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On the Horizon - New Receptor "Decoy" Drug Neutralizes COVID-19 Virus and Its Variants

(Source: An Article by World Pharma News)

Scientists at the Dana-Farber Cancer Institute have developed a drug that neutralizes SARS-CoV-2 and is equally effective against the Omicron variant, as well as every other tested variant. The drug is designed in a way that natural selection to maintain infectiousness of the virus should also maintain the drug's activity against future variants.

The investigational drug, described in a report published by *Science Advances*, is not an antibody, but a related molecule known as an ACE2 receptor decoy. Unlike antibodies, the ACE2 decoy is far more difficult for the COVID-19 virus to evade because mutations in the virus that would enable it to avoid the drug would also reduce the virus's ability to infect cells. The Dana-Farber scientists found a way to make this type of drug potently neutralize coronaviruses in animals infected with COVID-19 and to make it safe to give to patients.

This report comes at a time when antibody drugs used to treat COVID-19 have lost their effectiveness because the viral spike protein has mutated to escape being targeted by the antibodies.

The researchers, led by first author James Torchia, MD, PhD, and senior author Gordon Freeman, PhD, identified features that make the ACE2 decoys particularly effective and long-lasting. For example, they found that when they included a piece of the ACE2 protein called the collectrin-like domain, it made the drug stick more tightly to the virus and have a longer life in the body. Their experiments showed that ACE2 decoys have potent activity against the COVID-19 virus because they trigger an irreversible change in the structure off the virus by "popping" the top off the viral spike protein so it can't bind to the cell surface and infect cells.

The spike proteins (projections covering the COVID-19 virus) bind to the ACE2 receptor on the cell surface and it then refolds, driving the spike into the cell, enabling the virus to enter. ACE decoys lure the virus to bind to the decoy instead of the

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The next issue of the FOCUS Newsletter will be January 12, 2023.

The IFPW Team would like to wish everyone a joyous Holiday Season and a healthy New Year!

In Brief...

- **Walgreens Boots Alliance's (WBA)** has decreased its ownership of A**merisourceBergen's (ABC)** common stock from approximately 20% to 17%. The shares have been sold for approximately US$0.8 Billion and, subject to the completion of this Rule 144 sale, a concurrent share repurchase by ABC for proceeds of approximately US$0.2 billion. Proceeds to WBA will be used primarily for debt paydown and the funding of the company's strategic priorities, including the agreement for **VillageMD** to acquire **Summit Health-CityMD**, according to WBA sources.
- French pharmaceutical manufacturer **Sanofi** has officially moved to its new global headquarters in Paris. Named "La Maison Sanofi" the 9,000 square meter facility comprises two historic building and will house approximately 500 employees. The new facility is designed around hybrid work and sustainability, and reduces employee's carbon footprint by nearly 100%.
- Drugmaker **Amgen** has struck a deal with **Horizon Therapeutics** and will pay approximately US$28 billion for the company. The deal is expected to close in the first half of 2023, according to Amgen executives. Previously a bidding war ensued for Horizon between Amgen, Johnson & Johnson, and Sanofi.
- *Joaquim Duato* will assume the role of chairman of Johnson & Johnson as of January 2023, in addition to his CEO position. Current J&J chairman, *Alex Gorsky*, will depart from the company completely, and said that he "could not think of a better leader" than Duato to lead the J&J board.
- **Alliance Healthcare**, part of global healthcare company **AmerisourceBergen** and a leading wholesaler in pharma

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Using AI to Tailor DNA for Future Drug Development

(Source: A staff article from FiercePharma)

With the assistance of artificial intelligence (AI), researchers at Chalmers University of Technology in Sweden have succeeded in designing synthetic DNA that controls the cells' protein production. This technology can contribute to the development and production of vaccines, drugs for severe diseases and alternative food proteins much faster and at a significantly lower cost than is possible today.

How our genes are expressed is a process that is fundamental to the functionality of cells in living organisms. In other words, the genetic code in DNA is transcribed to the molecule messenger RNA (mRNA) which tells the cell's factory which protein to produce and in which quantities.

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On the Horizon (cont.)...

cell, rendering it inactive before it can enter cells. This explains the drug's surprising potency – not only does it function as a competitive inhibitor, but it permanently inactivates the virus. Since binding to the ACE2 is required for infection, variants can change but they must continue to bind to ACE2, making the drug persistently effective against all variants.

While the drug, called *DF-COV-1*, has not yet been tested in humans, manufacturing development is nearly complete and preclinical studies needed for regulatory approval are underway, with the goal of advancing the drug to clinical trials.

This work was supported by a U.S. Department of Defense CDMRP Peer Reviews Medical Research Program Technology/ Therapeutic Development Award. Additional support was provided by a National Institutes of Health grant, an Evergrande MassCPR award, and a grant from COVID-19 FastGrants.

