# Computers help chemists fight emerging infections

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Computer analysis of existing drugs may be key to fighting new infectious agents and antibiotic-resistant pathogens like deadly tuberculosis strains and staph 'superbugs.' Researchers in Canada say the use of such "emergency discovery" technology could save time, money and lives during a sudden outbreak or a bioterrorism attack. They reported here today at the 234th national meeting of the American Chemical Society.

Drug 'repurposing' or 'reprofiling' is not new: Pharmaceutical companies have been seeking new uses of old drugs to extend patent protections and whenever new, off-label uses of the drugs are found. But reprofiling to deliberately develop emergency drugs is a new concept, made possible by advances in chemoinformatics, a new field that merges chemistry with computer science, according to study presenter Artem Cherkasov, Ph.D., of the University of British Columbia in Vancouver, Canada.

"In the case of new infectious threats, there might be no time to develop a completely new drug 'from the ground up,' as the corresponding toxicological studies and regulatory investigations will take years to complete properly," says Cherkasov, a chemist with a background in computer-aided drug design and infectious disease. "Finding an already existing, well-studied therapeutic agent that will kill an emerging bug might provide a rapid, 'first line of defense' response option."

Under the new computer-aided system, the researchers plan to first identify vulnerable cellular components of a pathogen using proteomics,

or the study of proteins and their interactions. They will enter these key structures into the computer and, using elements of modern 'Artificial Intelligence,' will identify drugs that have the highest potential for activity against the target and for antimicrobial activity, says Cherkasov. Those compounds with the highest 'ranking' can then be quickly tested in the laboratory against the pathogen and eventually used to treat infected individuals, the researcher says.

The new approach is still in development for possible future use during an actual outbreak, Cherkasov notes. However, many non-antibiotic drugs have been shown to have antibiotic-like properties using this technique, he says. For example, computer studies have suggested that lovastatin, a drug marketed to lower cholesterol, and gentisic acid, an anti-inflammatory drug related to aspirin, both show promise as strong antibiotics. But more studies are needed before these compounds can be recommended for use as antibiotics in a clinical setting, he adds.

"It is not totally unexpected as there are thousands of existing drugs that are already enriched with target-binding structural features," Cherkasov says. "Many of them were not designed as antibiotics but have the potential to act as such."

"The chemical structures of compounds we identify usually look nothing like known antibiotics. But if a compound behaves like antibiotic in a computational model, it may act as one in a real life," says Cherkasov, who has programmed his computer system to identify 'antibiotic likeness,' or those chemical structures which have the most potential for antibiotic activity.

There is a growing need to expand and complement the range of available antimicrobial compounds, as many big pharmaceutical companies have withdrawn from the field of anti-infective agents, according to Cherkasov. Only two novel antibiotics have entered the

market in the last 20 years, he says.

The researchers plan to soon begin testing some of the newly identified antibiotic candidates against methicillin-resistant *Staphylococcus aureus* (MRSA). Also known as 'superbugs,' these bacteria are an increasingly worrisome cause of serious hospital-based infections and infections acquired in community settings.

Although Cherkasov's research team specializes in battling bacterial infections, similar techniques can be applied to emerging viral infections, such as SARS and bird flu, he says. Likewise, the technique also provides a potential means of identifying quick treatments for bioterrorism agents, such as new strains of anthrax, as well as rare infectious diseases such as those sometimes encountered in third-world countries.

Source: American Chemical Society