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Anti-CD45RB antibody therapy attenuates renal ischemia-reperfusion injury by inducing regulatory B cells

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Objectives: Regulatory B cells (Bregs) are a new B cell subset that suppresses immune responses. Recently, both anti-CD45RB and anti-Tim-1 treatments have been found to regulate immune responses by inducing Bregs; however, the role of Bregs in renal ischemia-reperfusion injury (IRI) has not been shown.

Methods: We investigated impacts of Bregs and anti-CD45RB on IRI and its mechanisms using mouse models of bilateral renal IRI.

Results:

Adoptive transfer of Bregs prior to or following IRI attenuated renal IRI. Anti-CD45RB treatment with or without anti-Tim-1 prior to IRI increased the renal infiltration of $CD19^{+}Tim\text{-}1^{+}$ Bregs and regulatory T cells. Anti-CD45RB decreased serum creatinine levels, pathologic injury score, and tubular apoptosis. Levels of IL-1β, IL-6, MCP-1, IFN-γ, and IL-17 were decreased, whereas IL-10 was increased in the CD45RB group. Following IRI, anti-CD45RB with or without anti-Tim-1 also induced Bregs, thereby improving renal function and tubular regeneration. In RAG1 knockout mice with B cell transfer, TCRα knockout mice, and wild-type mice with T cell depletion, anti-CD45RB increased Bregs and attenuated IRI. However, anti-CD45RB did not attenuate IRI in RAG1 knockout mice with T cell transfer or μMT mice and induced only mild improvement in wild-type mice with B cell depletion. Furthermore, B cells from IL-10 knockout mice did not show anti-CD45RB-mediated renal protection against IRI, in contrast to those from wild-type mice.

Conclusions: Anti-CD45RB treatment attenuated acute renal injury and facilitated renal recovery after IRI through induction of $IL\text{-}10^{+}$ Bregs. The present study suggests anti-CD45RB as a potential therapeutic strategy in renal IRI.