Pour Some Sugar on Me: The Sweet Side of Cancer, Glycosylation and Cancer Stem Cells

By Jordan Pavlic

Glycosylation, which might sound scary and super science-y at first, just means the process of adding sugar to a protein. Did you know that half of all proteins in the genome are potentially glycosylated (1)? For such an important process, you'd think it would get more attention! Glycosylation is an extremely significant process biologically, and plays a key role in many bodily functions including development, cell-to-cell communication, and immune system regulation (2). For example, glycosylation is very important to the biological process of embryogenesis, and the presence of correctly glycosylated extracellular proteins is critical for proper development (3, 4). As I am sure you can imagine, when things go wrong with glycosylation, things go wrong with your body as well, and there are many diseases linked to malfunctioning glycosylation mechanisms. But where does cancer fit into all of this?

Cancer is a devastating disease that has many forms and is estimated to kill over half a million people in the United States this year (5). Some cancers, such as breast cancer and pancreatic cancer, are more deadly than others; additionally, these cancers can be harder to diagnose. But what if I told you there was a way to diagnose cancer sooner than existing tests and that the secret to unlocking more cost-effective diagnoses and treatments lies within a subset of cancer cells called cancer stem cells?

Cancer stem cells are cells that have the ability to give rise to different tumor cell types and are able to form new tumors. Unfortunately, cancer stem cells are often resistant to treatment. As you can see in Figure 1, many treatments for cancer are ineffective because they don't actually target the cancer stem cell population, causing tumor recurrence. However, if there were a way to identify which tumors have cancer stem cells, and in what abundance, that could potentially change the way we approach cancer treatment entirely—and that is where glycosylation comes in! But how does glycosylation fit into all of this?

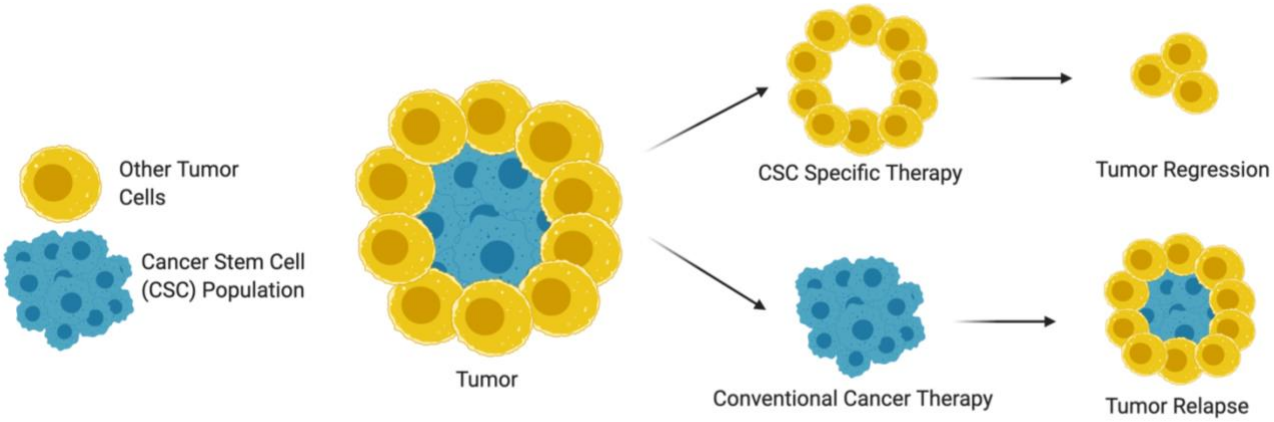

Figure 1: A schematic outlining the cancer stem cell hypothesis.

Cancer stem cells have a special glycosylation profile that distinguishes them from other cell types (6). From a diagnostic perspective, this offers infinite potential into characterizing cancer metastasis, prognosis, and recurrence. Cancer stem cells have markers that represent molecules expressed at higher levels, and these markers can be used to identify and isolate cancer stem cells from tumors. Markers for cancer stem cells have been identified in many different tumor types, and the vast majority of these markers are glycoproteins. This knowledge could unlock limitless potential for cancer stem cell targeting. For example, glycans, another name for sugars, on cancer stem cells, can be altered and transferred clinically to a glycan-based vaccine. These vaccines, in combination with FDA-approved cytotoxic drugs, could help to eradicate cancer stem cells and cancer cells present in the body. Additionally, these vaccines could inhibit tumor recurrence in many susceptible cancers. A big picture understanding of glycosylation as it relates to cancer stem cell populations could help healthcare providers make informed treatment decisions, while also giving cancer patients and their families much needed hope. And that, my friends, is the sweet side of cancer, glycosylation and cancer stem cells.

References

1. K. Ohtsubo, J. D. Marth, Glycosylation in cellular mechanisms of health and disease. *Cell* **126**, 855–867 (2006).

2. R. Goulabchand, T. Vincent, F. Batteux, J.-F. Eliaou, P. Guilpain, Impact of autoantibody glycosylation in autoimmune diseases. *Autoimmun. Rev.* **13**, 742–750 (2014).

3. F. Lo Schiavo, *et al.*, A carrot cell variant temperature sensitive for somatic embryogenesis reveals a defect in the glycosylation of extracellular proteins. *Mol. Gen. Genet.* **223**, 385–393 (1990).

4. P. M. Jacquinot, *et al.*, Change in glycosylation of chicken transferrin glycans biosynthesized during embryogenesis and primary culture of embryo hepatocytes. *Glycobiology* **4**, 617–624 (1994).

5. R. L. Siegel, K. D. Miller, A. Jemal, Cancer statistics, 2020. *CA Cancer J. Clin.* **70**, 7–30 (2020).

6. B. W. Mallard, J. Tiralongo, Cancer stem cell marker glycosylation: Nature, function and significance. *Glycoconj. J.* **34**, 441–452 (2017).