Glycosylation in cancer affects cellular receptor tyrosine kinases and regulates cancer cell biology

Celso REIS [1]

[1] Institute of Research and Innovation in Health, University of Porto, and Institute of Molecular Pathology and Immunology of the University of Porto, Portugal.

celsor@ipatimup.pt

Alterations of glycosylation in the tumour and its microenvironment are common molecular alterations with major biological implications for disease progression [1,2]. Cancer is a heterogeneous disease that requires multidisciplinary treatment. Current targeted therapy depends on patient stratification based on molecular features of the tumour. This presentation will report on the basis of alterations of glycosylation that occur in gastric cancer (GC). Recent results applying glycomic and glycoproteomic strategies have provided key information regarding the alterations of glycosylation occurring in cancer cells and their impact the activation of oncogenic receptors tyrosine kinase (RTK) in tumour samples, such as RON, MET, EGFR and HER2 (ErbB2) [3,4,5].

Our work demonstrates that ErbB2 is modified with both α2,6- and α2,3-sialylated glycan structures in GC clinical specimens. Glycomic and glycoproteomic analysis of ErbB2's ectodomain disclosed a site-specific glycosylation profile in GC cells, in which the sialyltransferase ST6Gal1 specifically targets ErbB2 N-glycosylation sites occurring within the receptor's binding domain of the therapeutic antibody approved and used in the clinics [3]. Abrogation of ST6Gal1 expression reshaped the cellular and ErbB2-specific glycosylation, expanded the cellular half-life of the ErbB2 receptor, and sensitized ErbB2-dependent GC cells to therapeutic antibody-induced cytotoxicity through the stabilization of ErbB dimers at the cell membrane, and the decreased activation of both ErbB2 and EGFR RTKs [3].

These results highlight the functional aspects of glycosylation modifications occurring in cancer and supports their potential application as biomarkers for patient stratification, personalize medicine and for novel and improved therapeutic applications [1,3].

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