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LOSS OF GLYCAN MODIFYING GENES, EFFECTS ON DIVERSITY, IMMUNITY AND REPRODUCTION

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All primate cells are coated by a complex layer of glycans (oligo- and polysaccharides) often attached to glycoproteins and glycolipids. Glycan repertoires differ between cells, tissues, populations and species. There are strikingly discontinuous patterns of glycan distribution across primate taxa. Glycans are used both, as molecular markers of self, mediating immune tolerance and cellular dialogues within an individual, or as markers of non-self by providing targets for innate immune receptors. In addition, the absence of certain glycans is often associated with the production of antibodies against the same glycans. The fixation of loss-of-function mutations in genes coding for glycan modification can affect the glycan repertoire of entire lineages. By analogy, such systems form "blood groups" at higher taxonomic levels including entire species (humans lacking the sialic acid Neu5Gc) or even parvorders (Catarrhines, lacking the alpha-Gal epitope). Pathogen exploitation of primate host glycans for recognition, attachment or manipulation is often assumed as the driving force behind primate glycan diversity. However, pathogen-mediated selection by itself, is more likely to result in balanced polymorphisms. We tested the notion that Glycan-based sexual selection could lead to fixation of glycan differences between species as mismatches between sperm or fetal glycans and maternal immunity may lead to reproductive incompatibility. In the process, this can contribute to protective glycan diversity, acting as a barrier to cross-species infection by enveloped viruses. We will present data from breeding experiments with mice genetically engineered to lack Neu5Gc, that strongly support this notion.

Keywords: glycosylation, self/non-self, viral infection, gene inactivation