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ANTI-GAL AND ANTI-NEU5GC RESPONSES IN NON-IMMUNOSUPPRESSED PATIENTS FOLLOWING TREATMENT WITH ANTI-THYMOCYTE GLOBULIN

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Background: Anti-lymphocyte or anti-thymocyte globulins (ATG) are polyclonal animal-derived IgGs, widely used as immunosuppressive drugs in the prevention or treatment of organ or bone-marrow allograft rejection, graft vs. host disease, and some autoimmune diseases. However, animal-derived glycoproteins are also strongly immunogenic and rabbit ATG induce serum sickness disease in patients when no additional immunosuppressive drugs are used.

In this study, we analyzed sera from patients of the START randomized phase II clinical trial, which evaluated the effect of Thymoglobulin[®] therapy in the auto-immune context of new-onset type 1 diabetes. The aim was to analyze various anti-ATG specificities developed by the patients, and especially anti-galactose- α 1-3-galactose (Gal) and anti-Neu5Gc. These two xeno-carbohydrate epitopes are present on rabbit IgG glycans and are lacking in humans.

Methods: Serial sera from patients at pre- or post-ATG infusion time points (1, 3, 6 and 12 months) were analyzed by ELISA for anti-ATG, anti-Gal and anti-Neu5Gc IgGs and IgMs. Results were compared to placebo-treated patients and healthy donors matched for gender and age.

Results: We showed that diabetic patients have pre-existing antibodies against the three specificities before treatment, although levels are similar to healthy individuals. ATG treatment resulted in highly significant increases of both IgMs (for anti-ATG and anti-Neu5Gc) and IgGs (for anti-ATG, -Gal, and -Neu5Gc), peaking at one month and still detectable one year post-infusion.

Conclusions: Treatment with rabbit polyclonal IgGs in the absence of additional immunosuppression results in a vigorous humoral response against Gal and Neu5Gc epitopes, contributing to an inflammatory environment that may compromise the efficacy of ATG therapy. Moreover, as diet-derived Neu5Gc is found on endothelial cells, elicited anti-Neu5Gc antibodies could play a role in vascular inflammation, with potential long-term clinical consequences.