Congratulations to Lauren!

Bullock Postdoctoral Fellowship 2016

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The Bullock Postdoctoral Fellowship for research is aimed at understanding and solving important biomedical problems. This multidisciplinary fellowship was created to foster interactions between researchers from diverse fields of science and medicine. The Fellowship provides one year of support, up to $60,000 direct costs.

A Highly Sensitive Microfluidic Imaging System for the Evaluation of CA125-Immune Cell Binding Profiles

Abstract

If found early, ovarian cancer is considered a highly survivable disease, with a 5-year survival rate greater than 90%. Frustratingly, however, over 70% of patients are diagnosed at advanced stages with the cancer having already metastasized. While aggressive surgery and chemotherapy leads to a response rate of 85%, an advanced stage diagnosis is largely regarded as a death sentence, with less than 30% of patients surviving beyond 5 years. Though the discovery of the tumor antigen CA125 over three decades ago provided hope that ovarian cancer could be detected early, its utility has been hampered by its lack of sensitivity and specificity. For example, approximately 20% of ovarian cancer patients register normal CA125 serum levels. Therefore, it is imperative to develop improved methods of ovarian cancer monitoring and early detection so that the disease can be caught early and treated effectively.

Increasing evidence has emerged suggesting an immunomodulatory effect of CA125, with the antitumor activity of NK cells being blunted after CA125 surface binding. While these studies have unveiled a new role of CA125 in the pathogenesis of ovarian cancer, the low level of CA125 binding events and the endogenous autofluorescence from immune cells currently limits the use of available technologies, such as fluorescence microscopy and flow cytometry, from more thoroughly investigating its immunomodulatory role. Therefore, in order to fully understand the ramifications of CA125-immune cell binding and explore its potential as an early diagnostic marker, there is an urgent need to develop a high throughput imaging technology that can not only quantify the level of CA125 binding but also identify the immune cell subtypes to which CA125 is bound. To address this critical need, the goal of this work is to develop a highly sensitive integrated all-in-one microfluidic flow-imaging device for the rapid quantification and characterization of CA125-immune cell binding in patient whole blood samples.

For the development of such an imaging platform, the proposed work integrates a highly interdisciplinary team of chemists, biologists, engineers, physicists and clinicians. By utilizing (1) a microfluidic device to isolate and align WBCs from whole blood into a single cell stream, (2) a high-resolution optical platform that combines dark field imaging optics and multichannel fluorescence detection, and (3) plasmonic gold nanoparticles for high sensitivity CA125 detection, we will develop and apply an innovative technology that has the potential to increase the imaging sensitivity 50 to 100-fold over currently available technologies. Using the proposed strategy, quantification of CA125 binding densities and bound immune cells will be possible on whole blood samples for future investigations into the differences between healthy patients and those with known ovarian cancer diagnoses. We anticipate the proposed imaging toolkit will have a major impact on the current state of disease monitoring and open the door for improved early detection methods for ovarian cancer.