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Tumor Necrosis Factor a Blockade to Ameliorate Renal ischemia Reperfusion Injury

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human (transplantation) setting. As the authors have already pointed out in their discussion, a transplant model was not used. As a result, their data will only elucidate the effect of infliximab on the acute, nonspecific immune response to a standardized amount of warm ischemic tissue injury. These kidneys did not suffer from any cold ischemic injury and the associated additional detrimental effect of rapid organ rewarming at reperfusion. Moreover, the model did not incorporate an alloresponse. We do not know the additional effect of TNF- α blockade in the context of standard clinical immunosuppressive agents, such as calcineurin inhibitors, mycophenolate mofetil, and prednisolone. Also, we cannot make a comparison between infliximab treatment and, for example, induction therapy with an anti-CD25 or anti-CD52 biological agent among the aforementioned common immunosuppressants. Finally, the study makes a comparison between the effect of splenectomy and anti-TNF- α treatment on IR injury. The authors assume that this effect is similar, but they have not made direct comparisons. Although the end result of both interventions in terms of reduced proinflammatory cytokine release and improved renal function may be comparable, the underlying molecular mechanisms could still be very different. However, Nagata and colleagues have taken an important first step towards unraveling the mechanism of action of TNF- α inhibition in renal IR injury. It should be applauded that they have not restricted their results to measurement of injury markers. One of the merits of this article is that it also demonstrated markedly reduced postischemic serum creatinine and urea levels in infliximab-treated animals, which is the best indication so far that TNF- α blockade might have the potential to improve clinically

relevant end points after IR injury. Forging ahead to the human renal transplant setting will be the next step to assess the potential value of infliximab as immunosuppressive therapy in this area.

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