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Sommario/riassunto

Organ transplantation is a life-saving surgical procedure through which the functionality of a failing organ system can be restored. However, without the life-long administration of immunosuppressive drugs, the recipient’s immune system will launch a massive immune attack that will ultimately destroy the graft. Although successful at protecting the graft from an immune attack, long-term use of immunosuppressive drugs leads to serious complications (e.g., increased risk of infection, diabetes, hypertension, cardiovascular disease, and cancer). Moreover, recipients suffer from limited long-term graft survival rates due to the inability of current treatments to establish tolerance to the transplanted tissues. Thus, there is a great medical need to understand the complex network of immune system interactions that lead to transplant rejection so that new strategies of intervention can be determined that will redirect the system toward transplant acceptance while preserving immune competence against offending agents. In the past 20 years, the discovery and growing understanding of the positive and negative regulators of the activation of the immune system have fostered new interventional procedures targeting one or the other. While pre-clinical results proved the validity of these strategies, their clinical implementation has been troublesome. These results underscore the need for additional methods to determine the most effective interventions to prevent long-term transplant rejection. New tools of genomics, proteomics and metabolomics are being implemented in

powerful analyses that promise the development of better, safer personalized treatments. In parallel, theoretical modeling has emerged as a tool that transcends investigations of individual mechanistic processes and instead unravels the relevant mechanisms of complex systems such as the immune response triggered by a transplant. In this way, theoretical models can be used to identify important behavior that arises from complex systems and thereby delineate emergent properties of biological systems that could not be identified studying single components. Employing this approach, interdisciplinary collaborations among immunologists, mathematicians, and system biologists will yield novel perspectives in the development of more effective strategies of intervention. The aim of this Research Topic is to demonstrate how new insight and methods from theoretical and experimental studies of the immune response can aid in identifying new research directions in transplant immunology. First, techniques from various theoretical and experimental studies with applications to the immune response will be reviewed to determine how they can be adapted to explore the complexity of transplant rejection. Second, recent advances in the acquisition and mining of large data sets related to transplant genomics, proteomics, and metabolomics will be discussed in the context of their predictive power and potential for optimizing and personalizing patient treatment. Last, new perspectives will be offered on the integration of computational immune modeling with transplant and omics data to establish more effective strategies of intervention that promote transplant tolerance.