Awards in Transplantation Science Recognize the Best Manuscripts Published in *Transplantation*

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The Transplantation Science Committee, together with The Transplantation Society and *Transplantation*, is pleased to announce the best manuscripts accepted by the *Journal* in 2014.

A selection committee including editors of *Transplantation*, The Transplantation Society, in addition to members and chairs of the Transplantation Science Committee, selected 2 winners from among a very competitive group of applicants.

The awards are named for 2 pioneering giants. The **Anthony P. Monaco Award** recognizing the best **translational submission** went to **Eytan Breman and coworkers** from Leiden University, The Netherlands, for their work exploring novel ways to monitor indirect allorecognition. The **Leslie Brent Award** for the best publication in basic transplantation research went to **Irene Kim and coworkers** from Cedars Sinai Medical Center, Los Angeles, California, for their work exploring the potential of IL-6 blockade in allosensitization.

The **Anthony P. Monaco Award** for the most outstanding translational paper for 2015 goes to **Breman and colleagues**[1] for their manuscript entitled "HLA Monomers as a Tool to Monitor Indirect Allorecognition." Transplantation has become a standard and effective therapy for many life-threatening conditions, as indeed kidney transplantation represents the gold standard of treatment for kidney disease. The success of transplantation rests upon the use of powerful immunosuppressive drugs that prevent the rejection response. However, even with modern immunosuppression and the reduction in acute graft loss, many grafts are still lost to late rejection. For example, development of antibodies against HLA molecules, particularly class II donor-specific antibodies, strongly associates with long-term poor kidney graft outcomes.[2] Recognition of donor antigens after transplantation can occur through distinct pathways of antigen presentation; namely, direct presentation of non-self HLA on donor cells or via an indirect pathway, whereby donor-derived peptides are presented in the context of self-MHC on recipient cells (see excellent review of allorecognition[3]). It is considered that the indirect pathway plays a major role in the development of humoral rejection, making this pathway of extreme interest clinically and potentially valuable as a read-out for both monitoring and predicting patient graft outcomes. However, to date, there has been no robust system to define the indirect pathway of T cell alloreactivity. In the manuscript by Breman and colleagues,[1] a system was established and defined whereby indirect activation of donor reactive CD4 T cell clones could be monitored. Using a CD4 T cell clone of known specificity directed toward HLA-A2 peptides restricted by HLA-DR1, Breman et al, could show strong and dose-dependent IFN-γ responses when co-cultured with HLA-DR1-positive monocytes or unpurified PBMCs. Similar response was achieved with purified HLA monomers, suggesting the system could be standardized. Importantly, the IFN-γ responses were specific for indirect presentation, as no CD8 T cell responses were detected in the same assay. Together with methods already in hand to measure direct alloreactivity, such as the mixed leukocyte reaction (MLR), cytotoxic T cell precursor assay, and the IFN-γ enzyme-linked immunosorbent spot (ELISPOT), the current assay can provide additional information on the development of an individual patient's alloresponse. Inclusion of new information on the indirect pathway could aid in the development of a precision medicine approach to managing immunosuppression needs and predicting graft outcomes.

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The **Leslie Brent Award** for the most outstanding basic science paper for 2015 goes to **Kim and colleagues** for their manuscript entitled "Anti-Interleukin 6 Receptor Antibodies Attenuate Antibody Recall Responses in a Mouse Model of Allosensitization."[4] Donor-specific antibodies that are either present pretransplantation or develop after transplantation are detrimental to graft survival and, in particular, to long-term outcomes where they are thought to play a role in chronic allograft dysfunction. Humoral immune responses are especially difficult to control, partly because of the challenge of targeting a complex interplay of cellular interactions between T, B, and plasma cells at the correct time. Methods to control alloimmune antibody responses are therefore critical to improving transplant outcomes in the long term. In the prize manuscript, Kim and colleagues examine the ability of a monoclonal antibody directed against the interleukin-6 receptor (IL-6R) in an effort to suppress antibody responses. IL-6 is a pro-inflammatory cytokine that is elevated in virtually all inflammatory states.[5] One function of IL-6 is the promotion of T, B, and plasma cell activation and maturation. In particular, IL-6 acts to activate follicular T helper cells to promote an antibody response. In the elegant study from Kim et al, the authors used a presensitized mouse skin transplantation model to examine recall antibody responses to the skin graft. Levels of DSA

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were examined after sensitization with or without anti-IL-6R treatment. Interestingly, treatment not only reduced the recall alloantibody response but increased the relative proportion of regulatory T cells in the spleens of mice. Moreover, anti-IL-6R treatment suppressed the production of IgG in allosensitized mice without impacting the proliferation of cells when tested in an in vitro assay. The group is now investigating the use of a humanized anti-IL-6R antibody (tocilizumab) together with IVIG in HLA-sensitized kidney transplant candidates as a method of desensitization. Results are eagerly awaited.

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Both the Leslie Brent Award and the Anthony P. Monaco Award are wonderful opportunities to highlight outstanding publications in *Transplantation*. We are looking forward to reviewing the best manuscripts from 2015 and will accept applications until June 30, 2016.

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