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BACTERIAL COAGGREGATION: A WAY DIFFERENT BACTERIA COME TOGETHER

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ALEX
AGE: 13

PABLO
AGE: 15

Bacteria are the smallest living organisms on this planet. While bacteria can live as free-floating single cells, many can specifically recognize other kinds of bacteria and stick to them. This ability is called coaggregation. Over 50 years ago, microbiologists first observed coaggregation between bacteria that grow in human mouths. However, it is becoming clear that coaggregation happens in many environments and may be an important and widespread phenomenon for bacterial survival. This article will help you understand bacterial coaggregation and hopefully inspire you to learn more about the microscopic behavior of bacteria.

STICKY SITUATIONS IN A MICROSCOPIC WORLD

We have all seen photographs or drawings of bacteria. Since the earliest drawings of these microorganisms, over 300 years ago, they have often been shown as small, individually arranged cells of various shapes. However, many species of bacteria are not solitary microorganisms and instead stick together to live in groups called aggregates. The most common type of aggregates are called **biofilms**, which are mixtures of microorganisms attached to interfaces (for example solid-liquid, liquid-oil, and air-liquid surfaces) and can contain tens to hundreds of bacterial species [1]. Examples of biofilms include dental plaque, the slime on the hulls of ships, and scum that forms on stagnant ponds.

BIOFILMS

A collection of bacteria that are stuck to an interface and each other.

AUTOAGGREGATION

The aggregation of bacterial cells of the same species.

COAGGREGATION

The specific recognition and attachment of different species of bacteria to one another.

ADHESIN

A protein on the surface of a bacterial cell that specifically recognizes and binds to a receptor on another bacterial cell.

RECEPTOR

A molecule containing complex sugars on the surface of a bacterial cell that is recognized by an adhesin.

COAGGREGATION NETWORKS

Coaggregates of more than two different species that are linked together through specific interactions.

The ability of bacteria to aggregate together is instrumental for biofilms to form. Some bacteria of the same species aggregate together through a process called **autoaggregation**, and this can help include more of the same species into developing biofilms. Interestingly, microbiologists have also realized that many bacterial species bind to *other* species through a highly specific process called **coaggregation** (Figure 1) [2]. Coaggregation might help biofilms form by allowing bacterial species to recognize and specifically stick to other species of bacteria that are already in developing biofilms [2]. Studies have shown that coaggregation mostly happens due to interactions between sticky proteins called **adhesins** present on the cell surface of a bacterial species and complex sugars called **receptors** located on the cell surface of another species (Figure 2). Adhesins and receptors are specific—they will only bind to each other if both are the right type. The interaction is a bit like a hand fitting into a glove, but a foot would not fit. Furthermore, bacteria can produce combinations of adhesins and receptors that allow for multiple species to coaggregate with each other and form a network of coaggregated cells. These **coaggregation networks** have been mapped for many bacteria in human dental plaque (Figure 3) (a type of biofilm that forms on the surface of teeth) and evidence suggests that these networks serve various functions [2]. Coaggregation networks are also being identified in many other environments. These include biofilms in drinking water, on human skin, and even on dogs' teeth. Coaggregation has been identified in so many environments that it may be a universal phenomenon among bacteria, making it important to understand why and how bacteria do it.

BRINGING BACTERIA WITH DIFFERENT ABILITIES TOGETHER

When thinking about why bacteria coaggregate, one of the most obvious reasons is summed up in the title of a well-regarded paper that focuses on coaggregation between dental bacteria: "Coaggregation: Adhere today, here tomorrow" [3]. Coaggregation helps bacteria to become part of biofilms, which stick tightly to surfaces and are not

