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Current Perspective on Immunology

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Introduction

While this phrase is intended to apply to all fields of science, I believe it is particularly pertinent to where we are now in the application of Systems methods to immunology. It's also a good reminder that all science starts with observation. This goes against common wisdom, which holds that one should start with a hypothesis and work their way to'mechanistic' facts by the conclusion of the paper. We certainly want to focus on hypotheses and mechanisms, but thorough observation and analysis must come first. Hypotheses are only worth having as additional data accumulates. I'm biassed, but I believe the modern form of Systems Immunology began in 2008–2009, with a relatively concurrent publication by me titled "A Prescription for Human Immunology" and the first data papers by Sekaly and Pulendran, where both groups used gene array data and other data to analyse Yellow Fever Vaccine responses. The common thread running through them all was that we required new methods to human immunology, because so much of what we do in mice can't be replicated in humans. We also wanted data that wasn't reliant on what we know about mouse immunology, because numerous failed translational efforts have shown that the mouse isn't a good predictor of human outcomes [1].

Also, because vaccination reactions activate the immune system extensively and are relatively straightforward to initiate, at least part of the way ahead was to look closely at vaccine responses. But first, some terminology and the big picture. I believe that the success of a systems approach to a problem is determined by how well the data collected captures the system's most significant features. Early systems research focused on signalling pathways in yeast, which makes sense for a single cell organism because cells may be conceived of as separate entities. As though they were uniform entities the immune system, on the other hand, is far more complicated, with numerous cell types and subsets, as well as variances in activation states. Furthermore, these cells communicate with one another via a variety of cytokines [2]. Also, diverse antigen receptor repertoires are formed as a result of experience. Fortunately, we now have advanced tools for phenotyping different cell types and quantifying the majority of cytokines. As well as new approaches for analysing the TCR and BCR repertoires. Importantly, this can be done at the single-cell level, which is useful for separating what distinct subpopulations are doing from the aggregate. The different tissues and organs where immune cells grow and mount responses are far less accessible in humans, but there has been significant progress recently in this area as well [3].

Description

But why is it important to understand the immune system as a whole? Because it is exactly how the various cell types and chemicals interact to mount and modify responses together. While taking a piecemeal approach to something as complicated as the immune system has been necessary for most of our field's history, we shouldn't stop there; the next step is to understand the interplay of its various components so that we can actually predict the contribution of each part to a given response. Blood is the most valuable resource because it is one of the most readily available clinical materials and contains the majority of significant cell types as well as many cytokines. And these cells circulate, particularly after any immunological procedure. Vaccinations and other forms of stimulation another reason this approach is particularly useful for human labour is that perturbations disclose a system's important interactivities, therefore the more and more different perturbations used, the more may be learned. With thousands of medicinal treatments, dozens of vaccinations, thousands of infectious diseases, and so on, humans have an embarrassment of riches [4].

Conclusion

In addition, different places of the world have diverse genetic variations and environmental exposures. Furthermore, because people live for a long time, longitudinal studies can be conducted to see how the immune system changes with age. However, inbred mice and monkeys can be highly beneficial in a systems approach as well; numerous immunological, viral, and genetic changes are well-known in mice and would swiftly and efficiently expose immune circuitry. Of course, going into mechanical detail would be much easier than with humans. Another rationale for parallel systems research in mice is to find variations in mouse versus human responses that could explain why mouse models of disease frequently fail to predict human responses or heterogeneity. Monkeys are appealing because they are more likely to elicit human-like responses, but they are a more limited option due to their high cost. Systems immunology, in my opinion, can be divided into four phases, as shown in the diagram. The first is a discovery phase, in which you utilize one of the many available technology platforms to 'cast a wide net' over a certain area or phenomenon of interest and see what you can find. This is mostly where we are presently, looking for predicted or surprising correlations between immune system components and diseases. A second phase would be to look at how different portions of the system interact in order to figure out if they correlate or anti-correlate. The third and fourth phases are when we have a good enough grasp of the primary activity drivers to forecast what will happen, first in a subsystem and then in the entire system [5].

Conflict of Interest

None

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