Frontiers in immunology and immune tolerance: new perspectives

Song Guo Zheng

In February of 2012, an International Forum entitled "Frontiers in Immunology and Organ Transplantation" was held in Shanghai, China. In attendance were 200 physicians and scientists from China, USA and the European Union. The conference, organized by Song Guo Zheng at University of Southern California, co-organized by Xin-Xiao Zheng at University of Pittsburg, and Huimin Fan at Tongji University, featured recent developments in the field of immune regulation and tolerance. The main and key findings reported at the meeting are summarized here.

The conference began with a keynote speech during which Xuetao Cao, an eminent Immunologist and President of Chinese Medicine Academy of Science, presented his studies focusing on the role of innate immune responses in immune tolerance. His group has independently investigated the regulatory DC subset and found that the long-term control of MTB infection, with 200 physicians and scientists from China, USA and the European Union. The conference, organized by Song Guo Zheng at University of Southern California, co-organized by Xin-Xiao Zheng at University of Pittsburg, and Huimin Fan at Tongji University, featured recent developments in the field of immune regulation and tolerance. The main and key findings reported at the meeting are summarized here.

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stem cells and immune responses. He demonstrated that inflammatory cytokines induce mesenchymal stem cells to release chemokines and NO. Chemokines and NO work in concert to exert a powerful immune suppressive effect, controlling immune and inflammatory diseases.

Regulatory T cells are another hot topic that was widely discussed in the conference. Song Guo Zheng (University of Southern California) has systematically described the development and function of CD4^+CD25^+Foxp3^+ Treg cells. While natural Treg cells are unstable and less suppressive under inflammatory conditions, he reported that all-trans retinoic acid, a vitamin A derivative, can stabilize murine and human natural Treg cells in an inflammatory milieu. Dr Zheng also described the unique role of transforming growth factor beta (TGF-β)-induced Treg cells in established autoimmune diseases. Using TGF-βRII DC conditional knock-out (KO) mice, he demonstrated that iTreg cells can induce tolerogenic DCs through TGF-β signals on DC and suggests this can lead to a phenomenon called ‘infectious tolerance’ and this mechanism can account for the long-term effect of Tregs in the treatment of autoimmune diseases.

Powel Kiela (University of Arizona) has developed TGF-βRII DC conditional KO (DC-Tgfbr2 KO) mice and reported the phenotypes of this novel mouse model. He has found that these mice develop highly activated self-reactive T cells and die prematurely with multi-organ autoimmune inflammation. Treg cell alteration in these mice is possibly associated with the breakdown of T and B cell tolerance. Despite no significant differences in antigen presentation, Tgfbr2-deficient DCs are more pro-inflammatory and incapable of directing antigen-specific Treg conversion due to overexpression of interferon-gamma. DC-Tgfbr2 KO mice show abnormal expansion of CD25^+Foxp3^+ Tregs with attenuated Foxp3 expression in vivo. Therefore, TGF-β signaling in DCs is critical in the control of autoimmunity through both Treg-dependent and independent mechanisms.

Feili Gong (Middle China University Medical School) has discussed the strategies to induce transplantation tolerance, including constructing hematopoietic chimerism, allogeneic-specific active immunity, blocking alloreactive T cell responses, preventing graft cell damage, regulating the differentiation of T cell subsets and adoptive transfer of immunocytes. He also updated the current status of research on the prevention of organ transplant rejection. Dr Gong suggests that humoral immunity, innate immunity, and chronic rejection responses should be strongly considered as mechanisms to be manipulated into order to control immune rejection responses. He also encouraged the development of more appropriate animal models for investigating relevant mechanisms.

Shuzhong Guo (Xi-Jing Hospital at the Fourth Military Medical University in China) and his colleagues reported the first case of rabbit allogeneic face transplantation in the world. They then also established human allogeneic face transplantation and demonstrated that the combination of bone marrow-derived cells and immuno suppressive reagents can significantly prevent the face skin rejection. This study is highly significant for patients with face injury.

Shusen Zheng (Zhejiang University Medical School) and his colleagues reported several interesting liver transplantation cases. Among them, they have conducted the two donors to one recipient transplantation case where two pieces of the liver from two donors were transplanted into one recipient and it has been survived >2 years so far, demonstrating their advanced clinical skill in the field.

The conference was then concluded by Zhong-Min Liu, President of Shanghai East Hospital at Tongji University and Chair of Department of Surgery with thanks to the organizers, speakers, and attendees. Jian-Guang Xu, a surgeon at the Fudan University Huashan Hospital and Head of Department of Health in Shanghai made a further conclusion speech where he also expressed his support for the development of high level of science in Shanghai. The conference will be held again in 2 years, on a date to be announced.