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The BNT162b2 vaccine's empty lipid nanoparticle is able to induce an NF-κB response

Amanda E Zelkoski[1], Katherine H.E. Ennis[1,2], Zhongyan Lu[1,2], and Allison M.W. Malloy[1]
[1]Uniformed Services University of the Health Sciences, [2]Henry M Jackson Foundation

Lipid nanoparticles (LNP) are essential components of messenger RNA (mRNA) vaccines that have been a cornerstone of the COVID-19 public health response. These LNPs are used for cell entry and protection of the mRNA. Others have shown that the LNP of the BNT162b2 vaccine is able to augment the immune response against the vaccine target. However, it is unknown how this LNP stimulates innate immune cells such as monocytes that participate in the engagement of the adaptive immune response.

We used a THP-1 monocyte reporter cell line for nuclear factor kappa B (NF-κB) and interferon regulatory factor (IRF) activation to understand if empty LNPs could stimulate innate cells in comparison with toll-like receptor (TLR) agonists. With this cell line, we show that the BNT162b2's LNP is able to initiate activation of NF-κB, but not IRF in a dose-dependent manner. The NF-κB response was similar to that of low doses of R848, a TLR 7/8 agonist, as well as LPS, a TLR4 agonist. Next, we evaluated NF-kB activation in the absence of MyD88 or TRIF using knockout reporter cell lines. We demonstrate that NF-κB activation is reduced in both knockout cell lines. In comparison, LPS primarily stimulated NF-kB activation through MyD88, and R848 relies on both pathways.

Our data show that LNPs can stimulate key innate immune cells through NF-kB pathways but not through IRF suggesting that this master regulator may participate in the immune activation induced by the current mRNA vaccine platform. Moreover, our data suggest that LNPs can use both MyD88 and TRIF signaling cascades to induce activation. Understanding the mechanisms behind the immunostimulatory capacity of LNPs can shed light on modulating these vaccine components to enhance vaccine design.