The research was performed by a collaborative team including scientists from Dana-Farber Cancer Institute, Massachusetts General Hospital Vaccine and Immunotherapy Center, Boston University Aram V. Chobanian & Edward Avedisian School of Medicine, the National Emerging Infectious Disease Laboratory at Boston University, Colorado State University and Boston Children's Hospital.

Using AI (cont.)...

Researchers have put a lot of effort into trying to control gene expression because it can, among other things, contribute to the development of protein-based drugs. A recent example of this is the mRNA vaccine against COVID-19 which is designed to instruct the body's cells to produce the same protein found on the surface of the coronavirus. The body's immune system could then learn to form antibodies against the virus. It is possible to teach the body's immune system to defeat cancer cells or other complex diseases if one understands the genetic code behind the production of specific proteins.

Most of today's new drugs are protein-based, but the techniques for producing them are both expensive and slow due to difficulties in controlling how the DNA is expressed. In 2021, a research group at Chalmers, led by Alekesj Zelezniak, an associate professor of systems biology, took an important step in understanding and controlling how much of a protein is made from a certain DNA sequence.

"First, it was about being able to fully read the DNA molecule's instructions. Now we have succeeded in designing our own DNA that contains the exact instructions to control the quantity of a specific protein," said Zelezniak, when discussing the research group's latest significant breakthrough.

The principle behind the new method is similar to when an AI program generates faces that look like real people. By learning what a large selection of faces looks like, the AI can then create completely new but natural looking faces. It is then easy to modify a face by, for example, saying that it should look older or have a different hairstyle. Adversely, programming a believable face from scratch, without the use of AI, would have been a much more difficult and time-consuming task. Similarly, researchers' AI has been taught the structure and regulatory code of DNA. The AI then designs synthetic DNA, where it is easy to modify its regulatory information in the desired direction of gene expression. In other words, the AI is told much of a gene is desired and then prints the appropriate DNA sequence.

"DNA is an incredibly long and complex molecule. It is thus experimentally extremely challenging to make changes to it by iteratively reading and changing, then reading and changing it again. This way it takes years of research to find something that works. Instead, it is much more effective to let AI learn the principles of navigating DNA. What otherwise takes years in now shortened to weeks or days," according to first author Jan Zrimec, a research associate at the National Institute of Biology in Slovenia and past associate of the Zelezniak group.

The researchers have developed their method in the yeast *Saccharomyces cerevisiae*, whose cells resermble mammalian cells. The next step is to use human cells. Researchers hope that their progress with have an impact on the development of new as well as existing drugs.

In Brief (cont.)...

products in Europe, along with **GIRP, the European Healthcare Distribution Association**, convened policymakers and leaders across the healthcare and pharma industries to discuss antimicrobial resistance (AMR), as well as AMR response efforts and opportunities to collaborate on initiatives to combat this global public health issue. The event featured remarks from member of **European Parliament**, the **European Commission** and organizations at the forefront of response efforts, as well as panel discussions led by healthcare and pharmaceutical executives.

- China will drop its travel tracing requirement as part of its exit from its strict "zero-COVID" policies. Residents' travels will no longer be traced and recorded via a smart phone app, thus potentially reducing the likelihood of people being forced into quarantine for visiting pandemic hot spots. China's government made the announcement following three years of lockdowns, travel restrictions and quarantines on those individuals moving between provinces and cities, requiring mandated testing, and requirements that a "clean bill of health" be shown to access public areas.
- **Bayer** announced the U.S. launch of the *Bayer Science Collaboration Explorer (BSCE)* as part of its ongoing efforts to enhance public trust in scientific innovations, processes, and R&D activities. The BSCE is a publicly accessible database where Bayer shares information on its science collaborations and new contracts with universities, public research institutions and individuals.
- **AstraZeneca** is initiating efforts to expand in the oncology cell therapy space with the acquisition of **Neogene Therapeutics Inc.** AZ will pay US$200 million up front plus up to US$120 million in potential milestone to acquire Neogene, which specializes in developing next-generation T-cell receptor therapies and has operations in the Netherlands and California, U.S.
- Singapore's **Agency for Science, Technology and Research (A*STAR)** announced a new partnership between its research communities and **GSK, Sanofi**, and **Takeda Pharmaceutical** to enhance the country's biologics manufacturing capabilities, including for recombinant therapeutic proteins and vaccine. The alliance will be finalized through the *Biologics Pharma Innovation Programme Singapore*, a consortium managed by A*STAR.

(Sources: Drug Store News, FiercePharma, NPR, Press Relases, Scrip Intelligence and World Pharma News)