

Antiviral properties of the NSAID drug naproxen targeting the nucleoprotein of SARS-CoV-2 Coronavirus

Anny Slama-Schwok

Sorbonne Université, France

Abstract

There is an urgent need for specific antiviral treatments directed against SARS-CoV-2 to prevent the most severe forms of COVID-19. By drug repurposing, affordable therapeutics could be supplied worldwide in the present pandemic context. Targeting the nucleoprotein N of the SARS-CoV-2 coronavirus could be a strategy to impede viral replication and possibly other essential functions associated with viral N [1-2].

Viral infection activates a cyclooxygenase-2 (COX-2) inflammatory cascade that is most marked in the initial inflammatory phase. SARS-CoV-2 infection also up-regulates COX-2 in human cell culture and mouse models [3]. The effectiveness of COX-1/ COX-2 inhibition by non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen discouraging the inflammasome activation could limit the cytokine storm.

The antiviral properties of naproxen, a non-steroidal anti-inflammatory drug (NSAID) that was previously demonstrated to be active against Influenza A virus [4-5], were evaluated against SARS-CoV-2. Intrinsic fluorescence spectroscopy, fluorescence anisotropy, and dynamic light scattering assays demonstrated naproxen binding to the nucleoprotein of SARS-Cov-2 as predicted by molecular modeling. Naproxen impeded recombinant N oligomerization and inhibited viral replication in infected cells. In VeroE6 cells and reconstituted human primary respiratory epithelium models of SARS-CoV-2 infection, naproxen specifically inhibited viral replication and protected the bronchial epithelia against SARS-CoV-2 induced-damage. No inhibition of viral replication was observed with paracetamol or the COX-2 inhibitor celecoxib. Thus, among the NSAID tested, only naproxen combined antiviral and anti-inflammatory properties. Naproxen addition to the standard of care could be beneficial in a clinical setting.

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Biography

Anny Slama Schwok has her expertise in drug design to design and develop new antivirals against Influenza, SARS-COV2 and RSV, mainly through initial hits involving drug repurposing. Combined with her expertise in biophysics, her group also developed novel fluorescent modulators of proteins involved in redox processes in the tumor microenvironment.