

New algorithm helps identify antibody genes

August 1 2022



A new paper describes an innovative tool for prediction of immunoglobulin (IG) genes and a comparative analysis of IG genes. Researchers discovered a new type of IG genes common in bat species, which are spreaders of viruses. Credit: Unsplash/CC0 Public Domain

In a study published in the journal *Genome Research*, investigators in UC San Diego's Department of Computer Science and Engineering and

Johns Hopkins University have illuminated the immunoglobulin (antibody) genes in 20 mammalian species, gaining new insights into their targets and evolutionary origins.

To make these findings, the three authors invented a [new algorithm](#) called IGDetective, which can predict immunoglobulin genes based on the genome assemblies they produce. This tool has tremendous potential to reveal immunoglobulin diversity throughout the mammalian world.

"IGDetective gives us an automated way to analyze antibodies and identify their genes of origin," said Pavel Pevzner, the Ronald R. Taylor Distinguished Professor of Computer Science at the Jacobs School of Engineering at UC San Diego, a Howard Hughes Medical Institute investigator and senior author on the paper.

While immunoglobulin diversity makes mammalian immune systems incredibly resilient, it also poses a tremendous challenge for researchers trying to reverse-engineer the machinery. Antibodies are built from three different gene types, called variable (V), diversity (D) and joining (J). Immune cells then "glue" these VDJ elements together, creating a virtually endless series of VDJ combinations that are highly responsive to the world's many immune threats.

This multiple-component design has allowed immunoglobulins to evolve rapidly, making VDJ collections unique to different species and even individuals. Prior to IGDetective, no algorithms could predict immunoglobulin genes based on their VDJ outputs, forcing researchers to manually annotate, a slow and laborious process. IGDetective gives scientists a powerful new tool to analyze these genes and possibly translate their findings into antibody therapies.

"Antibody diversity amongst different species offers tremendous therapeutic opportunities," said co-author Yana Safonova, a former

postdoctoral fellow in the Pevzner group and now an assistant professor in the Department of Computer Science at Johns Hopkins University.

Bats and viruses

This work could also reveal new details about some viruses, such as the coronavirus that causes COVID-19. While bats carry many of these viruses before they make the jump to humans, it's unclear why they rarely get sick from them. One hypothesis argues that bats have greater immunoglobulin gene diversity, giving them more antibody combinations to neutralize pathogens.

To address these questions, the team used IGDetective to analyze immunoglobulin gene evolution in 20 mammals, including four bat species. These efforts identified a new family of bat V genes that contribute to antibodies that are uniquely rich in the amino acid cysteine, a potential first step towards verifying the bat IG diversity hypothesis.

"By analyzing these newly identified [immunoglobulin](#) genes, we found new families of germline IG genes that are common in [bats](#) and some other species," said Vikram Sirupurapu, a Ph.D. student in the Pevzner lab and first author on the paper.

"We assume that these [genes](#) contribute to the production of highly stable antibodies and can recognize new types of epitopes (the molecules on pathogens that antibodies target)," he said. "Though we couldn't confirm the bat IG [diversity](#) hypothesis, we assume further investigations involving more bat species will shed light on their unique interactions with viruses."

More information: Vikram Sirupurapu et al, Gene prediction in the immunoglobulin loci, *Genome Research* (2022). [DOI: 10.1101/gr.276676.122](#)

Provided by University of California - San Diego

Citation: New algorithm helps identify antibody genes (2022, August 1) retrieved 19 June 2024 from <https://phys.org/news/2022-08-algorithm-antibody-genes.html>

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