Cancer cell death using metabolic glycan incorporation techniques

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Metabolic incorporation of glycan precursors possessing clickable units (*e.g.*, azide or alkyne) into cellular glycans has become a useful method to probe glycosylation in cells, tissues and organisms. This technique has been utilized to incorporate versatile unnatural monosaccharides into glycans for purposes of imaging, labelling and tracking glycans, conducting proteomic analysis, capturing glycan-binding proteins as well as inducing cancer cell death.
One major challenge in applying this method is to develop approaches that enable incorporation of glycans into specific types of cells. As part of this effort, glycan precursors containing linkages that are cleaved under specific conditions, such as UV irradiation and enzyme catalysis, have been developed. Also, ligand-targeted liposomes containing modified monosaccharides have been constructed to target specific receptor-expressing cells. In this study, we developed a method for inducing cancer cell death that utilizes metabolic glycan labelling combined with either ADCC or PDT. The strategy we devised to target cancer cells relies on use of the H_2O_2-activatable glycan precursor, PBA-ManNAz$(OAc)_3$, which contains a phenylboronic acid (PBA)-based molecular cage and an azidoacetyl group at C6–OH and C2–NH_2 positions of the monosaccharide, respectively. The design of this precursor is based on observations that hydrogen peroxide is present in high levels in most types of tumors and that a PBA-based cage can be eliminated selectively by H_2O_2. We reasoned that following entry of PBA-ManNAz$(OAc)_3$ into cancer cells, its PBA-based cage and three *O*-acetyl groups would be removed by H_2O_2 and intracellular esterases, respectively. The resulting substance, ManNAz, would then undergo the metabolic processes leading to incorporation of an azide-containing monosaccharide unit into cellular glycans.

References

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