Glycomics and glycoproteomics for mechanisms of healthy longevity

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We previously reported that characteristic *N*-glycans of plasma proteins in semi-supercentenarians (≥ 105 years old), who are recognized as a model of human longevity, were highly branched and sialylated *N*-glycans, and that one of carrier-proteins of these characteristic *N*-glycans was haptoglobin. In turn, we address to clarify the biological roles of these characteristic *N*-glycans in healthy longevity. Highly branched and sialylated *N*-glycans are known to be involved in inflammation, and so we hypothesized that these characteristic *N*-glycans would prevent inflammaging resulting in healthy extreme longevity. In this study, we tried to examine the relationship between *N*-glycans of plasma proteins and inflammaging using longitudinal and cross-sectional study, and to validate the biological roles in anti-inflammation mechanisms of these characteristic *N*-glycans using *N*-glycans remodeling mice.

Subjects were extracted using CRP levels as an inflammation marker, from the 3-year SONIC (Septuagenarians, Octogenarians, Nonagenarians Investigation with Centenarians) longitudinal cohort study and cross-sectional Japanese centenarian study. In plasma samples of subjects, we examined some inflammatory cytokines using ELISA. Furthermore, to prepare *N*-glycans remodeling mice, we used *in vivo* transfection technique with plasmid of human MGAT5 (α-1,6-mannosylglycoprotein 6-β-*N*-acetyl-glucosaminyl-transferase), which is involved in synthesis of highly branched *N*-glycans.

In CRP-increasing group, IL-6 and CD63 were increased significantly for 6 years, while in CRP-stable group, these cytokines were not changed. In centenarians with high CRP levels, IL-6 was more abundant than those in centenarians with low CRP levels. Furthermore, we examined hMGAT5 expression in mice liver and *N*-glycans of plasma proteins, resulting that *N*-glycans remodeling mice, which have highly branched *N*-glycans on plasma proteins abundantly, could be prepared 2 days after *in vivo* transfection. In future, we will perform *N*-glycoproteomics and multivariate analyses in cohort studies, and will clarify anti-inflammation mechanisms through haptoglobin with highly branched *N*-glycans in mice study.