Biofilms and Antibiotic Resistance.

# Introduction

Have you ever wondered why your dentist recommend flossing every time you brush? Or why do you still have to get your teeth cleaned every six months even if you have good oral health? What your dentist I trying to prevent is the formation of bacterial biofilms in your mouth, also known as plaque. Bacterial biofilms are found across nature; they are formed by a community of bacteria attached to a surface. Biofilms contain one or many types of bacteria and are protected by an extracellular protective barrier (Hoiby et al). Generally, biofilms can form in a moist environment where where planktonic (floating) bacterial cells are always present; they thrive in nature due to resistant mechanism such as their protective barrier. The human body is a good environment for biofilms to form; however, biofilms in the body are more often introduced by contaminated medical devices. When foreign bacteria can attach to any surface in your body, they create an infection that must be treated with antibiotics. These infections are often found in hosts with weakened immune systems and can become resistant to treatment (Hoiby et al, 2010). There are many treatment options that can be used in bacterial biofilm infections; however, treatments are limited and might not always work (Frieri, Kumar & Boutin, 2016). There are several types of bacterial biofilms can cause human diseases, these are found in the human body and on medical devices. In this chapter we’ll learn how biofilms are formed, where they are formed and represent a threat to human health, and how biofilm infections can be prevented.

# Biofilm formation

The formation of biofilms begins when a single bacterial cell attaches itself to a surface, the cell begins to divide and forms a colony; other bacterial cells join it and attach themselves to the same surface and begin dividing too, this process is constant, and it allows the biofilm to grow rapidly. (Rodney M. Donlan, 2001). Biofilms can form on any smooth or rough surface where bacteria are able to attach; when planktonic (floating) bacterial cells adhere to a surface, the cells become fixed and begin to multiply, forming small bacterial colonies. In the next stage, the colonies begin to secrete “extra cellular polymeric substances (EPS),” the biofilm begins to grow, a protective coat that isolates bacteria from environmental stressors (Hoiby et al, 2010). Biofilms can grow because they constantly have bacteria adhere to their surface; when a biofilm becomes too thick or too crowded, the bacterial cells on the surface dislodge and attach to a new surface to begin a new biofilm formation (Hoiby et al, 2010). But how can bacteria on the surface tell that it’s time to move on and start a new biofilm? And why do these bacteria decide to live in a biofilm rather than floating around? The answer to the first question is because bacteria can communicate with each other; bacteria, in general, have developed their very own language and it’s called quorum sensing. This mechanism allows bacteria to talk to each other through unique signals which allow these bacteria to know when the cell density within the biofilm matrix is too high. When too many bacteria are present, the lack of nutrients can compromise the biofilm viability; therefore, the bacteria on the surface to move on to form a new biofilm, (Hoiby et al, 2010).

The answer to the second question is persistence; bacteria that lives in biofilms become more resistant to environmental changes due to changes in their protein expression. The bacterial cells in the center of the biofilm change their genes in order to survive in an environment with a low amount of nutrients and oxygen (Rodney M. Donlan,2001). Cells closer to the surface of the biofilm also have differences in their gene, compared to planktonic cells. (Balcazar

et al, 2015).

