Medannex has developed a monoclonal antibody, MDX-124, that targets annexin-A1, a key component of the immune system. Annexin-A1 facilitates multiple steps in the lifecycle of viruses, together with their incorporation and proliferation in human cells, which is of particular importance in the current COVID-19 pandemic. By blocking annexin-A1, MDX-124 could disrupt the infectivity and transmission of SARS-CoV-2.

Annexin-A1 is a member of the annexin protein family of calcium-regulated phospholipid binding proteins and has been shown to influence a number of biological processes including inflammation, endocytosis/exocytosis and cell signalling. A growing body of evidence has revealed crucial roles for annexin-A1 and its receptor, formyl peptide receptor 2 (FPR2), in modulating the course of viral infections such as influenza A (IAV) (Ampomah *et al.*, 2018).

Lung epithelial cells (targeted by SARS-CoV-2) overexpress annexin-A1 and have been shown to have significantly higher IAV titers than cells that are deficient in annexin-A1 (Arora *et al.*, 2016). Furthermore it has been demonstrated that annexin-A1 deficient mice are protected against IAV infection via reduced viral replication and inefficient propagation in lung epithelial cells, resulting in increased survival (Arora *et al.*, 2016).

Annexin-A1 is known to be involved in multiple steps of the IAV lifecycle including binding to target cells, internalisation and subsequent intracellular trafficking to the nucleus, as well as facilitating IAV-induced apoptosis which leads to enhanced virus production (Arora *et al.*, 2016). These data highlight annexin-A1 as a novel host factor required by IAV to establish productive infection.

MDX-124 is a humanised monoclonal antibody that specifically targets and neutralises annexin-A1. By binding to annexin-A1 present in the envelope of a viral particle, MDX-124 could block interactions of the virion with FPR2 and impede its absorption into the host cell. This would prevent viral replication through FPR2 mediated ERK signalling. In addition, this would inhibit the release of cytokines/chemokines that lead to the cytokine storms and associated pneumonia seen in COVID-19 patients and promote the resolution of acute inflammation (Figure 1). MDX-124 could therefore prevent the generation of high viral loads, subsequent tissue damage in the lungs and overall viral pathogenesis.

Although there is currently no published literature discussing the role of annexin-A1 in respect of SARS-CoV-2, examining whether annexin-A1 is involved in the pathogenesis of this virus - and whether a targeted therapy to annexin-A1 (MDX-124) could prevent and reverse disease progression - could be of great importance in the global fight against COVID-19.

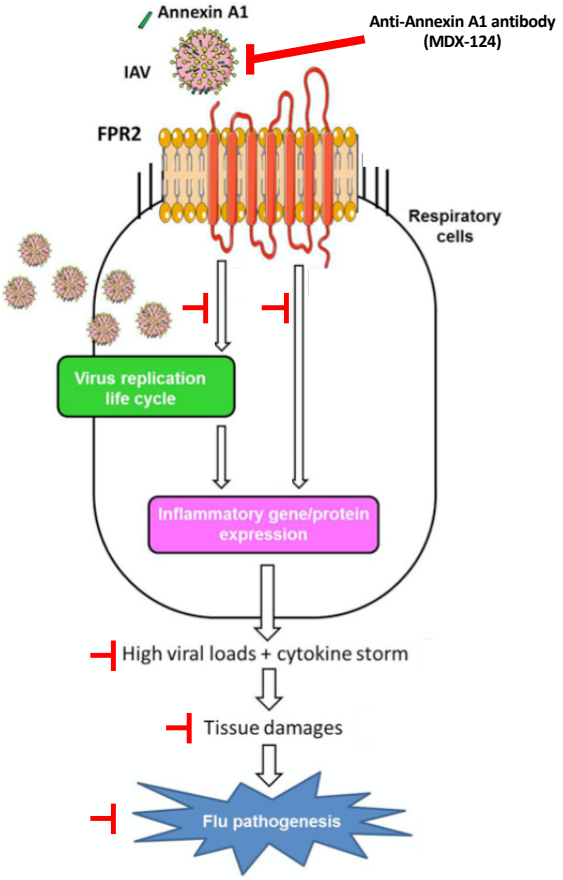


**Figure 1.** Schematic of the contribution of ANXA1 and FPR2 in influenza virus (IAV) pathogenesis and potential effect of anti-ANXA1 antibody (MDX-124). Adapted from Alessi *et al.* (2017).

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