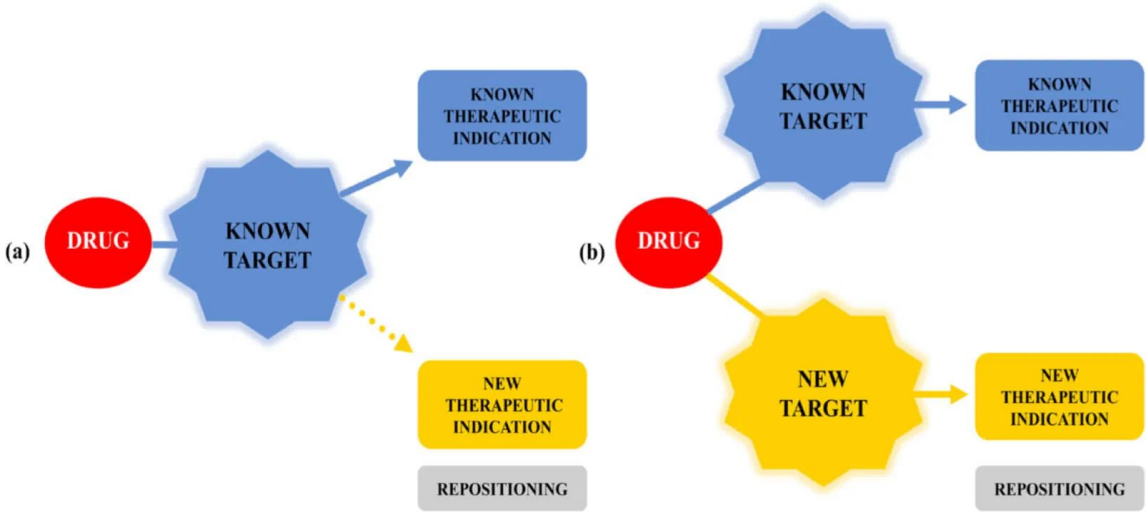
Drug Repurposing

Drug Repurposing (drug repositioning) involves the investigation of existing drugs for new therapeutic purposes.



Drug repurposing can serve as one of the effective solution to combat COVID-19 because the world needs an effective drug for COVID-19 as soon as possible but discovery of new drug, undergoing clinical trials, getting license for use, all this would take a long time,

Merits of Drug Repositioning

- Reduced number of required clinical trial steps could reduce the time and costs for the medicine to reach the market.
- Existing pharmaceutical supply chains could facilitate "formulation and distribution" of the drug.
- Known possibility of combining with other drugs could allow more effective treatment.

- The repositioning could facilitate the discovery of "new mechanisms of action for old drugs and “new classes of medicines",
- The removal of “activation barriers” of early research stages can enable the project to advance rapidly into disease-oriented research.