# Biofilms resistance mechanisms.

Biofilm infections thrive generally because they have a low susceptibility to environmental stressors such as antibiotics, low nutrient availability, and oxygen depletion, etc (Balcazar et al, 2015). There are several mechanisms that are used by bacterial biofilms to be able to survive. P. aeruginosa for example, is usually susceptible to penicillin; however, when it forms a biofilm, the cells that are in the inside of the biofilm are more deprived of nutrients and oxygen, which causes the cells to inhibit protein expression and become persistent (P.S. Stewart,2002). Note that persistent cells only partially shut down their protein expression which allows them to reduce the amount of nutrients that they use for surviving, at the same time, inhibited protein expression can result in antibiotic resistance; many antibiotics target the ribosome and if protein expression is inhibited, these antibiotics cannot target the ribosomal units that carry out translation. Another example is adaptive immunity; bacterial DNA undergoes mutations when bacteria are deprived of nutrients, it causes damage to their DNA, and can change their genetic material (P.S. Stewart, 2002). As it was mentioned before, the cells inside of the biofilm are persistent due to the lack of oxygen and nutrients; however, the bacterial cells on the surface of the biofilms are still receiving nutrients and oxygen, as a result, these cells develop a different resistance mechanism that is regulated by efflux pumps in their cell membranes. These pumps control what goes in and out of the cell, the biofilm reduces antibiotic penetrance which at the same time allows efflux pumps to maintain the inside of the cell free from toxic substances; however, this mechanism has been observed to be less successful (Frieri et al,2016). In addition, the high concentration of bacteria in biofilms could also be a defense mechanism which can trigger different stress responses within the biofilm (Hoiby et al, 2010). For instance, quorum sensing is essential for bacterial stress responses (Balcazar et al, 2015) These stress responses lead to the activation of secondary resistance mechanisms like horizontal gene transfer (HGT) in which bacteria can transfer resistance genes to each other via bacterial sex (Balcazar et al, 2015); moreover, bacteria has been observed to accelerate HGT in the presence of antibiotic low concentrations (Balcazar et al, 2015). Antibiotic resistant genes are more commonly developed in bacterial biofilms due to the different mechanisms that allow biofilms to become less susceptible to these; as a result, bacteria undergo mutations in their genes which can transfer not only to those species living in the biofilm but also among planktonic species (Hoiby et al, 2010). This process is believed to be one of the main reasons for antibiotic resistance increase in bacteria.

# Bacterial biofilm infections in humans

# The human body is a hospitable place for biofilm formation; many times, these biofilms are formed by foreign bacterial pathogens, fungi, or other common bacteria found on the skin. These microorganisms are introduced to the human body through medical devices; they can form on epithelial surfaces in the body or within the medical device itself for example: catheters, prosthetic joints, pace makers, mechanical heart valves, etc. (Rodney M. Donald, 2001). The formation of biofilms in the body can lead to infections. Biofilm infections in humans can be very challenging to treat and often impossible depending on the pathogenicity of its components (Frieri et al, 2015). These infections are often present in different parts of the body such as muscle tissue, lungs, urinary tract, bladder, mouth, pharynx, urethra, pancreas, etc. (Hoiby et al, 2010). When biofilm infections become difficult to clear, many antibiotics are used for their treatment which contributes to multidrug resistance. (Frieri et al, 2016) One example of this is the bacterial infection of P. aeruginosa in the lungs. This bacterium forms a biofilm in the lungs of people who suffers from cystic fibrosis, a rare disorder that promotes the formation of thick mucus in the lungs. P. aeruginosa can easily form biofilms in the lungs of these patients due to the abundant presence of oxygen, thickened mucus and moisture which contributes making these types of infections very hard to clear (Frieri, Kumal and Boutin, 2016). Other types of biofilm infections include urinary tract infections; biofilms form in the urinary track making UTIs more recurrent and harder to treat (Hoiby et al, 2010). Wound biofilms are usually formed in chronic wounds and they are yet another type of biofilm that can be detrimental to human health due to the many complications that it can present; thee biofilms are treated with mechanical methods such as wound dressings in addition to antibiotics. (Frieri et al, 2016). Biofilm formation can be prevented in some cases; however, there are many instances in which biofilm formation is unavoidable and irreversible. Preventative measures can be taken by identifying patients with higher risk of biofilm colonization due to having weak immune systems e.g. residents of long-term facilities (Frieri et al, 2016). Subsequently identify the potential risks of infection, and finally implementing measures to reduce the risk of infection. In cases in which bacterial biofilms are present in medical devices; replacing the medical device can be an effective treatment (Rodney M. Donlan,2001)

# Conclusion

Biofilms are formed by communities of bacteria and, or fungi that are present in the environment. They are more commonly formed in wet or moist environments. Biofilms are promoters of bacterial evolution due to the horizontal gene transfer that occurs among all bacteria, they are also responsible for deadly infections caused in humans due to the evolution of antibiotic resistant genes. Bacteria in biofilms have undergone mutation in their DNA which allows these to survive in harsh environments, those genes have been transferred to other bacteria in the regular environment and have led to the increase in antibiotic resistance. Biofilms can also be indicators of chemical pollution in water. E.g. waste water treatment facilities or contaminated rivers and lakes (Balcazar et al, 2015). This can become useful for humans to identify pollution in the water. Finally, biofilms are still being highly studied by scientist who are looking for ways to fight antibiotic resistance by understanding gene expression of bacteria that lives in biofilms.

References

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