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Antibiotic sensitivity and horizontal gene transfer in *Escherichia coli*

A genome-wide perspective

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ABSTRACT

Since their discovery in the early 20th century, antibiotics have truly revolutionized human medicine. They have allowed us to treat diseases that were previously untreatable and have become a staple of modern medicine. However, along with the human use of antibiotics pathogens resistant to antibiotics emerged. Over the last decades, an arms race between bacteria developing resistance and human medicine has been raging. Today, antibiotic resistance is a global problem with even the most potent antibiotics losing their efficiency.

Antibiotic resistance occurs when bacteria develop mechanisms to withstand the antibacterial effects of antibiotics. It is widely known that, once developed, resistance is selected for by the concentrations of antibiotics that are used to treat infections. In addition, it is becoming increasingly evident that even very low levels, often many times lower than those used in a clinical setting, can select for resistance. These low levels of antibiotics are commonly found in the environment where they contribute to the global reservoir of resistance by maintaining a constant level of resistance. Antibiotic resistance can also spread between bacteria through horizontal gene transfer. The major driving force behind this is believed to be bacterial conjugation. Despite this, the underlying mechanisms of conjugation are not fully understood.

In this thesis, antibiotic resistance and horizontal gene transfer is explored from a genome-wide perspective. The results indicate that the presence of resistance genes alone does not give the full picture when it comes to growth at sub-inhibitory levels of antibiotics. We also discuss how conjugation can be inhibited and found both genetic and environmental factors that can impair conjugation. Overall, our findings emphasize the importance of understanding the emergence, selection, and spread of antibiotic resistance at sub-inhibitory concentrations of antibiotics.

Keywords: antibiotics, antibiotic resistance, *Escherichia coli*, heavy metals, bacterial conjugation, pangenome, sub-inhibitory