



P8 O-GlcNAcylation Increases Constriction in Common Carotid Artery of Senescent-Accelerated Female Mice

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ABSTRACT

The glycosylation with *O*-linked-*N*-acetylglucosamine (*O*-GlcNAc) is an enzymatic process found on nuclear and cytoplasmic proteins. Augmented levels of *O*-GlcNAc-modified proteins have been associated to cardiovascular disease (CD) in male. However, the association of *O*-GlcNAc and CD in females it's not understood. Increased risk of CD in women is linked to menopause and occurs about 10 years later than in men. We tested the hypothesis that aging in females promotes vascular dysfunction, which is aggravated by augmented *O*-GlcNAc. We used 8-month-old female senescence-mice (SAMP8) and control (SAMR1). After euthanasia, the carotid artery (CA) was carefully removed and cleaned. The segments of CA were incubated for 24h in DMEM containing vehicle/or/Thiamet G (10-6M), a potent inhibitor of the *O*-GlcNAcase. Vessels from both groups were carefully mounted as ring preparations in standard organ chambers. Concentration-response curves to U46619 and phenylephrine (PE) (10-10 to 10-4M) were performed in vessels with endothelium in the presence or not of a COX inhibitor. Results are presented as mean \pm SEM, $n = 6$. Statistical analysis: ANOVA One-way, followed Bonferroni. $p < 0.05$. CA of SAMP8 ($R_{max}127 \pm 10$) exhibited increased PE-induced vasoconstriction, compared to SAMR1 ($R_{max}77 \pm 5$), which was abolished in the presence of the COX inhibitor. mRNA expression of COX-1/COX-2 was similar in both groups, but the eNOS decreased in CA of SAMP8. *O*-GlcNAcylation increased vasoconstriction in SAMP8 but not in SAMR1 female mice, indicating an important correlation between *O*-GlcNAcylation and aging process. Conclusion: the senescence is associated with vascular dysfunction mediated by abnormal activity of COX and eNOs, which is aggravated by augmented *O*-GlcNAcylation. FAPESP (2017/25116-2).

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