A new pre-print answers some questions about age-related immunopathologies associated with empty LNPs

And raises some more...

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A new preprint was uploaded on November 7, 2022 entitled: “Lipid nanoparticles (LNP) induce activation and maturation of antigen presenting cells in young and aged individuals” by a ‘non-conflicted group of researchers’ from… Acuitas? Wait, what?

This is worth writing a paper about, all on its own.

Check this out:

Under **Additional Declarations**

> **Yes** there is potential Competing Interest. Paulo Lin and Ying Tam are employees of Acuitas Therapeutic. Drew Weissman and Mohamad-Gabriel Alameh are named on patents and provisional patent applications about the use of lipid nanoparticles for nucleic acid delivery. Drew Weissman is named on patents on nucleoside modifications of mRNA.

In case you aren’t aware, Acuitas is the Canadian Biotech company that makes the proprietary Pfizer/BioNTech LNPs.

Anyway, the paper reveals some very interesting things, primarily age-related immune modulation induced by empty LNPs (eLNPs). The adjuvant effect of LNPs was always known but exactly how the adjuvant effect operates is still being elucidated. An adjuvant is an immunological stimulant and has been used historically in the context of vaccination since conventionally, the injection of attenuated viruses would require a bit of an immune system: AHEM! Vaccine producers have also typically used aluminum (salts) as adjuvants. Don’t get me started. Or maybe, that’s the only thing that matters?

Should I even write this up? Yes.

So let me quote the authors in their most interesting findings.

> These data showed a novel function of eLNP in eliciting [dendritic cell] DC maturation and innate immune signaling pathways and that some of these functions are impaired in older individuals providing some suggestion of why older individuals (>65 yrs of age) respond display lower immune responses and adverse events to SARS-CoV-2 mRNA-based vaccines.

The authors did quite a bit of work to establish that the responses to the empty LNPs were different amongst a small group of young (9; mean age 30) and old ()9; mean age 73) people. I think the part that interests me the most are the differences in a cytokine called Transforming Growth Factor beta (TGF-β). But before I get into that, I need to point something out that maybe a bit of a Freudian slip on their part.

The authors state:

> The ability of eLNP to induce TGF-β production and the differences observed between young and aged adults in the level of TGF-β that is induced are likely of importance, ***particularly in the use of eLNP during vaccination***, due to the essential roles that TGF-β plays in the differentiation and function of T cells.

Pardon? ***Particularly in the use of eLNP during vaccination?*** This made me do a triple re-read. Are they perhaps referring to this COVID-19 'vaccination' roll-out? Is this a thing, as many have suspected, and some claim to have evidence of? The roll-out of empty LNPs as 'placebos' into a proportion of the population? I mean, yes, this is absolutely the most critical aspect that required study and transparent data distribution, long before any roll-out should have commenced - if it was commenced at all! It was clear long ago from Pfizer's and Moderna's own safety data that the 'placebo' was inducing death, of all things. Check this out as a reminder. So maybe the 'placebo' was, as I have suspected, empty LNPs and maybe they are doing damage.

