Bankhead-Coley Cancer Research Program

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Department of Chemistry *2006 Program*
University of Florida *Bridge (1-year project)*

Project Title: Enrichment and Detection of Exfoliated Cancer Cells Using Aptamer/Nanoparticles

Project Summary: One of the most important aspects of cancer treatment is the early and accurate diagnosis of the disease. Early diagnosis enables current treatments to be much more effective and leads to greatly improved survival rates. Conversely, even the most effective treatments have poor survival rates when the cancer diagnosis is made at a later stage of the disease. Another limitation in the effective treatment of cancer is the diagnosis that is often based on subjective morphological examinations. A diagnosis based on the molecular fingerprints of the disease would be far more effective for not the diagnosis of the cancer but also for its treatment. Therefore, one of the major issues in improving cancer survival rates is the accurate and early diagnosis of the disease. Our grant addresses two important issues in molecular diagnosis of cancer cells: generation of molecular probes for the identification of cancer cells and the sensitive detection of exfoliated tumor cells. Molecular level differences are present between any two given types of cells. Making use of these differences to generate novel cell-specific molecular probes for the efficient capturing and detection of cancer cells is the major theme of this proposal. Recently, we have developed a novel cell-based aptamer selection strategy (cell-SELEX) to produce a group of aptamers (designer DNA/RNA probes) for the specific recognition of individual cells without prior knowledge of the biomarkers on the cells. The cell-SELEX uses whole cells as targets to select aptamers that can distinguish target from control cells. Using leukemia as a model, we have generated more than 20 aptamers. The selection process is fast and reproducible. The newly generated aptamers recognize target cells in a variety of samples including bone marrow and leukemia patient samples. In this grant, we will develop effective molecular probes for small cell lung cancer (SCLC) using cell-SELEX. SCLC is a very aggressive form of lung cancer with only 15 percent long-term, disease-free survival rate, partially due to the lack of methods for early diagnosis. SCLC and non-SCLC cells will be used as target and control cells for cell-SELEX, respectively. Once the aptamers highly specific for SCLC are generated, they will be conjugated to the magnetic nanoparticles (MNPs) and fluorescent nanoparticles (NPs) developed in our laboratory. The two NPs will then be incubated with SCLC samples for the enrichment and sensitive detection of exfoliated SCLC cells. The fluorescent NPs can report the SCLC cells with excellent sensitivity as each NP has tens of thousands of fluorophores embedded. The two-particle approach will allow fast enrichment and sensitive detection of trace amount of exfoliated SCLC cells in bodily fluids, thus enabling the potential for early diagnosis of the lung cancer. Once completed, the proposed work will not only show that cell-based aptamer selection can be widely applicable to various types of diseased cells, but also convincingly demonstrate the advantages of using cell-SELEX to generate aptamers for effective cancer studies and early cancer diagnosis. It is well accepted that the earlier a cancer is detected, the more treatable the disease is. Therefore, developing molecular techniques that allow for earlier detection of cancer allows current cancer treatments to be more effective.