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Expression of OGT correlates with migration and proliferation of colon cells lines

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The O-GlcNAc transferase (OGT) is a key regulator of the post-translational modification of proteins by O-linked β-N-acetyl glucosamine (O-GlcNAc) onto Ser/Thr residues. OGT uses the end product of the hexosamine biosynthetic pathway (HBP), UDP-GlcNAc, as a donor for O-GlcNAcylation processes. It is reported that OGT and O-GlcNAcylation levels are increased in cancers. We showed that in the colorectal cancers (CRC) cell lines (HT29, HCT116) the expression of OGT and O-GlcNAcylation level were elevated and that O-GlcNAcylation directly interfered with β-catenin stability and proliferation of cells. Previous studies showed that oncogenic factors such as p53, MYC or β-catenin are O-GlcNAcylated. The Wnt/β-catenin pathway is modified in most CRC by genetic alteration of β-catenin or one member of the destruction complex. Consequently, β-catenin is protected from proteasomal degradation and therefore induces cell proliferation. A similar observation was made when HBP flux was increased by culturing cells in high glucose medium. In these conditions, -catenin was protected against the degradation thus accelerating cell proliferation. In a recent study, we identified four O-GlcNAcylation sites at the N-terminus of β-catenin, one of those (T41) localized in the destruction box is crucial for the control of β-catenin degradation. In that context we studied the effect of OGT silencing in CRC cell lines and non cancer cell line CCD841CoN. We reported that silencing of OGT halved proliferative and migratory capacities of cancer cells. OGT knock-down also diminished cell adhesion corroborating previous observations that inhibiting O-GlcNAcylation decreases β-catenin/α-catenin interactions necessary for mucosa integrity which suggests that O-GlcNAcylation also affects localization of -catenin at adherens junction level.

Biography

Agata Steenackers defended her PhD thesis in the field of Biology and Biotechnologies in November 2013 at the Lille 1 University (France). During her PhD, she developed a project around the expression of GD3 synthase and gangliosides in breast cancer cells lines. She is now on a Post-doctoral position in Tony Lefebvre's team (UGSF) where she is studying the role of O-GlcNAcylation in colon cancer development.

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