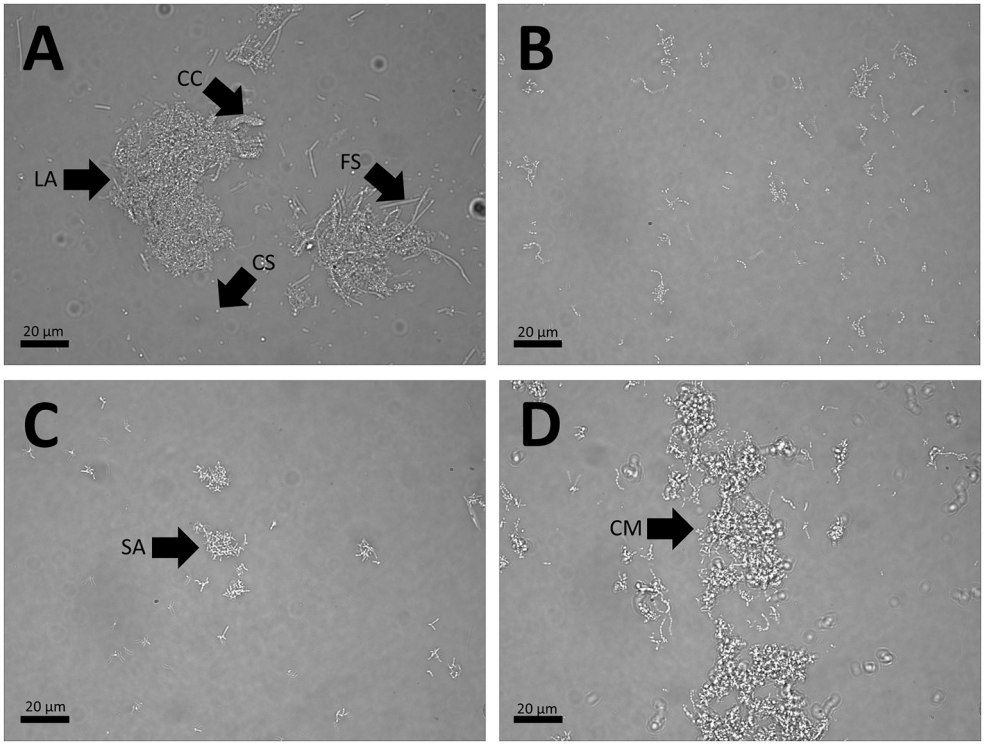

Figure 1

Microscopic images of aggregates and coaggregates. **(A)** A sample of human dental plaque, showing a large aggregate (LA) of bacterial cells, loose fusiform (rod)-shaped cells (FS), coccus (round)-shaped cells (CS), and a "corn-cob" (CC) coaggregated mass made by bacteria coaggregating around the fusiform cell. **(B)** Unaggregated dental bacteria *Streptococcus gordonii*. **(C)** Dental bacterium *Actinomyces oris* on their own and in small aggregates (SA). **(D)** A mixture of *Actinomyces oris* and *Streptococcus gordonii* cells that form a coaggregated mass (CM). The coaggregates formed within minutes after mixing the two species of bacteria.

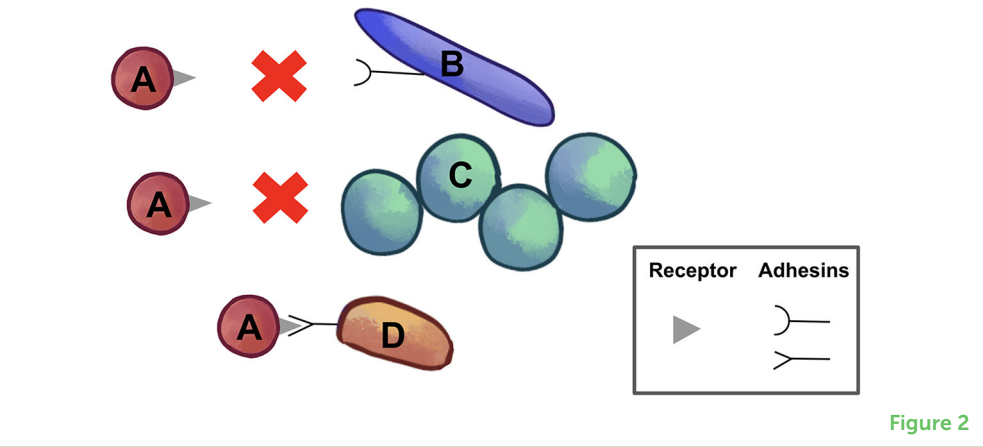

Figure 2

Specific interactions between adhesins and receptors allow coaggregation between certain species of bacteria but not others based on the molecular "shapes" of these molecules. Coaggregation does not occur between species A and B because the adhesin on species B does not fit with the triangle-shaped receptor on species A. Coaggregation does not occur between species A and C because there are no adhesins on the cell of species C. However, the adhesin on bacterial species D recognizes and sticks to the triangle-shaped receptor on cell of species A, allowing the two species to coaggregate.

easily washed away. Other reasons for coaggregation involve the ABCs—*alliances, battles,* and *conspiracies*. In the case of *alliances*, coaggregation can benefit both of the species involved. For example, the oral bacteria *Veillonella atypica* and *Streptococcus gordonii* coaggregate. *V. atypica* needs lactic acid to grow and *S. gordonii* produces it as a waste material. By coaggregating with *S. gordonii*, *V. atypica* can remove the waste material (which benefits *S. gordonii*) and use it for its own growth [4]. In terms of *battles*, coaggregation may allow one species to recognize and bind to another species to kill it! This may be the case for the bacterium *Lacticaseibacillus rhamnosus*, which lives in the human gut and coaggregates with *Escherichia coli* to kill it [5]. Finally, regarding *conspiracies*, coaggregation may allow

