

# ABSTRACT

We have utilized several models to describe the effects of interleukin (IL)-21 in chronic immune responses. A mouse model of chronic heart rejection was employed to demonstrate that an immune system devoid of IL-21 is largely incapable of developing cardiac allograft vasculopathy (CAV). This was true whether the transplant recipient mouse was IL-21 knock-out, a deficiency resulting in lack of IL-21 production, or a wildtype mouse treated with IL-21 receptor fusion protein (IL-21R.Fc) to block IL-21 function. Furthermore, deficiency of the BATF transcription factor regulating IL-21-dependent T follicular helper (Tfh) and T helper 17 (Th17) cells prevented CAV. In contrast, a mouse model of kidney allograft rejection demonstrated no dependency on IL-21 for the development of interstitial fibrosis (IF) and tubular atrophy (TA). These results created a new paradigm that CAV depends on IL-21. Finally, we showed that IL-21R.Fc was able to permanently reverse the development of type 1 diabetes (T1D). In summation, IL-21 is a chronic phase cytokine that is critical for the development of immune responses and it can be targeted clinically for therapeutic benefit.

## DISSERTATION COMMITTEE

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## DISSERTATION PRESENTATION

**Caitlin Baum**

**June 13, 2017**

**The Role of  
Interleukin-21 in  
the Chronic  
Rejection of  
Transplant  
Allografts and the  
Development of  
Type 1 Diabetes**

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Ph.D. in  
Biomedical Sciences

## ABSTRACTS & PRESENTATIONS

### PUBLICATIONS

**PD-1-dependent restoration of self-tolerance in the NOD mouse model of diabetes after transient anti-TCR $\beta$  mAb therapy.** Schroder PM, Khattar M, Baum CE, Miyahara Y, Chen W, Vyas R, Muralidharan S, Mierzejewska B, Stepkowski SM. *Diabetologia*. 58:1309-1318; 2015.

**Early acute antibody-mediated rejection of a negative flow cross-match 3rd kidney transplant with exclusive disparity at HLA-DP.** Mierzejewska B, Schroder PM, Baum CE, Blair A, Smith C, Duquesnoy RJ, Marrari M, Gohara A, Malhotra D, Kaw D, Liwski R, Rees MA, Stepkowski S. *Human Immunol*. 75(8):703-708; 2014.

**Current approaches in national kidney paired donation programs.** Mierzejewska B, Durlak M, Lisik W, Baum C, Schroder P, Kopke J, Rees M, Stepkowski S. *Ann Transplant*. 18: 112-124; 2013.

**Optimizing the use of regulatory T cells in allotransplantation: recent advances and future perspectives.** Baum CE, Mierzejewska B, Schroder PM, Khattar M, Stepkowski S. *Expert Rev. Clin. Immunol*. 9(12), 1303-1314; 2013.

### Future Plans

Caitlin plans to stay in Toledo for at least two years while she completes medical school.

**IL-21 Targeted Immune Therapy Regulates Creation of Tertiary Lymphoid Organs in Chronic Transplant Rejection.** Caitlin Baum, Mithun Khattar, Paul Schroder, Wenhao Chen, Stanislaw Stepkowski. Presentation, American Transplant Congress. Philadelphia, PA. May 2015.

**IL-21 Is a Key Regulator Coordinating Multiple Immune Responses in Chronic Allograft Rejection.** Mithun Khattar, Caitlin Baum, Paul Schroder, William Baldwin, Wenhao Chen, Stanislaw Stepkowski. Presentation, World Transplant Congress. San Francisco, CA. Jul 2014.

**Locally-Delivered CD4+CD25highFoxp3+ Regulatory T Cells Combined with Systemic KRP203 Therapy Induces Tolerance to Islet Allografts.** Caitlin E. Baum, Mithun Khattar, Ronghai Deng, Barry D. Kahan, Paul M. Schroder, Tammy Phan, Lynne P. Rutzky, Stanislaw M. Stepkowski. Presentation, American Transplant Congress. Seattle, WA. May 2013.

**EpHLA Software: A Tool to Perform Eplet-based Donor Selection for Sensitized Patients in a Kidney Paired Donation Program.** Caitlin E. Baum, Beata Mierzejewska, Herton Sales Filho, Annette Blair, Michael Rees, Jonathan Kopke, Rene Duquesnoy, Marilyn Marrari, Paul Schroder, Stanislaw Stepkowski. Poster, Cutting Edge of Transplantation. Chandler, AZ. Feb 2013.

**Anti-TCR $\beta$  mAb exerts potent effects on T cells to prolong islet allograft survival.** Ronghai Deng, Paul Schroder, Mithun Khattar, Caitlin Baum, Zhiyong Guo, Xiaoshun He, Wenhao Chen, Stanislaw Stepkowski. Presentation. 41st Annual Autumn Immunology Conference. Chicago, IL. Nov 2012.

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