Bad Bacteria and Their Harmless Kin Share, Swap Genes

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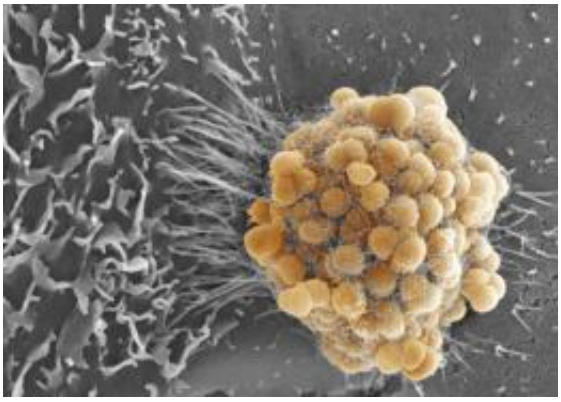

Neisseria bacteria (colored in orange) assemble pili, hollow protrusions made from an intricate protein structure (here visible as cob web-like structures wrapping around the bacteria), to exchange genetic information among each other and make contact with host cells. Here, Neisseria gonorrhoeae are pictured latching on to an epithelial cell found in the human cervix. (Credit: Dustin Higashi)

(PhysOrg.com) -- Comparing the genomes of disease-causing and harmless bacteria, University of Arizona microbiologists found no clear genetic demarcation between the two groups. The bacteria have swapped genes in the past, suggesting they can switch roles fairly easily.

In the bacterial world, good guys can potentially turn into bad guys and vice versa - just by swapping genes, microbiologists at the University of Arizona have discovered.

The researchers studied bacteria belonging to the genus Neisseria. These bacteria colonize the mucous membranes of humans.

Intrigued by the question of why some species of Neisseria are commensals - harmless colonizers whose presence in the body goes unnoticed - while others cause disease, the team identified the complete genetic codes of eight species of commensal Neisseria and compared them to the published genomes of the two known pathogenic species that cause gonorrhea and meningitis.

"The gene content of Neisseria species is fluid and not etched in stone," said lead author Magdalene So, who is a professor in the UA's department of immunobiology, where she directs the Microbial Pathogenesis Program. She also is a member of the UA's BIO5 Institute.

"These bacteria have the capacity to acquire new genes and drop others frequently," So said.

The study marks the first time scientists have determined the total gene content of a large group of related commensal bacteria and systematically compared it with the genomes of related pathogens. So's team reports its findings in Public Library of Science Online, or *PLoS One*.

To their surprise, the researchers found no clear genetic demarcation between commensal and pathogenic Neisseria. In fact, many commensals have the same genes known to promote virulence (the capacity to cause disease) in the two pathogens.

There is evidence that many genes, including virulence genes, have been exchanged between commensals and pathogens. Like the pathogens, the commensals have the machinery to acquire genetic information at high frequency. This leads the researchers to suspect that the Neisseria

species exchange genes with each other quite often.

"We know that the ability of pathogenic Neisseria to cause disease requires multiple virulence genes," said So. "If a commensal Neisseria by chance acquires the right combination of virulence genes, it would become pathogenic."

"What that combination is, we don't know yet. We have a good guess, and the huge data set we developed in this study will allow us to make much better guesses."

Neisseria use so-called pili, highly specialized structures made of proteins arranged like a spring, to take up large snippets of DNA - usually DNA from other Neisseria species. This process occurs frequently - about one in 10 bacteria take up DNA. The newly acquired DNA is then inserted in the genome. In this way, the bacteria acquire new molecular tools that are advantageous for their survival in a rapidly changing environment.

In previous work, So's group discovered that the bacteria also use pili to make contact with and communicate with their hosts' cells.

Bacteria even use their pili to crawl around: pili filaments grow from the bacterial body, tether to the cell, then are retracted into the bacterial body. This is analogous to the action of a fishing rod. Retraction of the pili allows the bacterial cell to move forward.

Pili are also used by the bacteria to congregate and form micro-colonies, which is an important part of the infection process.

"In the past, medical microbiology has focused on microbes that directly cause diseases," So said. "But there is a whole world of microbes living on and inside of us that we don't know a whole lot about."

While most of these commensals simply use our bodies as living space, others are necessary for us to survive. They help digest food, provide vitamins that our bodies can't make or ward off harmful microbes.

Given how successful commensal bacteria are in colonizing the human body, it may not be too far fetched to suspect these relationships could be beneficial to humans, in ways yet to be understood.

Recently, researchers were surprised to discover that bacteria also play roles in illness not usually associated with microbes, such as heart disease and diabetes.

"Commensals have many genes that are known to promote virulence in the pathogens," So said. "So we asked ourselves, what prevents them from becoming pathogenic?"

For example, Neisseria meningitidis, one of the most common causes of bacterial meningitis, makes a capsule that protects it from phagocytes, specialized cells of the immune system that gobble up intruders.

"The capsule, one would think, is key to a pathogen's ability to avoid being eliminated by the host," So said, "but surprisingly, not all Neisseria meningitidis strains have capsule genes."

The findings should prompt a renewed interest in the relationships between humans and microbes, she added, and help find targets for vaccines and antibiotics.

"For example, when you are trying to make an antibiotic targeting one of the Neisseria proteins, you want to make sure you choose one only the pathogen has. Otherwise you'll wipe out the commensals as well, which could open a niche for other, potentially harmful, microbes."

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