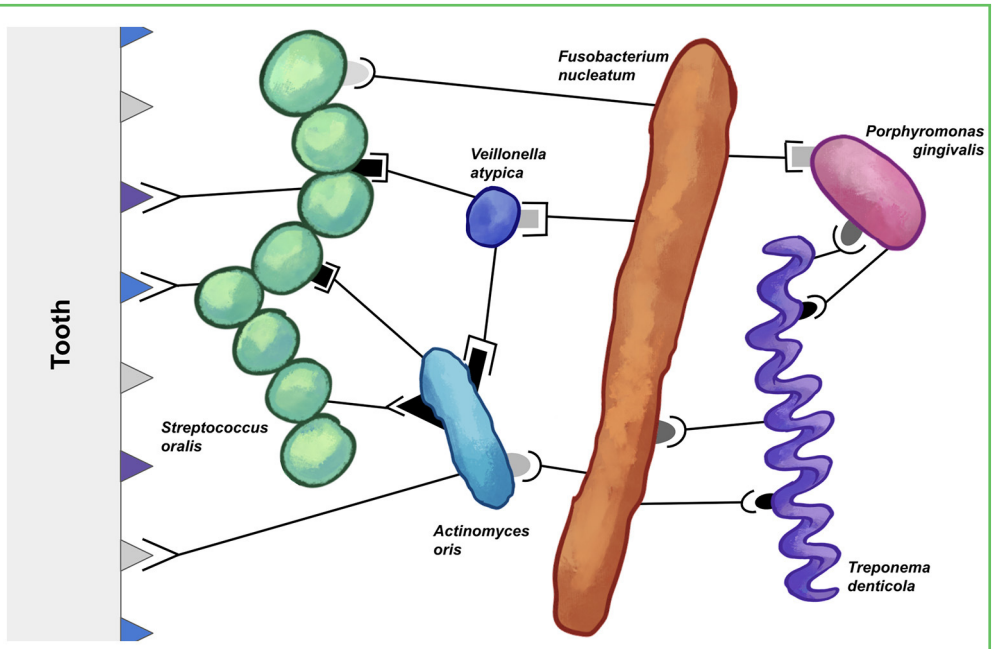

Figure 3

Figure 3

A simplified coaggregation network within dental plaque, a human oral biofilm. Certain oral bacteria, such as *S. oralis* and *A. oris* (shown here), stick to saliva and other substances that coat the tooth surface (gray, blue, and purple triangles). Then, other bacterial species stick to *S. oralis* and *A. oris* by specific adhesin/receptor interactions. This process creates a complex biofilm containing multiple bacterial species. Cells, adhesins, and receptors are not drawn to scale. A more complex coaggregation network is presented in Katharios-Lanwermeyer et al. [2].

bacteria to swap DNA, the genetic material required for building their cells. This may help the coaggregated bacteria gain new abilities, such as becoming resistant to an antibiotic [2].

WHY STUDY COAGGREGATION?

Biofilms are a huge problem in healthcare and can also damage homes, factories, and ships. For example, dental plaque forms on teeth and can cause cavities (and visits to the dentist). Biofilms inside pipes corrode their surfaces and can make the water look and taste bad, while biofilms on ship hulls cause damage and slow them down. Coaggregation may help biofilms to form and make them resistant to removal (e.g., with a scrubbing brush). It may also protect the bacteria from being killed by chemical treatments (e.g., with antimicrobial soap).

Preventing coaggregation may stop biofilms from forming as quickly and may make them easier to remove. For example, if we can exhaustively map coaggregation networks in biofilms, we might be able to identify a bacterial species that coaggregates with many other species and target that species to prevent alliances and conspiracies from developing. It may also be possible to use coaggregation to introduce species into biofilms to our advantage. For example, scientists are trying to find out if certain coaggregating **probiotic** (helpful) bacteria can help change how dental plaque develops, and possibly prevent tooth decay [6]. This kind of biological engineering could reduce our dependence on chemical treatments and antibiotics. Ultimately, if we understand how and why bacteria coaggregate, we

PROBIOTIC

Bacteria that can improve health by interacting with other bacteria.

can figure out how to select for coaggregating bacterial communities that will benefit our health and support a healthy environment.

CONCLUSIONS

Through coaggregation, bacteria can stick to other bacterial species and, once in a coaggregate, new behaviors and abilities emerge. Studying one species on its own will not necessarily reveal how it will behave in a biofilm that contains many species with which it can coaggregate. Alliances, battles, and conspiracies may be only some of the interactions that are happening in biofilms. There could be bacterial deception where, for example, one species coaggregates with another and tricks it into making a special nutrient. There could even be bacterial corruption, where coaggregation causes one or more species to damage other bacterial species, the **host**, or the environment. Ultimately, if we can manipulate coaggregation, we might be able to change which bacterial species are in a biofilm, how the individual species interact with the host or the environment, or the properties and activities of the entire biofilm community. Such manipulation could help us to treat disease or environmental problems caused by bacteria—from preventing cavities to protecting the hulls of ships.

HOST

A large organism (e.g., person) that is colonized by and shelters microorganisms.

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CONFLICT OF INTEREST: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

YOUNG REVIEWERS

ALEX, AGE: 13
My name is Alex. I am 13 years old and I am about to start 8th grade. In middle school, I enjoyed studying history, I also liked science because I am particularly interested in understanding how the microscopic world works, and how they interact with each other. Therefore, I would like to gain a deeper knowledge in this field, and possibly pursue it.

PABLO, AGE: 15
My Name is Pablo, I am half Mexican and half Spanish. I like to read and ask questions to improve my knowledge. I am very fond of science and technology and would like to become an engineer. My hobbies are to play the piano, videogames, football, and padel. I also like animals and cars, especially competition cars. My favorite animal is the eagle, and my favorite car is the Aston Martin Valkyrie. My idols are Adrian Newey and Fernando Alonso.

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