January 22, 2018 | By Ioana Patringenaru

New Algorithm Identifies Ten Times More Naturally Occurring Antibiotics than All Previous Studies

Drug resistance is a major concern worldwide. Many drugs, including antibiotics of "last resort" such as vancomycin and daptomycin, are Peptidic Natural Products (PNPs) that have an unparalleled track record in pharmacology. As a matter of fact, many antimicrobial and anticancer agents are PNPs. However, discovery of new PNPs is a difficult challenge, both experimentally and computationally.

In a paper published in Nature Microbiology on Jan. 22, a team of American and Russian computer scientists described a new algorithm that identified an order of magnitude, or roughly 10 times more, PNPs than all previous studies. Pavel Pevzner, a professor of computer science at the University of California San Diego, is the corresponding author on the paper.

PNPs represent one of the last bastions of the complex compounds that, until recently, remained virtually untouched by computational research. These compounds are produced by bacteria and fungi in a battle for survival and thus have a great potential to be natural antibiotics. With antimicrobial resistance becoming a global concern and medicine eager for new antibiotics, innovative methods for discovering natural product antibiotics are becoming of utmost importance.

In the study, researchers describe VarQuest, a novel computational approach for PNP identification. VarQuest can process immense amounts of mass spectrometry data (all spectra of natural products ever generated and made publicly available) in a single run and thus can be applied in high-throughput discovery pipelines such as the recently launched Global Natural Products Social (GNPS) molecular network. GNPS already contains over a billion of mass spectra collected worldwide, a gold mine for future bioactive compounds discovery. In contrast to existing competitors, VarQuest is able to identify not only known PNPs but also their novel variants, which are sometimes more clinically effective.

VarQuest analysis of the entire GNPS revealed an order of magnitude more PNP variants than all previous PNP discovery efforts. Moreover, VarQuest revealed a surprising diversity of PNPs that may reflect evolutionary adaptation of various bacterial species to changing environment and competition, for example, a continuous change of the repertoire of variants of peptidic antibiotics in response to developing antibiotic resistance.

"Researchers in the field of natural products are collecting large scale metabolomic data from microbial strains," said paper co-author Hosein Mohimani, former Pevzner's student who is now an assistant professor in the Computational Biology Department at Carnegie Mellon University. "Natural product discovery is turning to a big data field, and the field has to get prepared for this transformation, in terms of making sense of the Big Data. VarQuest is the first step toward making sense of the Big Data already collected in the field."

Mohimani earned his Ph.D. in the Department of Electrical and Computer Engineering at UC San Diego.

MEDIA CONTACT

Ioana Patringenaru, 858-822-0899, ipatrin@ucsd.edu

UC San Diego's Studio Ten 300 offers radio and television connections for media interviews with our faculty, which can be coordinated via studio@ucsd.edu. To connect with a UC San Diego faculty expert on relevant issues and trending news stories, visit https://ucsdnews.ucsd.edu/media-resources/faculty-experts.