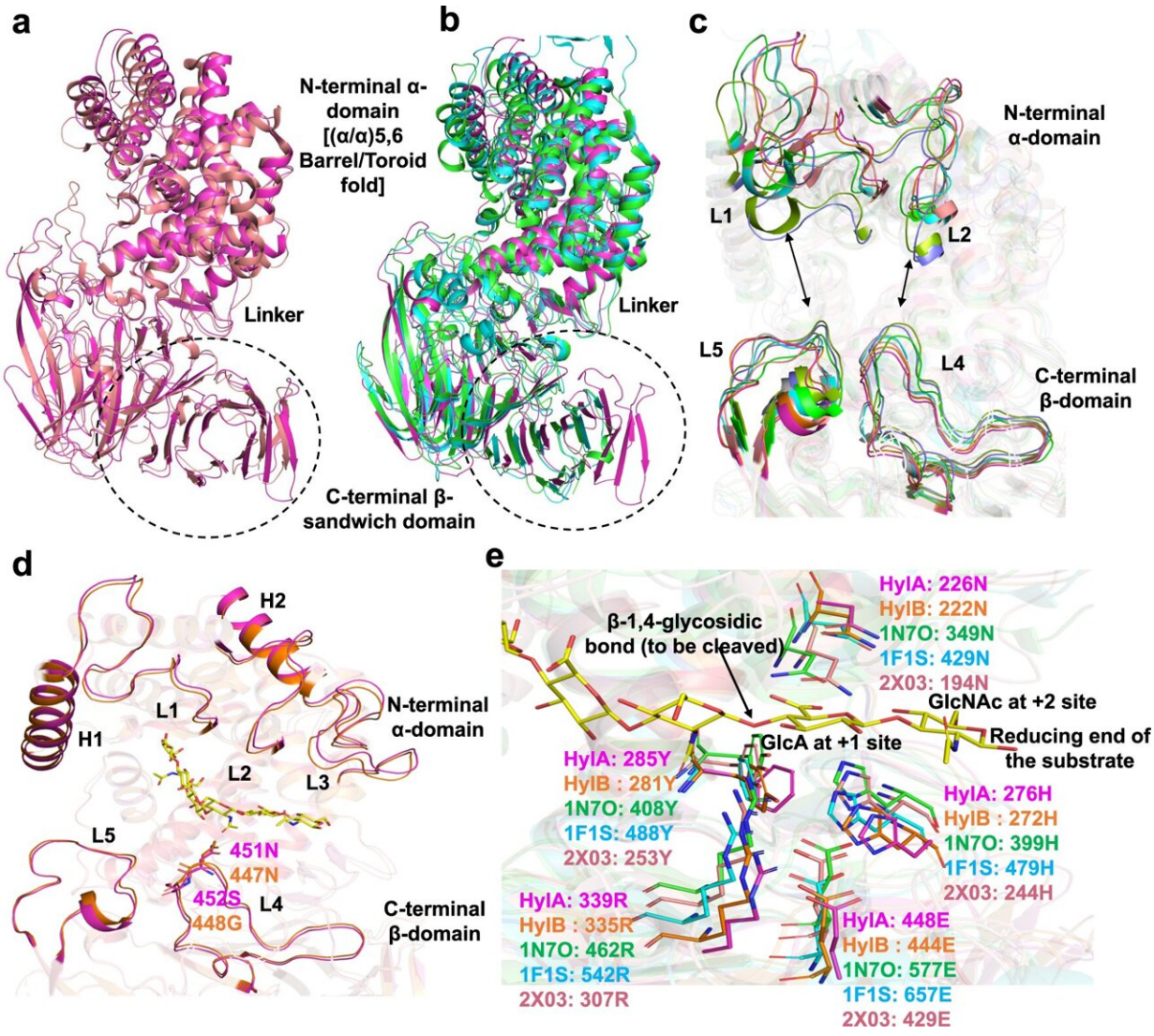
Bacterial enzyme research paves the way for acne vaccine

January 5 2024, by Sara Bock



Comparison of HylA and HylB with bacterial and animal Hyl. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-43833-8

In a groundbreaking development in the field of anti-acne therapies, a team of researchers at University of California San Diego School of Medicine has created an acne vaccine that successfully reduces inflammation in a mouse acne model. The vaccine neutralizes a specific variant of an enzyme produced by an acne-associated bacteria, while leaving the healthy bacterial enzyme intact.

