A New Solution to COVID-19 Also Prevents the Next Pandemic

With the approval of vaccines for the COVID-19 virus, SARS-CoV-2, the major looming concern is how the current pandemic will evolve -- and when the next pandemic will occur. As experts have said, it is inevitable. As they have also explained, it is likely to occur in one of two ways: either mutations that have already started occurring in the COVID-19 virus (such as the new variants discovered in the UK and South Africa) will ultimately render the current vaccines ineffective, or a new virus—SARS-CoV-3—will suddenly appear, just as SARS-CoV-2 did in late 2019. In either case, the world will be thrust back into another lockdown and panic.

A remarkable discovery from Prosetta Biosciences, a San Francisco biotechnology company, provides a straight-forward solution to both of those nightmare scenarios using a completely novel strategy for anti-viral drug development. *They have developed small molecule drugs that are effective against not only the COVID-19 virus but all major families of viruses causing respiratory disease including other coronaviruses and influenza.*

Prosetta's research showed that viruses such as SARS-CoV-2 reproduce in the body not by "self-assembly," as has long been thought, but by hijacking our cells' own machinery to accomplish the construction. So instead of targeting the virus itself—which is what relatively ineffective drugs such as remdesivir do—Prosetta targets what its scientists call the "assembly machines" that have been taken over by the virus. Since all viral mutants use the same assembly machine, future coronavirus variants will be just as susceptible to the new Prosetta drug candidates as is the COVID-19 virus.

Drugs that target the aberrant assembly machines, rather than the virus directly, make it hard for the virus to evolve around the drug. That means drug resistance, a problem that affects most conventional virus-targeted therapeutic drugs and vaccines at some point, is avoided. The combination of pan-respiratory viral effectiveness and avoidance of drug resistance makes these drugs unprecedented. The history of viral disease demonstrates that a lot of damage can be done by the time conventional drugs and vaccines are developed. A pan-respiratory drug with a barrier to drug resistance goes a long way toward solving these problems and preventing the pandemics of the future.

The most dangerous viruses not only hijack cellular mechanisms for their reproduction, they also interfere with the body's innate immune defenses. When innate immunity is compromised, the virus has a head start that enables it to spread widely before the infected host can develop antibodies to defeat the virus. As the arms race between the virus and the immune system rages, many secondary effects can develop, such as cytokine storm, that are themselves dangerous to the host. *Protecting innate immunity from viral attack is vital to restoring health.*

Viruses have figured out over eons of time through evolution how to modify the molecular basis of homeostasis - the chemical and biological balance needed for cellular health and defense. Viral reproductive strategy involves reprogramming of host machinery in order that it can be used to meet the virus' needs, rather than the host's. It does this by modifying multi-protein complexes within the cell that are needed for homeostasis. *Because the drugs that Prosetta is*

developing re-establish homeostasis, including restoration of key proteins of innate immunity, they not only stop the virus, but are also likely to repair innate immunity. This is unlike most other new approaches, such as genetic therapies, that deplete the cell of proteins needed by both the cell and the virus.

The Prosetta drugs also appear to avoid side effects. This could be the case for two different reasons. First, because the virus modifies the host's assembly machines to be optimal for viral reproduction. The Prosetta anti-viral drugs have been optimized to target the virally-modified aberrant versions, rather than the normal host assembly machines. By analogy, antibiotics that target the bacterial versions of host cellular machinery are generally non-toxic to us because of the difference between their machinery and ours. Beyond this point however, the analogy breaks down because bacteria code for their own machinery, and therefore can evolve around antibiotics. Viruses however are hijacking our machinery because they lack their own, and therefore can't do likewise. The second reason for non-toxicity is that the Prosetta drugs appear to work by restoring homeostasis, rather than by being toxic to both the virus and the cell.

Most antiviral drug discovery starts by targeting so-called active sites or protein-protein interaction sites on individual proteins. For instance, the spike protein on the SARS-CoV-2 virus, essential for its entry into cells, is the target of choice for both therapeutic drugs and antibody-promoting vaccines. Several variants of the novel coronavirus that may involve changes to the spike protein structure have already been seen. It is not yet known whether this adversely impacts the efficacy of current vaccines or antibody therapies, but further mutations can be expected to result in conventional drug and vaccine resistance over time.

In contrast, the Prosetta compounds go after the control panels (termed allosteric sites) of previously unappreciated collections of host proteins (that form the multi-protein complex assembly machines). The virally-modified aberrant assembly machines are essential for the virus in ways that are different from the way normal assembly machines serve the needs of the cell. Thus the Prosetta drugs avoid host toxicity. The virus found these allosteric sites over deep evolutionary time and modified them to promote its own reproduction. The trick is to get the virus itself to act as a "trufflehound," and reveal those hard-to-detect control panels – and the drugs that can be used to counter the virus – which is what Prosetta has succeeded in doing.

So far, Prosetta has obtained proof of concept for its drug discovery program and successfully tested its pan-respiratory drugs in both cells and animals. The company plans to advance these drugs through the drug approval process including clinical trials to obtain FDA approval. This could be achieved within a year, in time to rescue us from the feared impending mutations -- and before the next pandemic strikes.

If you have questions or would like more information, please contact vlingappa@prosetta.com