SYNTHESIS OF A CHONDROITIN SULFATE PROBE AND ITS APPLICATION IN PROSTATE CANCER CELLS

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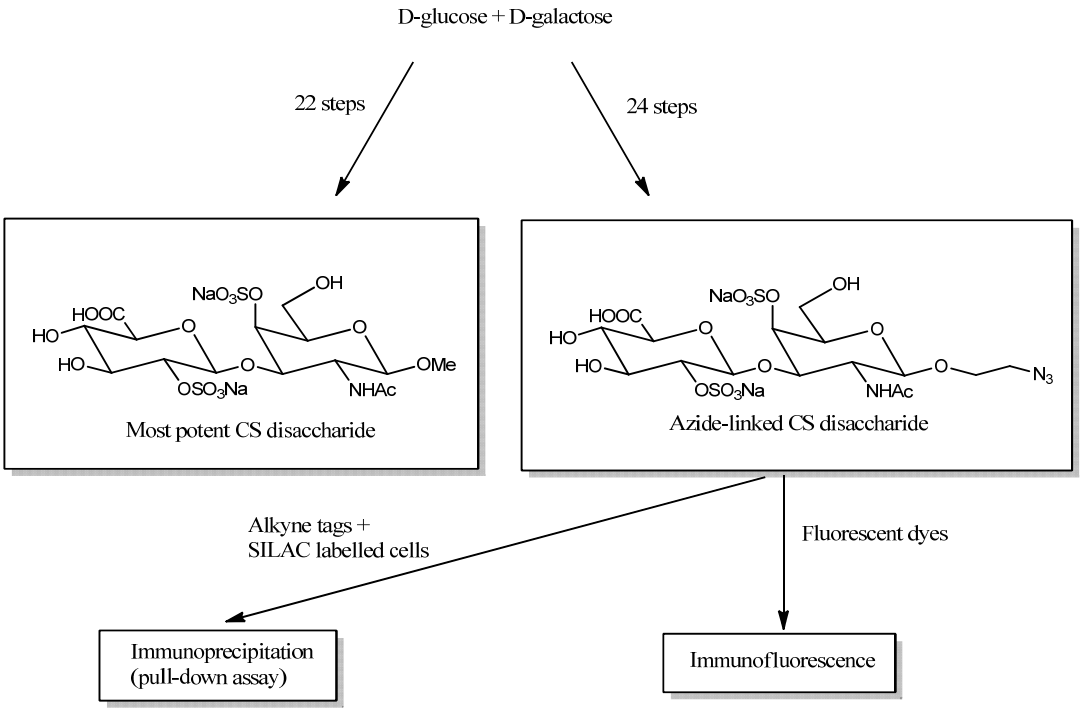
Chondroitin sulfate (CS) is a polysaccharide in the family of glycosaminoglycans (GAGs). It is overexpressed in various cancer cells, including prostate, testicular, gastric, pancreatic, and breast cancer. Recently, Poh et al described a divergent synthesis of 16 CS disaccharides and found that three of them were bioactive inhibitors of cancer cell proliferation, with C-2,4'-sulfated CS being the most potent [1]. However, the mechanism of action of CS in cancer cells is still unknown.

We modified Poh's synthesis to include an azide moiety on the non-reducing end of the CS disaccharide. Through the use of "click chemistry", different tags or dyes can be covalently linked to the CS disaccharide to probe for targets in mechanistic studies. For example, immunoprecipitation assays can be conducted on SILAC-labelled cancer cells to differentiate the binding of CS to its target proteins. Immunofluorescence assays can also be conducted to determine where the binding takes place in the cancer cell. We have investigated the biological activity of the CS disaccharide in human prostate cancer cell lines, and further mechanistic studies are currently being conducted.



[1] Poh, Z. W., Gan, C. H., Lee, E. J., Guo, S., Yip, G. W., & Lam, Y. *Scientific Reports* **5**, 14355 (2015).