

Abstract 77-P

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**Title:** HIGHER RISK OF KIDNEY GRAFT FAILURE AFTER REJECTION IN THE PRESENCE OF ANTIBODIES AGAINST ANGIOTENSI

**Abstract:**

**Aim:** Antibodies against AT1R have been observed in patients with acute rejection of kidney and chronic rejection of heart transplants. Our study sought to determine if AT1R antibodies are associated with graft failure after rejection.

**Methods:** We enrolled a total of 133 kidney recipients who had biopsy-proven rejection episodes. Serial post-transplant sera (n=873) were tested for the presence of both anti-AT1R and donor specific HLA antibodies (DSA).

**Results:** High levels of anti-AT1R were more prevalent in the failed patients than functioning patients (87% vs. 13%,  $P=0.0001$ ); 32% of failed patients had high anti-AT1R levels vs. 4% of the other patient group. Lower graft survival was observed in patients with both high-level anti-AT1R and DSA than in patients with DSA alone ( $P=0.0007$ ). Multivariate analysis showed that a high level of AT1R antibody is an independent predictor of poor graft survival and has the highest risk of graft failure (HR: 2.63,  $P=0.002$ ). Patterns of increasing development of high-level anti-AT1R were observed in 55% of the failed patients with high-level anti-AT1R. In contradistinction, high-level anti-AT1R detected in functioning patients were either transient (n=2) or stable (n=1).[figure1]

**Conclusions:** This longitudinal analysis of serial post-transplant sera showed the significant association of high levels of anti-AT1R with graft failure after rejection episodes. While high-level anti-AT1R is independently associated with the highest risk of graft loss, the development of both DSA and high-level anti-AT1R may augment the detrimental effect that leads to lower graft survival. The importance of monitoring and therapeutic targeting of non-HLA as well as HLA is emphasized.

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**Authors:** Michiko Taniguchi<sup>1</sup>, Lorita M. Rebellato<sup>2</sup>, Junchao Cai<sup>3</sup>, Paul G. Catrou<sup>2</sup>, Kimberly P. Briley<sup>2</sup>, Judy Hopfield<sup>1</sup>, Paul I. Terasaki<sup>3</sup>.

**Institutions:** <sup>1</sup>Research II, One Lambda, Inc., Los Angeles, CA, USA; <sup>2</sup>East Carolina University, Brody School of Medicine, Greenville, USA; <sup>3</sup>Terasaki Foundation Laboratory, Los Angeles, CA, USA.