

Infectious disease researchers unveil the secret life of flesh-eating bacteria

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Dr. James M. Musser, pathology and genomic medicine chair at Houston Methodist, led a research team that employed a tool first used for strep throat in horses to unveil the secret life of flesh-eating bacteria, giving them an in-depth understanding of the precise genes group A streptococcus uses to cause necrotizing myositis while living deep within muscle. Credit: Houston Methodist

Using a tool first used for strep throat in horses, Houston Methodist

researchers unveiled the secret life of flesh-eating bacteria and learned how it causes severe disease while living deep within muscle.

The team focused on necrotizing myositis, a devastating human infection with a very high mortality rate. Caused by group A streptococcus, this flesh-eating disease attacks the muscle, resulting in death up to 50 percent of the time and often leaves survivors with severe deformities and missing limbs.

"We call this identifying the secret life of group A strep because before this novel work was done we really did not understand the full range of different genes that were contributing to this terrible infection," said James M. Musser, M.D., Ph.D., chairman of the Department of Pathology and Genomic Medicine at Houston Methodist. "We were able to carefully dissect and pull back the curtain to identify what permits this organism to cause severe disease of muscle, the so-called flesh-eating disease. We now understand precisely what high-value targets we should be going after to disable or destroy."

Musser is the corresponding author on a paper appearing online Jan. 22 and in print Feb. 1 in the *Journal of Clinical Investigation*, titled "Gene fitness landscape of group A streptococcus during necrotizing myositis." Musser says his team now has an in-depth understanding of the precise genes that group A strep is using to cause this deadly infection in muscles.

"We used a special genetic tool that permitted us to one-by-one rapidly inactivate every gene in the group A strep genome, giving us the ability to hone in on the crucial genes responsible for causing or contributing to group A strep necrotizing myositis," Musser said. "By using this tool, we were able to identify 72 of group A strep's 1,800 genes as key genes to newly target for developing novel effective vaccines and antibiotics against this flesh-eating disease. So, in just one experiment, it enabled us

to identify every gene important for this bacteria to infect muscle."

The technique they used, called TraDIS, is a powerful genetic tool used in horses. It was first applied to an organism that is a cousin to human group A strep, called *Streptococcus equi*, which is a pathogen that causes an infection similar to severe [strep throat](#) in horses called strangles.

"We now have a genetic roadmap of how group A strep causes this flesh-eating disease. We can exploit this crucial information to begin developing new strategies to prevent the disease, make better treatments for our patients and, hopefully, create an effective vaccine against group A strep that finally wipes this organism off the face of the earth."

Used by scientists at the Animal Health Trust, a scientific and veterinary research charity in the UK, this new technique has only recently been applied to a small number of other pathogens, with Musser's lab being the first to use it in group A streptococcus.

Musser's UK collaborator, Andrew Waller, Ph.D., Head of Bacteriology at the Animal Health Trust, has used TraDIS for studies in horses and explains that the Houston Methodist Research Institute team did not have to adapt the tool that much for use in group A streptococcus, since the strangles bacteria is more than 80 percent identical to group A strep in humans. He says it has turned out to be an effective tool in many different bacterial pathogens, giving scientists a full listing of the genes contributing to deadly organisms.

"A key discovery was that we identified one family of specialized genes in the group A strep called transporters responsible for bringing nutrients into the bacterial cell that permit it to survive and thrive in places where we don't want it to be, for example in human muscle," Musser said.

"This understanding that transporters contribute extensively to this severe invasive disease in humans was very unexpected. Before this

study was done, we really didn't know these transporter [genes](#) were so important in causing the flesh-eating [disease](#)."

More information: Luchang Zhu et al, Gene fitness landscape of group A streptococcus during necrotizing myositis, *Journal of Clinical Investigation* (2019). [DOI: 10.1172/JCI124994](https://doi.org/10.1172/JCI124994)

Provided by Houston Methodist

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