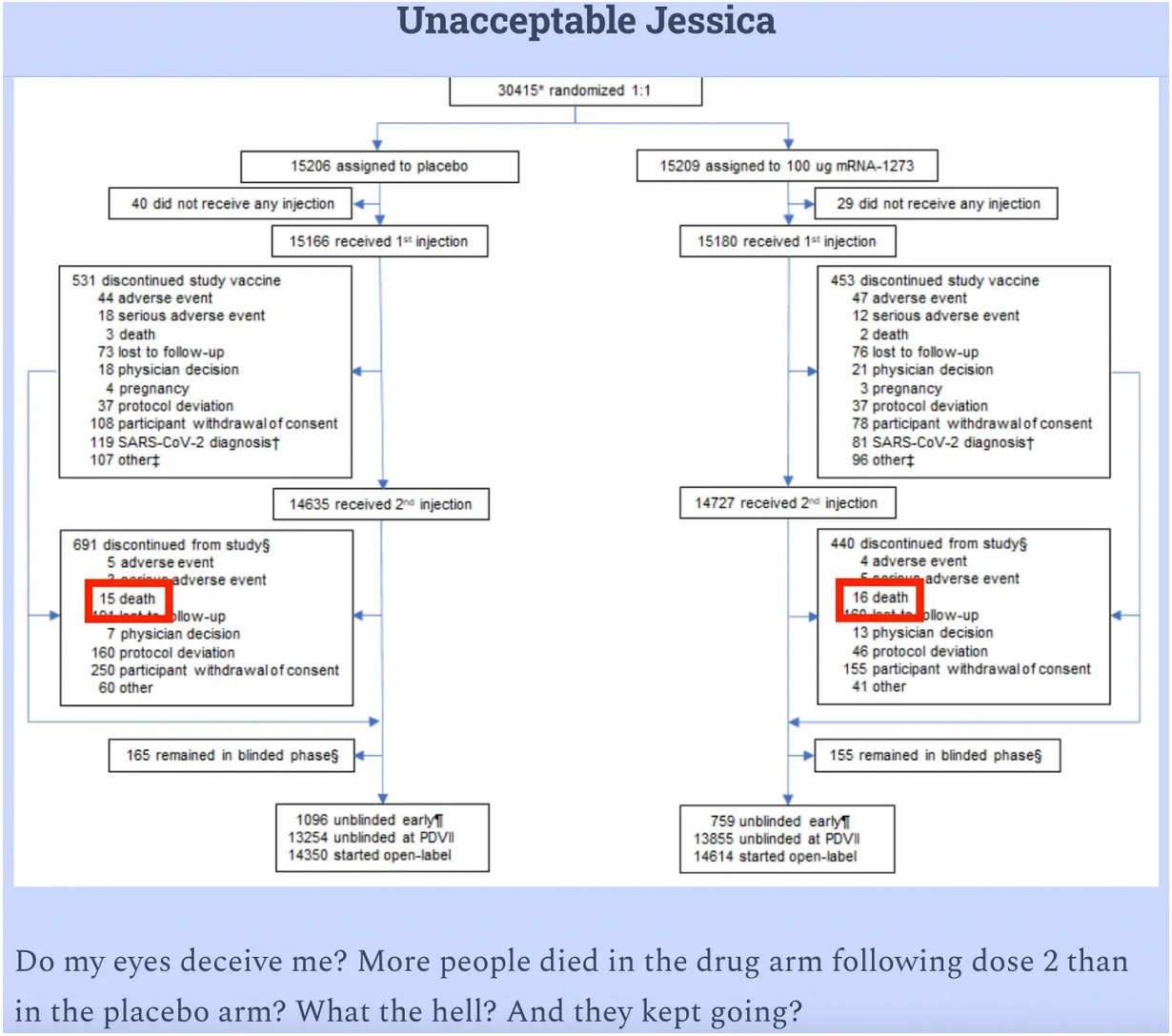

Figure 1: https://jessicar.substack.com/p/i-dont-know-what-to-say

I am going to leave that alone for now. Back to TGF-β.

On TGF-β

TGF-β is implicated in many essential (immunological) functions including cell differentiation, apoptosis and cell proliferation. It's really important to regulation of immunological functions and can play anti-or pro-inflammatory roles. To alter its production levels, is to alter many (immunological) functions. Because of its essential role in cell proliferation, it is also heavily implicated in tumorigenesis. [1]

