Fc-linked N-glycosylation of murine IgG1 variants

P-37-015

O. Zaitseva[I], J. Krištić[I], M. Pezer[I], G. Morahan[II,III], G. Lauc[I,IV]

[I]Genos Glycoscience Research Laboratory, Zagreb, Croatia, [II]University of Western Australia, Center for Medical Research, Perth, Australia, [III]Harry Perkins Institute of Medical Research, Centre for Diabetes Research, Nedlands, Australia, [IV]University of Zagreb, Faculty of Pharmacy and Biochemistry, Department of Biochemistry and Molecular Biology, Zagreb, Croatia

The structure of N-glycans attached to the Asn297 in fragment crystalizable (Fc) region of immunoglobulin G (IgG) affects the affinity of IgG to its ligands and consequent immune responses. Great inter-individual variation in Fc-linked N-glycome of IgG is observed both in human populations and between mouse strains. Mice have four IgG subclasses (IgG1, IgG2a/c, IgG2b and IgG3) each with distinct immune functions and specific N-glycosylation profile. In our recent study we identified a single nucleotide change (rs51376262) in the *Ighg1* gene as one of the candidate genetic variants influencing total IgG N-glycosylation in mice. Allelic state of rs51376262 defines the amino acid residue (phenylalanine or isoleucine) preceding the N-glycosylated Asn297 in the Fc of mouse IgG1 subclass. The aim of our study was to test if this mutation is associated with the changes in IgG1 Fc-linked N-glycome. We analyzed IgG Fc-glycopeptides with liquid chromatography-mass-spectrometry in 95 strains of the powerful Collaborative Cross (CC) resource of recombinant inbred mouse strains (Geniad Pty Ltd, Animal Resources Centre, Murdoch, WA, Australia). The CC strains were genotyped using the MegaMUGA platform (GeneSeek; Lincoln, NE). We performed quantitative trait loci mapping of subclass-specific IgG Fc-linked glycosylation traits using online tools (www.sysgen.org/GeneMiner). We observed that lower levels of galactosylated, mono- and disialylated N-glycans in the IgG1 Fc-linked glycome were associated with the 296Ile IgG1 variant. Functional studies would be needed to obtain further proof of the effect of amino acid composition of mouse IgG1 heavy chain on its N-glycosylation.