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Bacterial Persister Cells and Development of Antibiotic Resistance in Chronic Infections: An Update

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The global issue of antimicrobial resistance poses significant challenges to public health. The World Health Organization (WHO) has highlighted it as a major global health threat, causing an estimated 700,000 deaths worldwide. Understanding the multifaceted nature of antibiotic resistance is crucial for developing effective strategies. Several physiological and biochemical mechanisms are involved in the development of antibiotic resistance. Bacterial cells may escape the bactericidal actions of the drugs by entering a physiologically dormant state known as bacterial persistence. Recent findings in this field suggest that bacterial persistence can be one of the main sources of chronic infections. The antibiotic tolerance developed by the persister cells could tolerate high levels of antibiotics and may give rise to persister offspring. These persister offspring could be attributed to antibiotic resistance mechanisms, especially in chronic infections. This review attempts to shed light on persister-induced antibiotic resistance and the current therapeutic strategies.

Keywords: bacterial persister cells, biofilms, chronic infections, antibiotic resistance, antibiotic tolerance

INTRODUCTION

Persister cells are a subset of bacteria that can survive high levels of antibiotics with genetic changes by reducing their metabolism and becoming metabolically inactive. When bacteria acquire genetic mutations or come into contact with an environment that restricts their growth, it leads to antibiotic tolerance [1]. The tolerance developed by persister cells is slow and reversible, allowing them to switch back to their active state once antibiotics are removed [2].

Several bacteria cause persistent infections, and the emergence of persister cells is a significant contributor to chronic infections and antibiotic resistance [1–3]. In recent times, it has been discovered that there are viable sub-populations of persister cells in fungal strains like C*andida albicans* that can survive high concentrations of antifungal agents [4, 5]. This shows that persister cells have the ability to survive antibiotic treatments, which is a common feature among all microbial persisters. Essentially, bacterial persisters are phenotypic variants of regular cells that can survive harsh antimicrobial treatment. If the antimicrobial agent is removed, persister cells can resume their growth and could facilitate infection [3–5].

Formation of persister cells is not an inherited process and is mainly controlled by growth phases and various environmental stress factors. Persisters make up a small fraction of exponentially growing cells and do not reproduce in the presence of antibiotics. However, these cells switch back to

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