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Grant Title: Biosynthesis and function of O-GalNAc glycans in the cell nucleus

Abstract

Glycosylation is a very frequent post-translational modification in proteins, and the initiation of O-GalNAc glycosylation has been recently described on relevant nuclear proteins. Here we evaluated the nuclear elongation of a second sugar residue in the biosynthesis pathway of O-GalNAc glycans to yield the terminal core 1 glycan (C1G, Galβ3GalNAcαSer/Thr). Using confocal microscopy, enzymatic assay, western blot, affinity chromatography and mass spectrometry, we analyzed intact cells, purified nuclei and soluble nucleoplasms to identify the essential factors for C1G biosynthesis in the cell nucleus. The enzyme C1GalT1 responsible for C1G synthesis was detected inside the nucleus, while catalytic activity of C1Gal-transferase was present in nucleoplasm and purified nuclei. In addition, C1G were detected in the nucleus inside of intact cells, and nuclear proteins exposing C1G were also identified. The present evidences are the first demonstration of core 1 O-GalNAc elongation on proteins in the human cell nucleus. These findings reveal a novel post-translational modification on nuclear proteins, with relevant repercussion in epigenetic and chemical biology areas.