This work was conducted in collaboration with colleagues at Cedars-Sinai Medical Center and University of California Los Angeles School of Medicine.

Approximately 70 to 80% of individuals develop acne at some point in their lifetime, most often during adolescence, with multiple factors—genetic, environmental and bacterial—to blame.

Through this new work, the scientists are now one step closer to helping drastically reduce the severity of this common condition with a more precise and less disruptive treatment than is presently available.

"We're working to develop a therapy that's much more tailored toward exactly what we know causes acne, rather than just generically blocking inflammation," said George Y. Liu, MD, Ph.D., professor and chief of the Division of Pediatric Infectious Diseases at UC San Diego School of Medicine.

"We hope that by understanding how bacteria induce acne, we can come up with a single or combination vaccine that would take care of acne much more effectively than we can right now."

More than a decade in the making, this research began with an attempt to answer a longstanding question regarding a type of acne-associated

bacteria called Cutibacterium acnes (C. acnes), which is plentiful on everyone's skin: If we all have C. acnes on the surface of our skin, then why do only some people develop acne?

In a paper published in *Nature Communications*, the researchers identified two variants of hyaluronidase, an enzyme produced by C. acnes. One variant, called HylA, is strictly made by C. acnes that are associated with acne. The other variant (HylB) is made by C. acnes associated with healthy skin.

In examining the structural and genetic differences between the two forms of the enzyme, the team found that while HylA worsens acne by causing inflammation, HylB actually appears to reduce inflammation and promote healthy skin. Their work further revealed that HylA and HylB originated from a common ancestor but evolved to have divergent effects.

In particular, the researchers investigated the differences in the way the two variants break down hyaluronic acid in the skin, revealing that HylA produces larger fragments of hyaluronic acid—leading to a more robust inflammatory response—while HylB produces smaller, anti-inflammatory fragments.

When the researchers removed the hyaluronidase genetically from both health- and acne-associated C. acnes, the bacteria became similarly non-inflammatory.

Based on this newfound knowledge, said Liu, who is one of the paper's senior authors, the team then developed therapeutic approaches, including a vaccine and inhibitors, that targeted HylA, the acne-causing variant, and successfully reduced inflammation. The study points to the value of understanding the genetic factors of C. acnes to inform the development of targeted acne treatments.

According to María Lázaro Díez, a former postdoctoral researcher in the George Liu Lab and one of the paper's five lead authors, this novel approach could potentially benefit a large number of acne patients, as there is no specific acne treatment of its type available to date.

"A major strength of this work was the interdisciplinarity and diversity of the team, working together with two common objectives: to expand the knowledge about acne pathogenesis and to use it as an approach for acne therapy," said Lázaro Díez.

The work builds on a 2019 study in which Liu led a team that used a synthetic sebum to develop a new mouse model that closely resembles human acne, allowing them to directly compare "good" and "bad" strains of bacteria.

As the researchers move forward in fine-tuning the use of selective HylA inhibitors and vaccines for acne therapeutics, they are encouraged by this preliminary success and hope to create a product that could be life-changing for many individuals who suffer from acne or are at risk of developing it.

"Our anti-acne directed approach has the potential to revolutionize acne therapies by offering more targeted treatments," said Irshad Hajam, a postdoctoral fellow in the Liu Lab and one of the paper's lead authors.

"What is truly remarkable about this work is we can now have more directed and effective anti-acne therapies while preserving the healthy skin microbiome, and that is a significant advancement in acne therapy."

More information: Irshad A. Hajam et al, Functional divergence of a bacterial enzyme promotes healthy or acneic skin, *Nature Communications* (2023). DOI: 10.1038/s41467-023-43833-8

Provided by University of California