

P017 Action of a library of O-glycosylation inhibitors on the growth of human colorectal cancer cells in culture

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O-glycosylation is thought to play a significant role in the regulation of cell growth. However, only limited information is available and few specific and selective inhibitors have been found. We have synthesised a library of O-glycosylation inhibitors based on benzyl-O-N-acetyl-D-galactosamine. These inhibitors were tested with an established series of human colorectal cancer cell lines, which model the adenoma-carcinoma sequence.

Cancer cells were incubated with the inhibitors and examined for cell growth patterns and cellular and subcellular glycosylation using a range of lectins with confocal microscopy. The specificity of O-glycan inhibition was confirmed for the library, relative to other forms of glycosylation. All inhibitors tested resulted in smaller cell yields. However, a differential effect on O-glycosylation was detected using the lectins showing variation of localisation at a subcellular level in the various cell lines. Further differential action of the inhibitor library was observed for apoptosis and on the cell cycle with the cell lines tested.

This work demonstrates that O-glycosylation is closely involved in the regulation of cell growth in colorectal cancer cells and that the generation of a library of small molecular weight inhibitors offers a valuable means of examining this regulation at the molecular level