Drug development platform could provide flexible, rapid and targeted antimicrobials

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Anushree Chatterjee working with graduate student Dana Stamo in her lab at CU Boulder within the Department of Chemical and Biological Engineering. Credit: College of Engineering & Applied Science, University of Colorado Boulder

When disease outbreaks happen, response time in developing and distributing treatments is crucial to saving lives. Unfortunately, developing custom drugs as countermeasures is often a slow and difficult process.

But researchers at the University of Colorado Boulder have created a platform that can develop effective and highly specific peptide nucleic acid therapies for use against any bacteria within just one week. The work is detailed in Nature *Communications Biology* and could change the way we respond to pandemics and how we approach increasing cases of antibiotic resistance globally.

The Facile Accelerated Specific Therapeutic (FAST) platform was created by Associate Professor Anushree Chatterjee and her team within the Department of Chemical and Biological Engineering. It can quickly produce new antibiotics for any system or disease—from highly adaptive microbial super bugs to radiation poisoning in astronauts—that are specifically designed to selectively target just the bacteria of interest. The paper demonstrates significant growth inhibition and other positive responses in resistant bacteria such as E. coli, which are adapting to current treatments much faster than new drugs can hit the market.

Traditional drug discovery methods usually take 10 or more years and are specific to one bug or another. That is because they are based on identifying molecules from one bacteria that can then be used against other bacteria to promote human health. Unfortunately, evolution over billions of years has resulted in bacteria strains today that are increasingly resistant to this kind of approach—aided in part by recent over prescription of antibiotics by doctors. FAST, on the other hand, can be used for any bug and enables speedy identification and testing of molecules that target new mechanisms in pathogens—getting ahead of that curve.

Kristen Eller, a Ph.D. candidate in the Chatterjee Group, is the first author on the new paper. She said the FAST system utilizes bacteria's genetic makeup to design specific and targeted antibiotics that stop their natural means of producing essential proteins, causing them to die. She added that the platform also provides a unique strategy to deliver these treatments to bacteria that are traditionally hard to target because they reside within our own host cells. To get around this, the platform essentially utilizes bacteria's natural ability to invade our own cells and manipulates it instead to be a carrier of the therapeutic.

"The applications for the real world are immense in that we have created a platform—not just a single therapeutic," she said. "It is adaptive, dynamic and can be altered to target any bacterial species that is a threat while also being modulated to develop antivirals as needed."

Recently, another paper published in *PNAS* showed the use of the FAST platform to create novel antibiotics against a clinical isolate of carbapenem-resistant E. coli that was found to be resistant to pretty much all antibiotics.

Chatterjee said that last aspect is particularly important as particular strains evolve, change and become more resistant over time. The goal, she said, is to rapidly create tailored treatments specific to the region in question, the person seeking treatment or even the global health situation for example.

"The technology we use to treat these kinds of health issues has to be smart enough to keep up with evolving organisms and also quick enough to respond to real-time crisis," she said. "Within this platform there are multiple steps where you can design and create new drug targets, which is really key."

Chatterjee said the platform could eventually be modified to develop

antivirals for treatment of common colds, the flu and most pressingly, COVID-19. For now, her team is working on collecting more data to develop potential COVID-19 treatments and beginning to work towards clinical trials.

"We need to think out of the box when it comes to keeping up with pathogens because they are always advancing and changing," she said. "If we can establish these processes and techniques now, then we will be much better prepared next time there is a pandemic or outbreak."

More information: Kristen A. Eller et al, Facile accelerated specific therapeutic (FAST) platform develops antisense therapies to counter multidrug-resistant bacteria, *Communications Biology* (2021). DOI: 10.1038/s42003-021-01856-1

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