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Preface

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Guest Editors

Solid organ transplantation has become the therapy of choice for many end-stage organ diseases. Over the last two decades, the field of basic transplant immunology has developed rapidly and is beginning to provide the basis for many of the advances in the clinical field. The major challenge for clinicians and experts in laboratory medicine is to take this wealth of basic knowledge and translate it into clinically applied information that can be harnessed to improve the short and long term outcomes of solid organ transplantation. An important goal of translational transplant immunology is to provide to the clinician, prior to and after transplantation, the tools to prospectively predict an individual's risk for complications such as rejection, drug toxicities, malignancy and infection. Furthermore, with the introduction of novel therapies that may promote graft acceptance, assays that might predict graft acceptance will aid in the individualization of immunosuppressive drug regimens, optimizing efficacy while minimizing undesirable side effects.

The articles in this issue of *Clinics in Laboratory* Medicine provide insights into the role of cytokines and growth factors in promoting graft rejection and acceptance. Relevant information will be discussed regarding the key immune cells that participate in allograft rejection and acceptance and the state of the art laboratory tests that allow us to determine the specificity and magnitude of the immune response will be emphasized.

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The issue begins with a discussion of the role of dendritic cells (DC), the most potent antigen presenting cells, in promoting allograft rejection and acceptance. The function of DC and their ability to regulate alloreactivity is dependent on several factors including various chemokines and cytokines. Drs. Colvin, Matta and Thomson discuss the importance of chemokines in directing the trafficking of various subsets of DC and their potential impact on allograft outcomes.

The next article continues with the theme of trafficking of immune cells during allograft rejection. Drs. Schenk, Rosemblum and Fairchild provide an excellent overview of the role of chemokines released in the graft that engage chemokine receptors on T cells and other graft infiltrating leukocytes. The feasibility of the clinical use of chemokine receptor antagonists and the potential application of chemokines/chemokine receptors as biomarkers for ongoing immune response in the allograft are discussed.

In the third article, Drs. Wadia and Tambur summarize the importance and the type of cytokines that influence the immune response and promote either rejection (Yin) or acceptance (Yang) of the allograft. They emphasize the importance of the balance of these mediators that ultimately may determine the fate of the transplanted organ.

Drs. Benitez and Najafian concentrate on the need for non-invasive laboratory assays that provide a qualitative and quantitative assessment of alloreactive cytokine producing cells. They discuss several assays that can assess donor-specific alloreactivity pre-transplant and post- transplantation and how the clinician might use these assays for tailoring immunosuppressive therapy.

In the next article, Drs. Zarkhin and Sarwall review the *pros* and *cons* of assays that have been used to monitor allografts, not only for risk of rejection, but also for identifying stable patients who may benefit from minimization of immunossuppression. They expand on potential mechanisms of allograft tolerance and the development of non-invasive biomarkers to monitor a stable/quiescent state.

The genetic background of the patient and donor may also contribute to the overall outcome of transplantation. There are individuals that may have a genetic propensity to produce more pro-inflammatory cytokines and less regulatory cytokines and in those individuals the balance of the immune response is towards inflammation and rejection of the graft. In contrast, other individuals may exhibit a genetic profile that favors a lower immune reactivity and those patients may exhibit less rejection. The following three articles of this issue provide an overview of the clinical impact of cytokine gene and drug metabolism polymorphisms on allograft outcome.

Drs. Girnita, Webber and Zeevi discuss the impact of single nucleotide polymorphisms (SNPs) or combination of SNPs on thoracic transplantation. They emphasize how these results should be validated as independent risk factors associated with various outcomes in heart and lung transplantation. Dr. Nickerson provides an excellent review of the findings relative to

the role of gene polymorphism in the context of renal and liver transplantation. His review also examines the limitations of the current studies and the potential of this technology in the future care of transplant recipients. The last paper in this series by Dr. Burckart examines the potential role, and the hurdles that need to be overcome, to take full advantage of the science of pharmacogenomics to better understand key processes of drug selection and patient response after transplantation.

Dr. Webber and I would like to express our gratitude to all our collaborators who we were fortunate to work with for the creation of this issue. When we first discussed this project, we hesitated because of the very ambitious task of summarizing a clinical laboratory view of the cytokine network in transplant rejection and acceptance. Nevertheless, we took the challenge because we trusted in the help of great friends, well established experts in the field, who can share their knowledge, wisdom and above all can identify the challenges and opportunities we have in laboratory medicine.

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