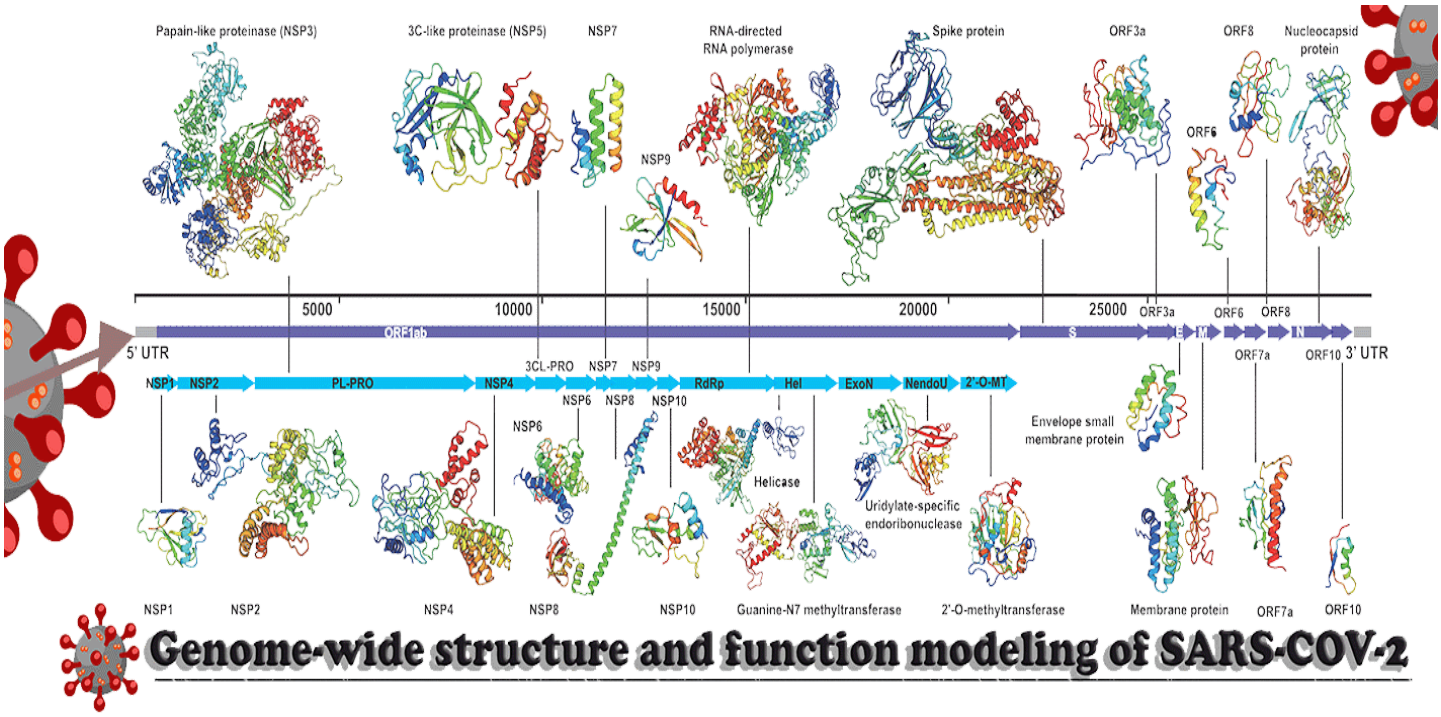
Druggable Targets of SARS-CoV-2

In January, scientists deciphered a piece of very bad news: the genome of SARS-CoV-2, the virus that causes Covid-19. The sample came from a 41-year-old man who worked at the seafood market in Wuhan where the first cluster of cases appeared.

Researchers are now racing to make sense of this viral recipe, which could inspire drugs, vaccines and other tools to fight the ongoing pandemic

Viruses must invade the living cells to replicate and spread. When the coronavirus finds a suitable cell, it injects a strand of RNA that contains the entire coronavirus genome. The genome of the new coronavirus is less than 30,000 “letters” long. Scientists have identified genes for as many as 29 proteins, which carry out a range of jobs from making copies of the coronavirus to suppressing the body’s immune responses.

Some of the proteins encoded by the coronavirus genome are shown below



Four Druggable targets of SARS-CoV-2

- **Spike (s)**

  Spike Protein mediates host cell invasion via binding to a receptor protein called angiotensin converting enzyme-2 (ACE-2) located on the surface membrane of host cells.

- **Main protease/ 3 chymotrypsin-like cysteine protease (Mpro/3CL)**

Upon entry, the viral genome is translated into viral polyproteins using host cell protein translation machinery, which are then cleaved into effector proteins by viral proteinases like 3CLpro and PLpro.

- **Papain-like protease (PLpro)**

  PLpro behaves as a deubiquitinase that may deubiquinate certain host cell proteins, including interferon 3 (IF-3) and NF-κB, resulting in immune suppression.

- **RNA-dependent RNA polymerase (RdRp)**

  It synthesizes a full length negative RNA template to be used by RdRp to make more viral genomic RNA.

References

1. https://www.nytimes.com/interactive/2020/04/03/science/coronavirus-genome-bad-news-wrapped-in-protein.html
2. https://www.thelancet.com/coronavirus
3. https://zhanglab.ccmb.med.umich.edu/COVID-19/