

Immune-Oncology Symposium Debate

As the least experienced and the least competent member of the anti-vaxxers, I'm obliged to don the tinfoil helmet...

And I'd like to begin by using the **most triggering phrase** in the English language: I'd like to talk about COVID vaccines.

Counter to what one might expect, having more COVID boosters actually makes you **more** likely to contract COVID, with an increasing likelihood the more boosters you've had.

The question of course is: why? And what does that have to do with cancer vaccines?

The connection is in the targeting and overstimulation of the wrong part of the immune system.

With neoantigen vaccines, the aim is targeted stimulation of the adaptive immune system.

However, for respiratory infections like COVID, the frontline immune response comes not from adaptive but from mucosal compartment immunity.

Similarly, with cancer, it is the innate immune system that underpins the body's cancer defence mechanisms.

Overstimulation of the adaptive immune system can **downregulate** both innate **and** mucosal compartment immunity.

And because resources are finite, that will **deplete** rather than **enhance** the desired immune response, which is what we see with COVID.

There is an additional risk of T-cell exhaustion through chronic overstimulation, which has also been observed.

With an evolving disease, a neoantigen-based vaccine must adapt as quickly as the disease, which becomes more difficult when resources are misdirected.

So just as we see a reduction in mucosal compartment immunity in response to multiple COVID mRNA vaccines, so we may also cause a weakening of the innate immune response to cancer if we focus so strongly on developing cancer vaccines targeted primarily at adaptive immunity.