

❖ THE NEED FOR PUBLIC-PRIVATE PARTNERSHIPS TO BOOST TRANSPLANTATION RESEARCH

Michel GOLDMAN

*Director, the Institute for Medical Immunology, Université Libre de Bruxelles, Charleroi, Belgium
Coordinator, the RISE consortium, 6th Framework Programme of the European Union*

Research networks dedicated to translation of immune tolerance in the clinic currently support pilot trials aiming at immunosuppression withdrawal in kidney or liver allograft recipients. Results obtained so far indicate that significant hurdles still need to be overcome before large scale clinical trials aiming at the induction of transplantation of tolerance can be safely launched. Therefore a key question for the transplantation community is: how can we translate our current knowledge of transplantation immunology into improved standard of care for solid organ transplant recipients? Beside the development of new pharmaceutical products with reduced toxicity and more comfortable mode of administration, tailoring immunosuppression according to the immune status of each patient would obviously represent a significant advance. Although a number of immunological methods have been proposed to monitor alloreactivity in humans, the only tests which are accepted as robust biomarkers are those measuring humoral parameters. It is well established that the presence before transplantation of antibodies directed against donor HLA molecules is a major risk factor for early severe renal graft rejection and more recently pre-transplant antibodies against major histocompatibility complex class I-chain A (MICA) antigens were also found to be associated with an increased frequency of renal allograft loss. Whereas tests assessing allo-specific T cell-mediated immune responses will probably be difficult to standardize and to introduce in routine clinical practice, several recent studies suggest that gene profiling might become a clinically relevant monitoring tool. Indeed, microarray analysis of peripheral blood mononuclear cells samples from cohorts of drug-free patients with a functional graft allowed to propose molecular fingerprints or signatures for operational tolerance in kidney and liver transplantation. In cardiac transplantation, a similar approach has been suggested to differentiate graft quiescence from rejection, although additional studies will be necessary for definitive qualification of this assay for the detection of cardiac transplant recipients with low risk of acute cellular rejection. Since it is likely that the most informative biomarkers should be sought at the graft level, one can predict that molecular imaging of transplanted organs will become an area of intense investigation in the near future

Patients' stratification: towards a new paradigm in transplantation medicine

As in other areas of modern medicine, future advances will depend on tailoring therapy according to individual patient needs. In the context of transplantation, this would mean to reduce immunosuppression to the minimal level required to prevent rejection. Stratification of transplant recipients will be based on established risk factors (e.g. cold ischemia time, preformed anti-HLA or anti-MICA antibodies) and on post-transplant monitoring of non-invasive biomarkers. Although several candidate biomarkers are available, the challenge now is to validate these biomarkers in order to make them acceptable by the medical community and regulatory agencies. Large clinical trials will have to be specifically designed for that purpose. In view of the important resources needed to implement such studies, public-private partnerships supporting collaborative efforts between the industry and academic centers appear as the most appropriate means to move this type of research forward.

Prof. Michel Goldman, will present What's hot, what's new in basic science during the Presidential & Awards Session – Wednesday 2 September, 11:00 - 13:30