful for clinical diagnosis and monitoring the progression of disease, particularly in cancer. Called exosomes, these vesicles are secreted by most types of cells and are therefore present in most biological fluids. Unfortunately, the exploration of exosomes as biomarkers has been limited, principally by fundamental technical challenges to their isolation and characterization due to their small size (30 nm-200 nm diameter). To achieve the desired biomarker goals of specificity and sensitivity requires meeting the current requirement for a large number of exosomes to be isolated and concentrated. Because cell debris may interfere with analysis, lengthy and rigorous sample preparation is required. Clearly, exosome isolation and characterization is impractical in all but a research setting, but their compelling use as a clinical biomarker for cancer offers enormous potential to improve patient care. To address the unmet need for a robust and readily accessible methodology for the analysis of exosomes in a clinical setting, David proposes to miniaturize the technology for their isolation and characterization by developing a microchip-based platform. His strategy combines recent advances in microfluidic device technology together with his contemplated development of a multichannel sensitive fluorescence-based assay system. After partitioning the sample into millions of isolated droplets, where each drop contains at most a single exosome, he will perform ultra-sensitive immunoassays for surface proteins on individual exosomes as potential markers of disease. If David is successful, his microchip-based platform will enable clinical research scientists to readily map tumor exosome surface markers, which potentially could lead to new advances in cancer diagnosis and therapy, especially in terms of predicting metastasis. High-throughput and high-precision assays with small sample volume, reduced equipment cost and low analysis time should facilitate point-of-care use of exosomes as biomarkers for the prevention, diagnosis, and treatment of disease. Such advances in personalized medicine have the potential to reduce cancer morbidity and associated mortality, especially among young children.