

Twitter Thread by UNSW RNA Institute

UNSW RNA Institute

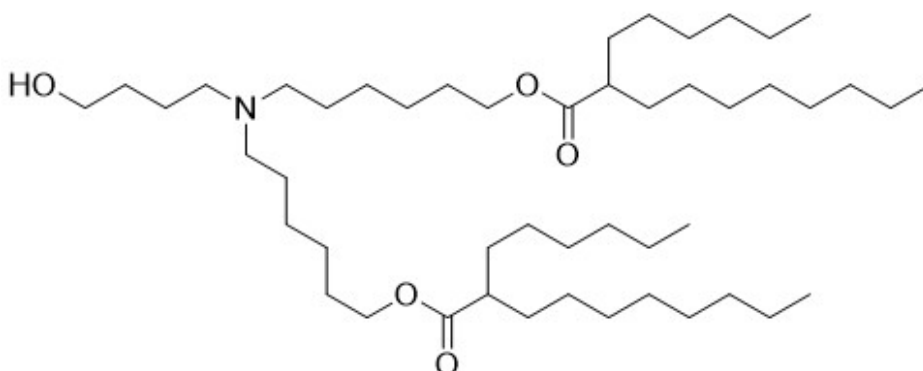
@UNSWRNA



mRNA vaccine is finally arriving in Australia. It is very similar to the @BioNTech_Group / @pfizer #mRNA The main difference is in the lipid nanoparticle (LNP) that deliver the mRNA. This is both in terms of the lipid chemistry and how the LNP's are formed 1/10

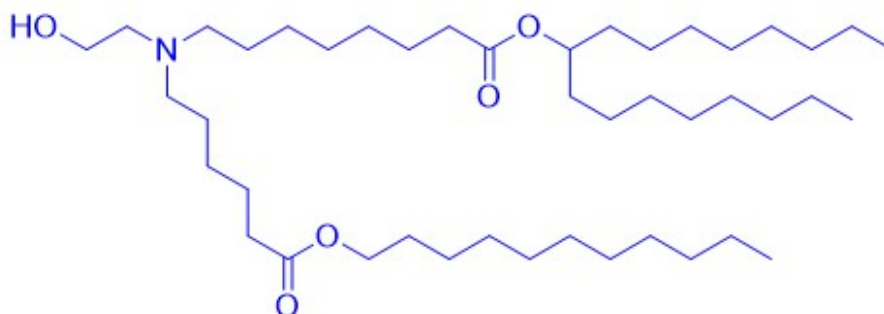
The mRNA binding lipid in:

BioNTech / Pfizer (BNT162b2)



ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)

Moderna (mRNA-1273)

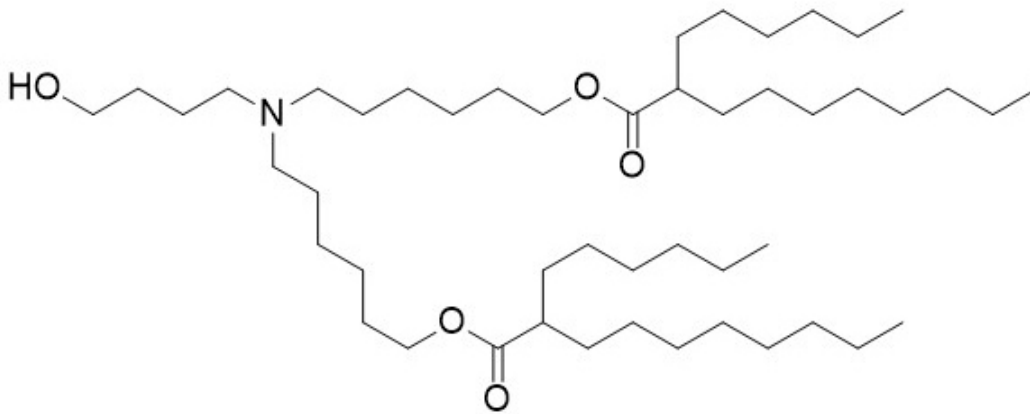


SM-102 = (9-Heptadecanoyl 8-((2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino)octanoate)

