TMPRSS2 binds TMPRSS2 inhibitors

Acencio, ML., Gillespie, ME., Jassal, B.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

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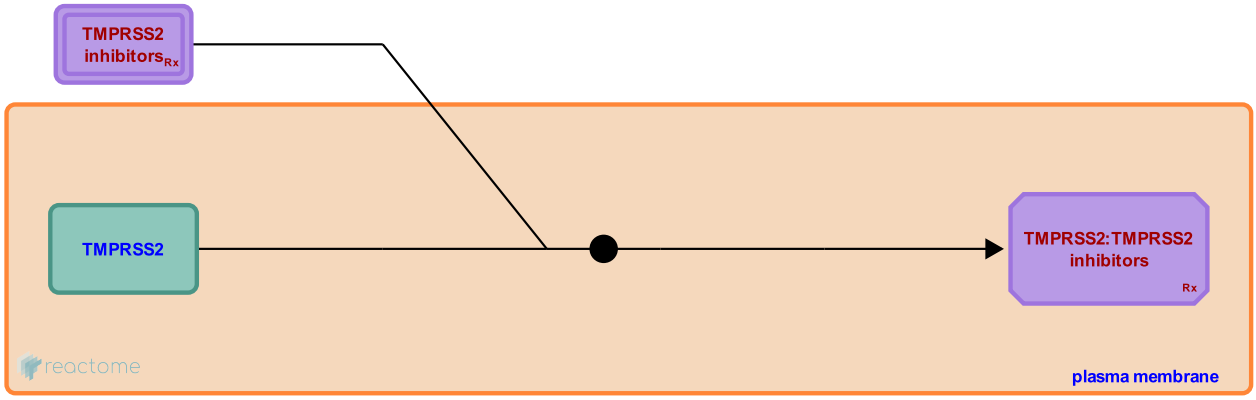
Stable identifier: R-HSA-9681514

Type: binding

Compartments: extracellular region, plasma membrane



Entry of influenza, parainfluenza and coronaviruses into airway epithelial cells requires binding of a viral spike protein to a host cell receptor, followed by cleavage and activation of the viral spike protein mediated by the host cell. Without this cleavage, fusion of the viral and host cell membranes is blocked. The primary receptor for the human SARS-CoV-1 virus is angiotensin converting enzyme 2 (ACE2) (Li et al. 2003). The resultant complex is cleaved by the protease transmembrane protease serine 2 (TMPRSS2) (Shulla et al. 2011, Heurich et al. 2014). Therefore, active site inhibitors of these airway proteases could have broad therapeutic applicability against multiple respiratory viruses (Laporte & Naesens 2017). The approved drug camostat is a protease inhibitor that may block SARS-CoV-2 entry into cells by inhibiting the actions of TMPRSS2 (Kawase et al. 2012, Hoffmann et al. 2020). Nafamostat, another serine protease inhibitor, was found to be a potent inhibitor of S-mediated membrane fusion and blocked MERS-CoV infection in vitro (Yamamoto et al. 2016).

Otamixaban (FXV673), an anticoagulant, is a potent and selective direct inhibitor of coagulation factor Xa. Virtual docking studies suggest that otamixaban may bind to the serine protease TMPRSS2 (Rensi et al. 2020, preprint). Inhibition of TMPRSS2 is being examined for antiviral activity but its inhibitory potential and/or antiviral activity have not yet been determined so it is annotated here as a candidate drug. I-432 is another inhibitor of TMPRSS2 under investigation for anti viral potential (Pászti-Gere et al. 2016).

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Editions

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