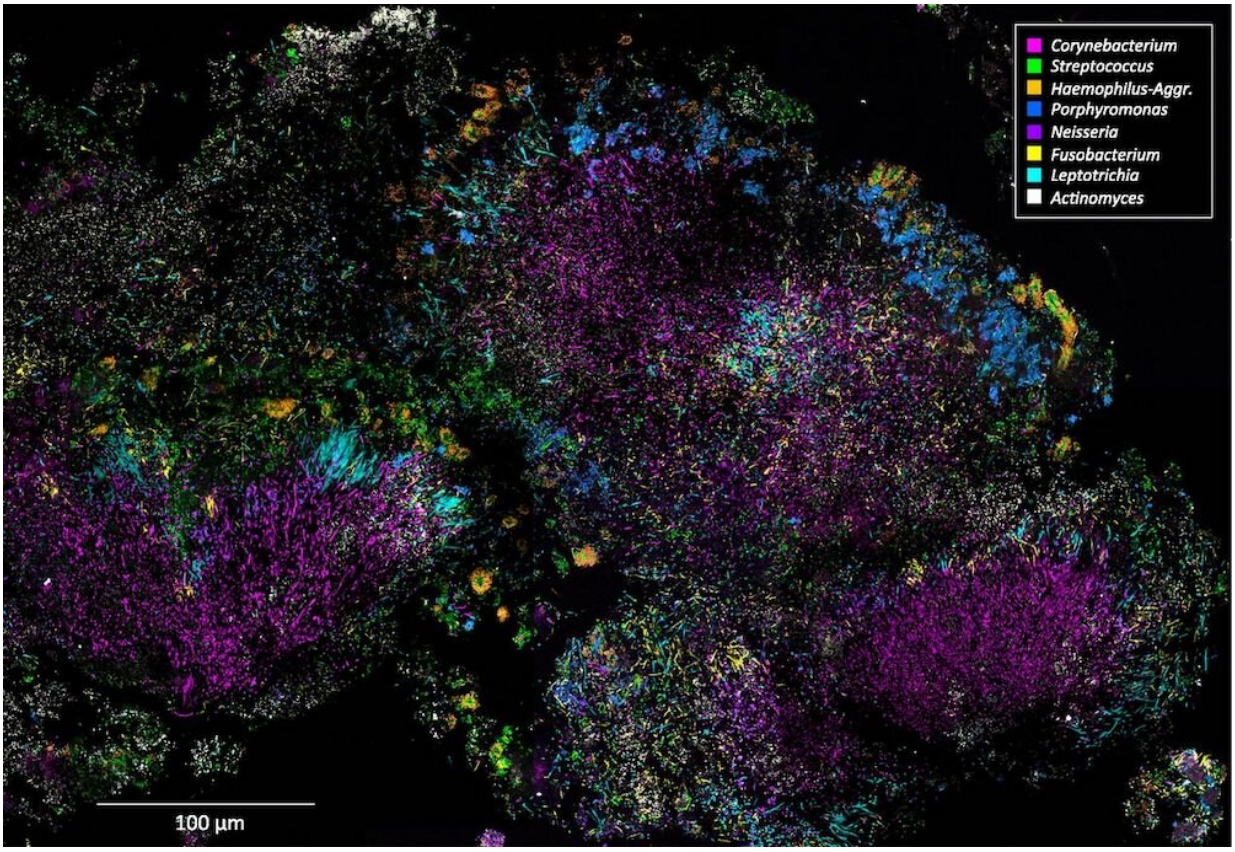
Oral bacteria 'battle royale' helps explain how a pathogen causes hospital infections

April 8 2019



Scientists know the genetic makeup of about 70 percent of oral bacteria. What they don't know is which species would live the longest without nutrients in a 'battle royale' -- so they decided to find out. Credit: Jessica Mark Welch and Gary Borisy, PNAS.1522149113

Hundreds of different bacterial species are living inside your mouth. Some are highly abundant, while others are scarce. A few of these oral bacteria are known pathogens. Others are benign, or even beneficial.

Scientists know the genetic makeup of about 70 percent of oral bacteria. What they don't know is which species would live the longest without nutrients in a "battle royale"—so they decided to find out. The results help explain how certain dangerous bacteria are able to persist in a sterile hospital environment and infect patients.

In a paper publishing later this week in the *Proceedings of the National Academy of Sciences* journal, researchers from the Forsyth Institute, the J. Craig Venter Institute, the University of Washington, and the University of California, Los Angeles, describe their discovery that three closely related species of bacteria belonging to the family Enterobacteriaceae outlived all other oral bacteria in long-term starvation or "doomsday" experiment.