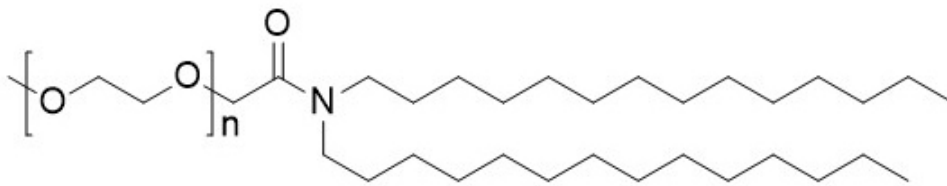
Both companies use a mixture of 4 lipids/PEG-lipids in their LNP formulations. The most important of those is the lipid that binds to the mRNA during the LNP formulation. These are the so-called ionisable lipids. Why? Because at certain pH levels

they are positively charged 2/10

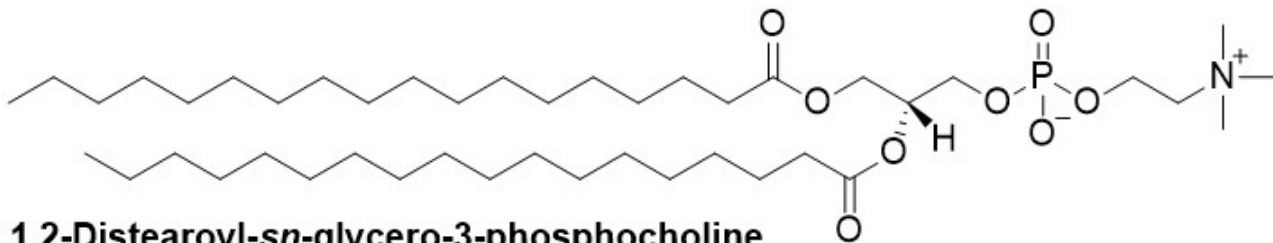
So at a fairly low pH, they are positively charged and bind strongly to the mRNA. This is how the two form a nanoparticle. The other 3 lipids/PEG-lipids (see the ones for the Pfizer below) are "helper" lipids, each playing different role in forming the LNP and making it work 3/10



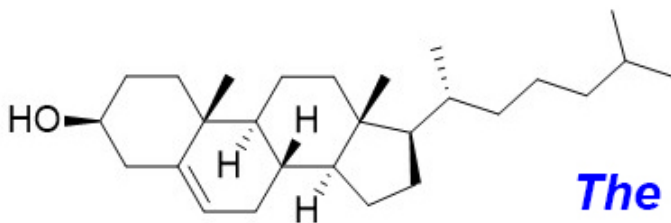
ALC-0315 = ((4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate)



ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide



1,2-Distearoyl-*sn*-glycero-3-phosphocholine



cholesterol

The 4 lipids used in the mRNA BioNTech/Pfizer vaccine against COVID-19

Prof. Pall Thordarson (Palli), School of Chemistry, UNSW Sydney, Australia

Once the LNP is formed the pH is raised to neutrality, and the lipids are no longer positively charged. After vaccination, the LNP then gets into your cells and into the acidic endosomes, where the pH drop again charges these lipids which now helps releasing the mRNA. 4/10

But is that all then in terms of the differences between the "Pfizer" and Moderna LNPs? We think not! A key research area for the @UNSWRNA is RNA delivery systems and based on our own experience it is not just what you use to form a LNP but HOW they are made that matters! 5/10

And we have strong clues that these two companies use different approaches to make their LNP's. Pfizer has been quite open about their process. You can even watch a video of the process below. It is a simple process using an impingement jet mixer. 6/10 <https://t.co/zZ2avu3OEj>

Moderna on the other hand has been less open about how they make their LNP's (see below). And no wonder! Somehow they cracked the problem to make them more stable than the Pfizer ones - we would keep this as an industrial secret too in their shoes;-) 7/10 <https://t.co/atpjOsowox>

The end results is that due to the combination of slightly different lipid chemistry and probably more importantly, slightly different formulation process, the Moderna vaccine is not as fragile and can be stored at -20 C instead of the recommended -80 C for the Pfizer one 8/10

But when it comes how effective they are or indeed side-effects, the differences seem negligible. As explained below there are also subtle difference in the mRNA code + slightly more mRNA in the Moderna vaccine but the end results seems to be the same 9/10 <https://t.co/fV5BmZSrzm>

We here in Australia are lucky to have now 3 very good vaccines: AstraZeneca, Pfizer and now Moderna, so if you haven't been vaccinated grab one now and it doesn't matter which one! But we do hope you enjoyed this journey around the Moderna vs Pfizer LNP's. 10/10