IFPW FOCUS

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Repurposing Approved Drugs to Treat Coronavirus

(Source: A staff article by World Pharma News)

Since the beginning of the pandemic, researchers worldwide have been looking for ways to effectively treat COVID-19. And while the COVID-19 vaccines represent the best measure to prevent the disease, therapies for those who do get infected remain in short supply. A new groundbreaking study by University of Michigan (U-M) reveals several drug contenders already in use for other purposes - including one dietary supplement - that have been shown to block or reduce SARS-CoV2 infection in cells.

The study, published recently in the Proceedings of the National Academy of Science, uses artificial intelligence-powered image analysis of human cell lines during infection with the novel coronavirus. The cells were treated with more than 1,400 individual FDA-approved drugs and compounds, either before or after viral infection, and screened, resulting in 17 potential hits. Ten of those hits were newly recognized, with seven identified in previous drug repurposing studies, including remdesivir, which is one of the few FDA-approved therapies for COVID-19 in hospitalized patients.

"Traditionally, the drug development process takes a decade and we just don't have a decade," said Jonathan Sexton, Ph.D., Assistant Professor of Internal Medicine at the U-M Medical School and one of the senior authors on the paper. "The therapies we discovered are well positioned for phase 2 clinical trials because their safety has already been established."

The team validated the 17 candidate compounds in several types of cells, including stem-cell derived human lung cells to mimic SARS-CoV2 infection of the respiratory tract. Nine showed anti-viral activity at reasonable doses, including *lactoferrin*, a protein found in human breastmilk that is also available over the counter as a dietary supplement derived from cow's milk.

"We found *lactoferrin* had remarkable efficacy for preventing infection, working better than anything else we observed," Sexton said. He adds that early data suggest this efficacy extends even to newer variants of SARS-CoV2, including the highly transmissible Delta variant.

The team is soon launching clinical trials of the compound to examine its ability to reduce viral loads and inflammation in patients with SARS-CoV2 infection. The trials are adding to the list of ongoing studies of promising repurposed drugs. Sexton noted that over the course of the pandemic, other drug repurposing

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In Brief...

- **Bayer AG** announced the acquisition of **Vividion Therapeutics, Inc.**, a U.S.-headquartered biopharma company utilizing novel discovery technologies to unlock high value, traditionally undruggable targets with precision therapeutics. The deal is worth US$1.5 billion with success-based milestone payments valued up to US$500 million. Separately, **Bayer Yakuhin** has named *Julio Truiana* as its President effective September 1, replacing *Heike Prinz* who will move to the position of overseeing Bayer's pharma business in Europe, Middle East and Africa.
- **Profarma Group** announced financial results Q2 of 2021, with gross revenue growth of 25.2% at R$1.8 billion (US$341.1 milllion) and 26.0% growth in its distribution business. Net income totaled R$33.7 million (US$6.4 million) in line with the 2nd quarter of 2020. Separately, Profarma will sell its entire joint-venture interest in **Cannes RJ Participações S.A.** to **CM Hospitalar S.A.** The transaction doesn't involve AmerisourceBergen's equity stake in Profarma.
- U.S. wholesaler **Cardinal Health** will continue to distribute phrmaceuticals to **CVS Health's** retail pharmacies and distribution centers under an extension of current agreements. "We value our long-standing partnership with CVS Health, and we are honored to continue our important work together to bring our best-in-class abilities together for their customers," Cardinal

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Full Approval of the Pfizer Vaccine Has Arrived

(An article by David Leonhart for the New York Times)

Within hours of U.S. FDA full approval of Pfizer's *Comirnaty* vaccine announcements from the Pentagon, universities and numerous large companies imposed new vaccine mandates. The Biden administration also urged organizations to require vaccination of employees or institute strict testing requirements for those who choose not to be vaccinated.

The lack of full approval has been a point of contention leaving some Americans skeptical of the vaccine's safety. With the insurgence of the Delta variant, infection rates have risen dramatically with more than 1,000 Americans per day dying of Covid. It is estimated that vaccination would have saved approximately 95% of those patients.

Many have wondered why the FDA has been so slow to approve these critical vaccines. The answer lies in bureaucratic caution. FDA leaders wanted to proceed as closely as possible to their normal approval process. Months were spent reviewing clinical trial results before granting full approval. Emergency

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Repurposing Drugs (cont.)...

studies have identified different compounds with potential efficacy against SARS-CoV2.

Remarkably, the U-M study also identified a class of compounds called *MEK-inhibitors*, typically prescribed to treat cancer, that appear to worsen SARS-CoV2 infection. The finding sheds light on how the virus spreads among cells.

"People going in for chemotherapy are at risk already due to a lowered immune response. We need to investigate whether some of these drugs worsen disease progression," said Sexton. The next step, he noted, is to use electronic health records to see whether patients on these drugs have worse COVID-19 outcomes.

