During this module, discuss Optimal Tumor Cancer Treatment. What is the muddiest point? What surprises you the most? What else can you add to what we've learned on this topic in this module (provide references to resources)?

**What is the muddiest point?**

The challenge in optimal tumor cancer is that this treatment needs to inhibit proliferation and induce differentiation.

* If you decrease proliferation, you get fewer cycling CSCs, which also means there are fewer CSCs available for differentiation. Slowing down CSC proliferation also leads to a larger pool of non-cycling CSCs, which remain resistant.
* If you only promote differentiation, you increase the number of DCs that eventually die, but you will also reduce proliferation; and with not enough cycling CSCs, you will also end up slowing down differentiation: with fewer cycling CSCs, differentiation slows, as cycling CSCs ultimately divide into two non-cycling CSCs.

**What surprises you the most?**

I was surprised to learn how quorum sensing acts as a regulatory feedback mechanism on both differentiation and proliferation, particularly that the differentiation probability increases as CSC density increases. This makes sense, as a high-density CSC environment may trigger differentiation to free up space for proliferating CSCs, since differentiated cells (DCs) have a limited lifespan. What also is counter-intuitive is the fact that reducing the proliferation rate does not affect non-cycling CSCs.

What else can you add to what we've learned on this topic in this module (provide references to resources)?

I looked for recent clinical trials combining differentiation-inducing agents with antiproliferative cancer agents.

Targeting MDSC differentiation using ATRA with pembrolizumab