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**non-HLA-antibodies targeting Angiotensin type 1 receptor and antibody mediated rejection.**

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**Source**

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**Abstract**

Antibody-mediated mechanisms directed against non-HLA related targets may exert negative impact on allograft function and survival. Angiotensin type 1 receptor (AT(1)R) emerges as a functional target for non-HLA allo- and autoantibodies (AT(1)R-Abs) comprising of IgG1 and IgG3 subclasses. Proof of concept for pathophysiologic relevance of AT(1)R-Abs in antibody mediated rejection (AMR) in renal transplants was provided by passive transfer studies in animal model and therapeutic rescue of patients. Although AT(1)R-Abs may belong to complement fixing IgG subclasses, C4d positivity in renal transplant biopsies was not frequently detected implicating complement independent mechanisms of injury. AT(1)R-Abs exert direct effects on endothelial and vascular smooth muscle cells by induction of Erk1/2 signaling and increased DNA binding of transcription factors associated with pro-inflammatory and pro-coagulatory responses. Establishment of enzyme-linked immunosorbent assay employing extracts of cells overexpressing AT(1)R in its native conformation was instrumental for recent studies in independent cohorts. Assessing the AT(1)R-Ab-status along with the HLA-antibodies may help to identify patients at particular risk for irreversible acute or chronic allograft injuries and improve overall outcomes. This review summarizes the current state of research in AT(1)R biology, development in diagnostic strategies, discusses recent clinical studies, and provides perspectives on further refinements in understanding AT(1)R-Ab-actions.

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