The work is one of the first major discoveries to come out of the new U-M Center for Drug Repurposing (CDR), which was established in November 2019, just as the pandemic began. The Michigan Institute for Clinical & Health Research (MICHR), with partners across campus, launched the Center with the goal of finding potential therapeutics for the thousands of human diseases for which there is no treatment.

Monoclonal antibody therapy has been around for decades and.COVID-19 monoclonal antibodies (lab-made antibodies given to a person that help their immune system stop the infection from spreading) have been gaining credibility as a key tool for protecting people most at risk of severe COVID-19. Preliminary research shows the treatment reduces risk for hospitalization or death by about 70%.

These treatments are authorized for emergency use in the U.S. by the Food and Drug Administration for people who are 65 and older and certain people age 12 and older, including people with obesity, diabetes and heart disease. Importantly, antibody treatment has to begin before COVID-19 progresses into severe disease or hospitalization, usually within the first 10 days of symptoms.

Monoclonal antibodies aren't a substitute for the preventative COVID-19 vaccines, but some public health officials have criticized the lack of awareness and access to monoclonal antibody therapy.

Dr. Rajesh Gandhi, an infectious disease physician at Massachusetts General Hospital, told the New York Times that more people need to be educated about how effective monoclonal antibodies can be at preventing severe disease.

Another surprising discovery occurred in the early days of the COVID-19 pandemic when doctors in Wuhan noticed something surprising. Many of the elderly patients who survived the virus were poor, an unlikely demographic expected to fare well in a health crisis. A review of the survivors' medical records revealed that a significant number suffered from chronic heartburn and were taking an inexpensive drug called *famotidine*, the key ingredient in *Pepcid*.

UVA Biomedical engineering professor and Dean of College of Data Science, Phil Bourne, and UVA senior scientist Cameron Mura worked with an international team of researchers to analyze information from a database that holds the medical records of millions of COVID-19 patients living in 30 different countries. The team narrowed that number down to around 22,000 people, the largest sample size for a study on *famotidine* and the disease to date.

"The power of the electronic health record, which is really yet to be fully realized as a research tool, is that you've suddenly got all this data you can mine to see whether what you determined in passing or anecdotally has any basis," Bourne said.

The team's analysis, which appeared in the journal Signal Transduction & Targeted Therapy (from the Nature publishing group), showed that the data supported findings from other smaller-scale studies. When delivered at high doses (the equivalent of about 10 Pepcid tablets), *famotidine* appears to improve the odds of survival for COVID-19 patients, especially when it is combined with aspirin. It also seems to hinder the severity of disease progression, making patients less likely to reach the point where they require intubation or a ventilator.

Vaccine Approval (cont.)...

authorization was granted to get as many vaccinated as possible.

The FDA defended its approach, pointing out that a full and careful approval process would increase confidence in the vaccines. Officials also claim that their hands were tied and had no choice but to follow the path that they did. However, this is inconsistent with facts.

Two basic ways show that the FDA did have a choice and could have acted more quickly. First, the agency did acknowledge that it moved more expeditiously than normal. Typically, a vaccine approval takes between eight and 12 months. Pfizer's vaccine received full approval three and a half months after the company filed its application. Once the FDA moved away from its usual process, it could have done so more aggressively than it did, something experts have been urging for months. Indeed, FDA leaders has already decided to grant approval long ago about the substantive part of the decision to grant full approval.

Secondly, American history is rife with examples of government officials overhauling such approval processes during a time of crisis. Frankliin D. Roosevelt repeatedly broke with tradition during the Great Depression and during World War II. More recently, Federal Reserve Chairman Ben Bernanke employed creative solutions to avoid another depression during the 2007-2009 financial crisis. They used legal "gray areas" to provide leeway and alternate avenues so that several approaches could be considered and instituted.

National emergencies can change the equation. Sometimes the concrete benefits of creative solutions far outweigh the benefits of beaucratic continuity.

In Brief (cont.)...

CEO *Mike Kaufmann* said.

- **Johnson & Johnson (J&J)** CEO *Alex Gorsky* is stepping down for personal reasons, effective 3 January. He will hand over the reigns to board vice-chairman *Joaquin Duato*. The transition is expected to be smooth given Duato's already significant role in executing J&J's pharmaceutical and consumer business strategies. He will also assume responsibilities for J&J's medical device business. Separately, J&J has received emergency use authorization for its single-dose COVID vaccine, according to India's Union Health Minister *Mansukh Mandaviya*.
- **Pfizer Inc.** and **BioNTech** announced they have submitted Phase I data to the **U.S. Food and Drug Administration** to support the evaluation of a third, or booster, dose of the companies' COVID-19 vaccine for future licensure. The data will also be submitted to the **European Medicines Agency (EA)** and other regulatory authorities in coming weeks.

Sources: Company Press Releases, Drug Store News, FiercePharma, and World Pharma News