ABSTRACT

We have explored the role of Cd40 signaling in the kidney on the development of renal interstitial fibrosis (IF) in a rat model of chronic renal allograft rejection. To this end, we used genetically hypertensive salt-sensitive Dahl (Dahl-S) and Dahl-S *Cd40 mutant* (*Cd40*^{mutant}) rats (both displaying hypertension ≈180 mm Hg at 6 weeks of age). These Dahl-S or *Cd40*^{mutant} rats served as kidney donors to normotensive, allogeneic Brown Norway (BN) rats in a transplant study to model chronic renal allograft rejection. Recipients animals were euthanized at 97-129 days post-transplant, and the native and transplanted kidneys were harvested and examined for IF. We hypothesized that proximal tubular CD40 signaling regulates IF in chronic renal allograft rejection, and that recipients of a renal allograft from a *Cd40*^{mutant} donor will show reduced IF. All normotensive BN recipients were treated for 30 days with tacrolimus at a dose 1.5 mg/ in order to block acute rejection according to standard protocols. BN recipients of *Cd40*^{mutant} kidneys displayed significantly reduced IF in comparison to recipients of kidneys from Dahl-S rats. Kidney transplants from *Cd40*^{mutant} donors had reduced collagen 1A1 (COL1), COL3A1 (COL3), transforming growth factor β (TGF-β), MCP-1, and PAI-1 expression compared to Dahl-S kidney grafts, suggesting a CD40 mechanism involving PAI-1/MCP-1 signaling for fibrosis. These data for the first time connect IF with CD40 signaling in proximal tubules in both hypertension and chronic allograft rejection.

COLLEGE OF MEDICINE AND LIFE SCIENCES
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THESIS PRESENTATION
by

Vassili Bletsos

July, 26, 2018

The Role of CD40 Signaling in Chronic Renal Allograft Rejection in a Hypertensive Rat Model

M.S. in Biomedical Sciences

FUTURE PLANS

This fall, Vassili will be starting a post-baccalaureate certificate program at Duquesne University in Pittsburgh, Pennsylvania to prepare to apply to dental school in the following application cycle.

INVITED ORAL PRESENTATIONS

VS Bletsos, J Breidenbach, ST Haller, and SM Stepkowski. The Role of CD40 Signaling in Chronic Renal Allograft Rejection in a Hypertensive Rat Model. Presented at the American Transplantation Congress Annual Meeting, June 2-6 2018, Washington State Convention Center, Seattle, Washington.

OTHER PRESENTED ABSTRACTS

VS Bletsos, J Breidenbach, ST Haller and SM Stepkowski. Role of CD40 Signaling in Chronic Renal Allograft Rejection in a Hypertensive Rat Model. Presented at the 2018 Graduate Research Forum, University of Toledo Health Sciences Campus March 2018, Toledo, Ohio.