

Investigating Leukocyte Dynamic Response to Stimuli in an Integrated Microfluidic-Ion Mobility-Mass Spectrometer

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Short Abstract — Leukocytes, including T cells and monocytes, play a critical role in the function of the immune system. Any alteration of the phenotypic state of these cells can lead to a potential change in immune response. Toxins and drugs are likely culprits of these leukocyte alterations. By studying leukocyte dynamic response to stimuli using a coupled microfluidic-ion mobility-mass spectrometer (MF-IM-MS), a greater understanding of leukocyte behavior may result and potentially lead to the ability to predict and control cellular dynamics.

Keywords — microfluidics, ion mobility-mass spectrometry, immune response

I. PURPOSE

DEFICIENCIES in the immune response can lead to a host of issues ranging in severity from minor infections to cancer and cardiovascular disease. These immunodeficiencies, while in some cases are caused by a number of genetic conditions, can result from changes in mood, drug use, pathogens and toxins. Changes in the immune response can potentially be attributed to variations in immune cell state: a result of alterations in the production or uptake of chemical species. Altered immune cell state, however, may be a transient feature only evident under stressful conditions. Steady-state approaches to determining cell state, such as analysis of cellular effluent from a culture flask, lack the ability to detect the dynamic response of immune cells, or any cell population, to a given experimental condition. A method of real-time exposure and analysis is required in order to determine these potential transient cell states.

The development of a joint microfluidic and ion mobility-mass spectrometry platform, capable of investigating dynamic response of a cell population to a stimulus, is

currently in progress. A microfluidic bioreactor, shown previously to be capable of reporting real-time signaling in T cells [1], is specialized for constant perfusion of cell populations. When combined with the rapid fluid analysis by IM-MS, an innovative technology platform arises which proves to be capable of immediate monitoring of alterations in species transport across the cell membrane, whether small molecule, metabolite, carbohydrate, lipid, protein, etc. Knowledge concerning changes in species transport provides information on the current state of the leukocytes which can lead to a more thorough understanding of a particular cell's biology.

II. RESULTS

The integration of these two technologies has begun by means of offline experimental set-ups and steady-state analysis conditions in both yeast and T cell populations with promising results [2]. As advances in the uniting of these technologies continues, alterations in leukocyte populations in response to stimuli, such as those previously reported in response to staphylococcal enterotoxin B (SEB) [3], may be accomplished, leading to a platform for real-time analysis of dynamic cellular response to stimuli.

III. CONCLUSION

This integrated microfluidic and mass spectrometry platform is uniquely suited to capture the dynamics of the cellular response to a wide variety of stimuli. This particular application of the technology is aimed at identifying leukocyte dynamics; bringing immunology to a whole new dimension. As our understanding of the immune response deepens, we will gain new insights into disease treatments and prevention strategies.

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