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Anti-Neu5Gc responses in kidney allograft recipients after treatment with Rabbit Anti-Thymocyte Globulins

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Non-human immunoglobulins including Anti-Thymocyte Globulins (ATG) display galactose-α1,3-galactose (α-Gal) and N-glycolyneuraminic acid (Neu5Gc) glycans which are highly immunogenic in humans, due to loss-of-function mutations of the key genes involved in their synthesis. Because ATG is the most popular induction treatment in allograft recipients, it is important to decipher the response against these antigens, particularly against Neu5Gc, which has been associated to formation of immune complexes and to xenosialitis, an systemic inflammation possibly causing damages to the transplant and to the host.

We conducted a prospective study on the response against α-gal and Neu5Gc after ATG induction treatment on a kidney transplant recipient cohort (n=60) compared to transplanted patients not receiving ATG (n=30). Using quantitative ELISA and sialoglycan microarrays, we analyzed quantitatively and qualitatively the response against these carbohydrates.

We show in a serial analysis that, despite observing a drop in the levels of anti-Neu5Gc antibodies compared to the pre-existing levels at 6- and 12-months post-graft likely due to the immunosuppression, there was a significant increase in the anti-Neu5Gc levels at 6 months post-graft, between the ATG-treated and non-treated patients (p=0.007). Anti-α 1,3-Gal antibodies, in contrast, remained unchanged. Furthermore, the sialoglycan microarray analysis shows greater anti-Neu5Gc reactivity against multiple different Neu5Gc-containing glycans in patients treated with ATG, as well as a greater shift in their anti-Neu5Gc repertoire for some Neu5Gc specificities that were lacking in the sera at baseline.

In conclusion, kidney graft recipients receiving ATG develop anti-Neu5GC antibodies. These finding warrant further investigation into their possible role in graft dysfunction.

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