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Editorial

Immunoproteomics: from Reductionist to Systems Immunology - ∂

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Early explorations into the workings of the immune system have generally taken a reductionist approach. Analysis of the role of cellular subsets in the immune response focused on the interactions of two cells types in culture. Similarly, in order to understand the function of a particular protein, it was isolated, expressed and analyzed *in vacuo*. The introduction of mass spectrometry allowed for the analysis of *in situ* protein abundance, interactions and post-translational modifications, yet dynamic interactions were still beyond reach of this powerful technique.

While technological advancements in imaging greatly expanded the complexity of investigations into cellular interactions during the immune response, comprehensive protein analysis lagged behind, relying on western blot and budding flow cytometry. Intravital microscopy and multiphoton imaging made possible investigations into the location and multicellular interactions during an active immune response *in vivo*. These, and other, new technologies led to real-time visualization of the interactions of numerous cells types in the lymph node, spleen and other tissues responding to infection or allergy.

Despite being able to localize proteins within a tissue sample and determine their abundance, proteomics focused on a single parameter. The widespread demographics of the proteins expressed during the immune response (immunoproteome) remained circumstantial. Analyses of limited numbers of highly abundant proteins in select locations were correlated with known immune related activities. Studies focused on understanding what happened to an individual protein, or proteins, within a given pathway. Interactions between the class I and class II antigen presentation were interrogated using mass spectrometry to analyze peptide presentation following perturbations in the pathway [1]. Top-down proteomics has been used in numerous studies to identify peptide epitopes potentially recognized by immune T cells that could lead to new vaccines [2,3].

However, the immunoproteome is more than simply the presentation of epitopes and a correlation between immune proteins and immune function. The dynamic immunoproteome includes these but adds cytokines, signaling proteins, effector proteins and activation/differentiation proteins. This vast snarl of proteins involved in an immune response presents further dimensions that must be considered to understand the immunoproteome, in particular, variations in systemic expression and temporal kinetics. New proteomics approaches aimed to combine improved instrumentation with bioinformatics analysis to generate a systems biology view of the developing immune response.

Current advances in the sensitivity and resolution of proteomic technology and bioinformatic analyses allow for the possibility to analyze the immuoproteome of an entire system kinetically over the course of an immune response to various infections. As the immune response against more and more infections is analyzed in greater detail and at a systems level, it is becoming more evident that not all immune responses are created equal. High resolution, high throughput proteomics can analyze not only the abundance of various proteins in the immune response but also their modification. However, without systems bioinformatics and big data computing power, the temporal kinetics of the immunoproteome will remain a snap shot in time. As the field of proteomics further advances to answer such big data questions, concomitant or even greater advances in bioinformatics will be needed to break this hurdle. By defining the immunoproteome in such detail, proteomics may move from simply an analytical technique to the driving force behind directing future generations of immunology research.

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