"A number of species from that family are known to cause infections in hospitals," said Dr. Xuesong He, an Associate Member of Staff at the Forsyth Institute and co-author of the study.

To create a battle of bacteria, researchers placed hundreds of samples of oral bacteria from human saliva into test tubes. The bacteria, which are accustomed to living in the nutrient-rich mouth, were starved in their new environment. Each day, scientists checked the samples to see which bacteria were still alive.

Nearly every bacterial species died within the first couple of days. But three species—Klebsiella pneumoniae, Klebsiella oxytoca, and Providencia alcalifaciens—survived the longest, with Klebsiella pneumoniae and Klebsiella oxytoca surviving for more than 100 days.

Researchers were surprised to find that Klebsiella were among the champions of this bacterial combat. In their natural environment of the oral cavity, Klebsiella are considered an underdog. They account for only about .1 percent of all microbes in the mouth. But in an extreme environment deprived of all nutrients, Klebsiella reigned supreme while the bugs normally found in high abundance rapidly died off.

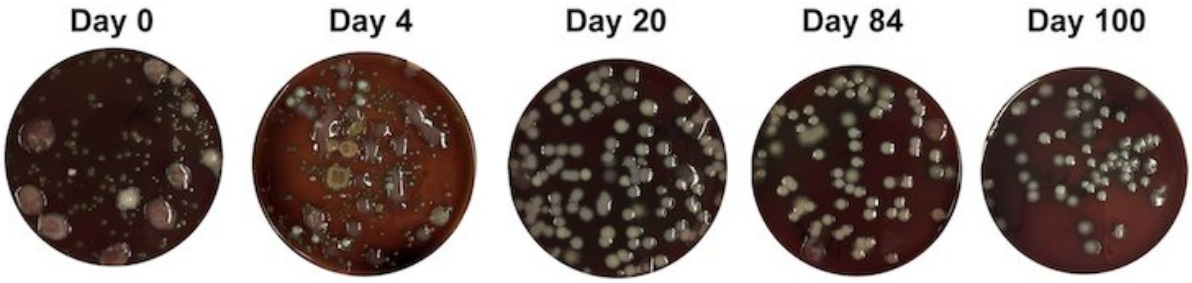


Fig. 2. Colony morphology during long-term starvation. Representative image of the PBS:saliva community on SHI agar following the indicated number of days of long-term starvation.

Credit: Forsyth Institute

How did Klebsiella pull off such a feat? To answer this question, scientists analyzed the genome of the bacteria on the first day of "battle" and then again on day 100.

"When we look at the genome content, it turns out that these Enterobacteriaceae species have larger genomes than other oral bacteria, giving them the capacity to tap into more diverse energy sources," said Dr. He. The researchers found that the Klebsiella had undergone genetic mutations that may have allowed them to survive and continue to function, even without a food source.

Scientists describe Klebsiella species as opportunistic pathogens. In

healthy people, they live in the mouth peacefully, crowded by other microbes and unable to grow or cause trouble. But outside the mouth, where few other bacteria survive, Klebsiella is king. They persist on hospital surfaces, like sinks or tables. If a patient with a compromised immune system makes contact with Klebsiella, that patient could develop an infection.

"Oral fluids like saliva are a rich source of bacteria and viruses. We want to understand how pathogens, that are typically rare, can become dominant and then also persist for long periods outside the body to be later transmitted," explains co-author Dr. Jeff McLean, a Professor at the University of Washington.

Infections by Klebsiella can result in a number of dangerous conditions including pneumonia and meningitis. One of the reasons Klebsiella infections are so dangerous is that Klebsiella are particularly adept at developing resistance to antibiotics, as well as transferring this drug resistance to neighboring bacteria.

"The finding that these Klebsiella species survive longer than their more benign neighbors in mixtures of saliva is likely to have a great deal of clinical significance, as multiple virulent outbreaks of antibiotic-resistant Klebsiella have been traced back to hospital sinks and drains," said Dr. Jonathon L. Baker, Ph.D. Baker is the Ruth L. Kirschstein NRSA Fellow in the Department of Genomic Medicine at the J. Craig Venter Institute and lead author of the study.

This research also helps illuminate a key ecological dynamic of bacterial communities.

"From a big picture point of view, this is a huge step forward towards understanding microbial social structure and ecology," said Dr. Wenyuan Shi, CEO and Chief Scientific Officer at the Forsyth Institute. "This

study begins to address a fundamental question in biology—how, evolutionarily, was a microbial community built, and what takes place as the community dies?"

More information: Jonathon L. Baker el al., "Klebsiella and Providencia notch a tag-team victory in a battle royale of oral bacteria," *PNAS* (2019). www.pnas.org/cgi/doi/10.1073/pnas.1820594116

Provided by Forsyth Institute