SELECTED TALK:

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The complexity of *O*-GlcNAc-mediated regulation of galectin expression and secretion

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Post-translational glycosylation of intracellular proteins with *O*-linked N-acetylglucosamine (*O*-GlcNAcylation) is an important mechanism cells use to control both gene expression profiles and trafficking of regulatory molecules such as transcription factors and hormones. Emerging evidence suggests that *O*-GlcNAc homeostasis is specifically relevant for processes regulating cellular stress responses, cancer cell stemness, and cellular differentiation. My laboratory elaborates the hypothesis that this regulation involves galectins, soluble β-galactoside-binding proteins with diverse glycan-dependent and glycan-independent functions outside and inside cells. Two different approaches have been exploited in this context including (1) *in silico* analysis of correlations between expression of genes encoding *O*-GlcNAc cycle enzymes and galectins from TCGA database and (2) experimental cellular models of granulocytic (HL-60 cells) and trophoblastic (BeWo and JEG-3 cells) differentiation. Multiple significant correlations in expression between genes of interest (*O*-GlcNAc-related genes versus galectins and cell stemness transcription factors) were observed for samples representing normal and breast cancer tissues, normal bone marrow, and acute myeloid leukemia. Furthermore, significant differences between pairwise correlations of gene expression in normal and cancer tissues were detected, suggesting a possible global switch in *O*-GlcNAc-dependent mechanisms controlling the expression of galectin genes in cancer. Our findings with cell culture models revealed that the basal levels of global *O*-GlcNAc varied between different cell lines and dropped down during neutrophilic differentiation of HL-60 cells induced by either all-*trans* retinoic acid or high dose of DMSO while no significant changes were detected for placental cell differentiation induced by 8-Br-cAMP. Remarkably, the expression profiles of galectin genes and proteins changed in both models of cellular differentiation, whereas those were modified by inhibitors of *O*-GlcNAc cycle only in case of HL-60 cells. Moreover, secretion of many galectins (galectin-1, galectin-3, and galectin-9) by HL-60 cells was readily increased under low *O*-GlcNAc conditions either due to the cell differentiation or biochemical inhibition. Galectin-specific patterns were also revealed in the effects of recombinant galectins and galectin inhibitors on *O*-GlcNAc homeostasis and differentiation of HL-60 cells. Overall, these results support a complex role of *O*-GlcNAc/galectin pathway in regulating specific types of cellular differentiation and relevant aspects of cancer cell stemness.