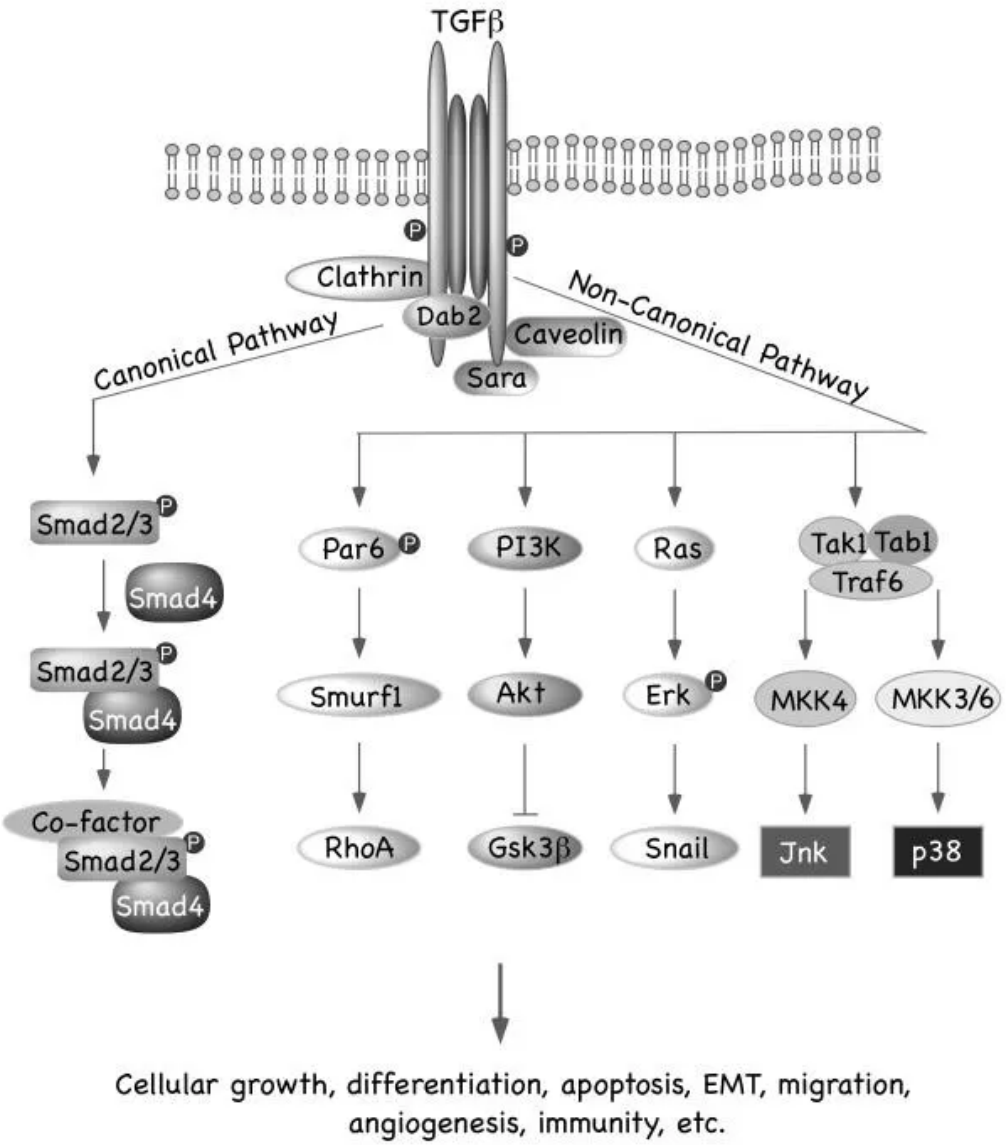

Figure 2: Schematic Representation of Canonical and Non-canonical TGFβ Signaling Pathway. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2810629/

Due to the essential roles that TGF-β plays in the differentiation and function of T cells in particular, the fact that the authors found differences in production levels of this cytokine based on age has implications with regard to injecting people with LNPs since it alters 'vaccine responsiveness'. Should we really have done this without bloody knowing how these eLNPs alter cytokine profiles?

> TGF-β is a potent modulator of proliferation, differentiation, and function of all of lymphocytes, dendritic cells, and macrophages, essentially regulating both innate and antigen specific immunity.
>
> We show that TGF-β expression was significantly increased following eLNP stimulation in PBMCs from older individuals.

So if TGF-β expression levels are higher in older people following injection with eLNPs, then might this be inducing other physiologic problems in addition to the ones noted (impaired innate immune signaling) like proteinaceous deposits? I found an article written by an M.D. named Puya Yazdi in November 2021 about TGF-β, and I found the last paragraph quite interesting. I recommend reading his article: it's easy to get through and is quite comprehensive.

> Scientists think that TGF-beta may have the following activities, mostly based on animal and cell culture data:
>
> - May decrease: acetylcholine, slow-wave (or deep) sleep, muscle regeneration, the activity of the vitamin D receptor, bone density, red blood cell formation and lymphocytes (T and B cells), cytotoxic T Cell (CD8) and Natural Killer cell activity, macrophages activity, inflammation
> - May increase: free radicals, tissue growth, damage in response to infections, wound healing and new blood vessel formation (angiogenesis), local inflammation and fibrosis, extracellular matrix deposition, switch to IgA [6], cognitive function (when very mildly elevated), the chance of EBV (Epstein Barr Virus)-associated diseases [6]
>
> **Proper human studies have not confirmed many of these activities.**.

It's that extra-cellular matrix deposition and fibrosis bit that interests me. Think: amyloids. Maybe the proteinaceous deposits are not true amyloids? I don't know. Again, I digress.

The paper is important because it addresses the reality of immune dysregulation due to the presence of the empty LNPs in real people, and shows that in older people, this dysregulation is more astute. I am quite impressed at the number of human subjects they recruited actually: human trials are hard to do. Kudos.

The authors claim that the results suggest that we need better vaccines for older people.

I claim that LNPs should not be used as delivery vehicles for other toxic products like modified messenger RNAs.

I will end this review here. It wasn't excellent, but it might prompt thought in yous.

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1 Chaudhury A, Howe PH. The tale of transforming growth factor-beta (TGFbeta) signaling: a soigné enigma. IUBMB Life. 2009 Oct;61(10):929-39. doi: 10.1002/iub.239. PMID: 19787707; PMCID: PMC2810629.