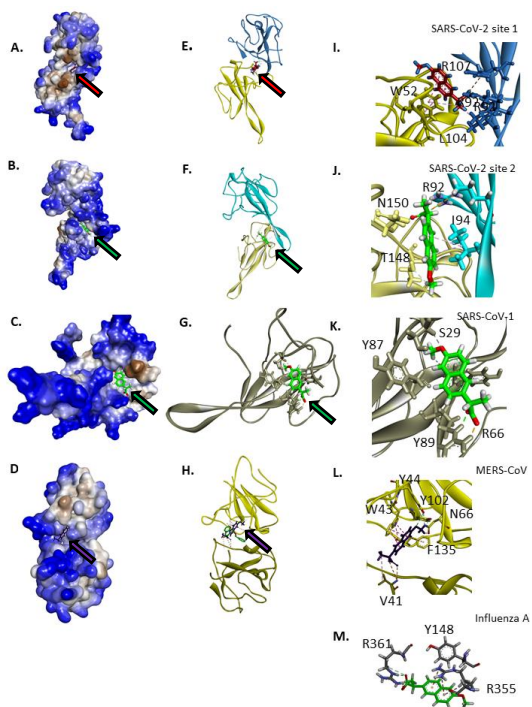


Broad-spectrum antiviral activity of naproxen: from Influenza A to SARS-CoV-2 Coronavirus

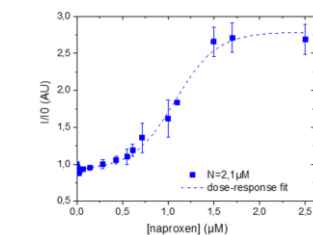
Olivier Terrier, Sébastien Dilly, Andrés Pizzorno, Julien Henri, Francis Berenbaum, Bruno Lina, Bruno Fève, Frédéric Adnet, Michèle Sabbah, Manuel Rosa-Calatrava, Vincent Maréchal and Anny Slama Schwok

Abstract: There is an urgent need for specific antiviral drugs directed against SARS-CoV-2 both to prevent the most severe forms of COVID-19 and to reduce viral excretion and subsequent virus dissemination; in the present pandemic context, drug repurposing is a priority. Targeting the nucleoprotein N of the SARS-CoV-2 coronavirus in order to inhibit its association with viral RNA could be a strategy to impeding viral replication and possibly other essential functions associated with viral N. The antiviral properties of naproxen, belonging to the NSAID family, previously demonstrated against Influenza A virus, were evaluated against SARS-CoV-2. Naproxen binding to the nucleoprotein of SARS-CoV2 was shown by molecular modeling and fluorescence spectroscopy. In VeroE6 cells and reconstituted human primary respiratory epithelium models of SARS-CoV-2 infection, naproxen inhibited viral replication and protected the bronchial epithelia against SARS-CoV-2 induced-damage. The benefit of naproxen addition to the standard of care is tested in an on-going clinical study. <https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001301-23/FR>; NCT04325633

Naproxen binds to viral nucleoproteins (N) in silico and in vitro



structure	SASA (Å ²)
N alone	14650
N + NAP	14497



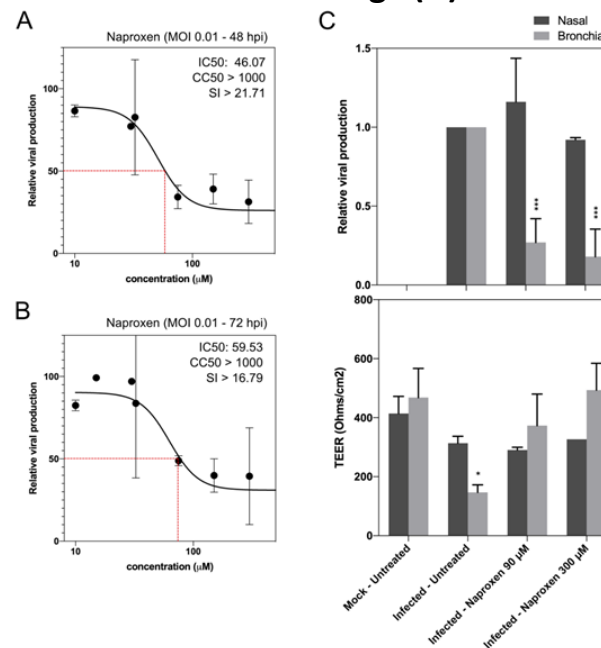
Change of SARS-CoV2 N intrinsic fluorescence upon naproxen binding

Naproxen was identified in a virtual screening (using a library of compounds selected from Sigma) targeting N

Dual effect of naproxen :
-Antiviral effect:
inhibition of transcription/replication of the virus by targeting the nucleoprotein

-Well-known anti-inflammatory effect:
Inhibition of cyclo-oxygenase COX (NSAID) and prostaglandin synthesis;
COX1: inhibition of thrombosis;
COX2: inhibition of inflammation & pain

Naproxen inhibits SARS-CoV2 replication in VeroE6 cells (A,B) and in a model of reconstituted epithelium (C) and protects the epithelium against viral-induced damage (D)



*Efficacy of Addition of **NA**proxen in the Treatment of critically ill Patients Hospitalized for **COVID-19** Infection*

*Promoted by APHP _ DRCI-Siege, DRCI-URC Iariboisière-St Louis
PI: Pr Frédéric ADNET*