Achelois BioPharma, Inc.
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Variant-resistant therapeutics for pandemic viruses

Achelois developed molecular velcro-based antiviral technology to build next-generation therapeutics to pre-empt emerging pandemic viruses.

Despite significant advancements in developing vaccines, antibody-based neutralizing therapeutics, and oral antivirals for severe acute respiratory syndrome (SARS) coronaviruses, we are still unprepared for the next virulent variants or emerging pandemic. Current pandemic preparedness methods are often reactive and easily defeated by virus evolution, leading to only partial and temporary protection—as seen during the coronavirus disease 2019 (COVID-19) pandemic. Similar approaches have also failed to produce effective vaccines or therapeutics for influenza, hepatitis B virus (HBV), and other viruses with pandemic potential. Moreover, vaccine hesitancy and economic inequality present significant social obstacles to successful pandemic control through vaccination, which requires widespread and repeated administration. Therefore, there is an urgent need for game-changing therapeutics for SARS coronaviruses and other pandemic viruses. To this end, Achelois BioPharma developed variant-resistant antivirals with unique antiviral mechanisms to pre-empt future pandemics.

Molecular Velcro-based antivirals

Scientists at Achelois have been pondering the unique strategies that viruses employ to enter host cells while eluding the control of vaccinations, neutralizing antibodies, and antivirals. One particularly notable feature of virtually all enveloped viruses is the presence of hundreds of trimeric or oligomeric viral spikes, which can interact simultaneously with multiple copies of host cell receptors and attachment proteins. This evolutionarily conserved feature maximizes the virus's ability to infect cells through multivalent, Velcro-like spike interactions with the corresponding entry receptors on target cells. Although each individual molecular interaction may be modest, their collective strength enables them to outcompete bivalent neutralizing antibodies and other low-valency or monovalent binders. However, no treatments have been developed to counteract this spike multivalence—at least, not until now.

Taking inspiration from viruses, Achelois scientists have created 'antiviruses' using genetic programing to produce virus-like particles that display thousands of copies of multimeric spike-binding proteins, mirroring viral spikes. These antiviruses operate as a form of 'virus Velcro', turning one of the virus's strengths against it. They provide an attractive 'lure' that encourages the target virus to engage in Velcro-like interactions, thereby counteracting its multivalency and preventing it from entering a cell. Unlike vaccines and antibody treatments that must continually adapt to new variants, antiviruses target viruses with the same entry receptor, making them resistant to variants and ideal for both prevention and treatment.

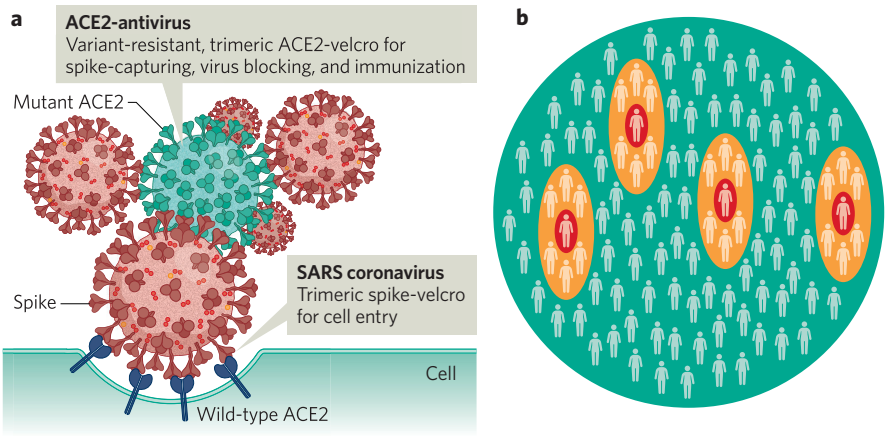

Fig. 1 | Pandemic control by variant-resistant ACE2-antivirus. a, ACE2-antivirus forms Velcro-like interactions with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). **b**, Effective pandemic control is achieved by treating and immunizing only the infected (red) and those in close contact (orange) with ACE2-antivirus.

Therapeutics for SARS coronaviruses

The company's lead antiviral product is the ACE2-antivirus, a novel multivalent neutralizing therapeutic targeting all SARS coronaviruses utilizing ACE2 as a cell-entry receptor (Fig. 1). Because the surface of ACE2-antivirus is covered in more than 2,000 copies of enzymatically inactive mutant ACE2 proteins in oligomeric patterns that mirror spike proteins on SARS coronavirus 2 (CoV-2) virions, SARS-CoV-2 preferentially binds to ACE2-antiviruses. The ACE2-antivirus is orders of magnitude more potent than clinically-approved neutralizing antibodies and has comparable potencies against all major variants tested so far, including the original, beta, gamma, and omicron variants. Intranasal delivery of ACE2-antivirus has been shown to save human-ACE2 transgenic mice from lethal infection by multiple SARS-CoV-2 strains—illustrating its potential as a highly potent therapeutic against these types of SARS coronaviruses. More importantly, ACE2-antivirus treatment in preclinical models also resulted in robust and broad protective immunity against future infections by multiple variants, indicating that ACE2-antivirus can function as a therapeutic vaccine for SARS-CoV-2. Finally, ACE2-antivirus is stable at 4°C and at room temperature for at least three months, can be efficiently aerosolized for localized delivery into the lungs, and is well tolerated in rats and non-human primates, thus having many favorable drug-like properties.

In summary, by using the ACE2-antivirus to counteract viral multivalence, Achelois has established a new variant-resistant therapeutic and immunization approach for pandemic control and preparedness. Notably, this new antiviral approach is pre-emptive, variant-resistant, and efficient because it only requires treating the infected people and their close contacts, whereas vaccines need repeated population-wide vaccination.

Ready to partner

Antivirus therapeutics were enabled by Achelois' proprietary technology to precisely control the number and oligomeric patterns of ACE2 proteins on engineered vesicles. Moreover, antivirus displaying any virus-capturing protein on its surface—including spike-recognizing antibodies—can be generated. Consequently, Achelois can produce highly potent variant-resistant antivirus against any viruses with or without defined high-affinity entry receptors. The company has proof of concept and patents for other programs in its pipeline, including candidates for Middle East respiratory syndrome, influenza and HBV, and is also applying the technology to build multivalent therapeutics to treat cancer, autoimmune, and inflammatory diseases.

Achelois is interested in finding partners to co-develop ACE2-antivirus and build a novel antivirus toolbox for all pandemic viruses. The antivirus technology is a powerful and versatile platform. It enables the rapid development of new antivirals to preempt more virulent variants of SARS-CoV-2 and emerging future pandemic viruses.

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