Epigenetic Investigation of Antibiotic-Tolerant Persister Wake-up Chronic Infection Mimicking Conditions

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In today’s world uncontrolled and unconscious antibiotics usage cause huge risk to human health due to rapid development of resistant bacterial strains. Infectious bacteria have the ability to change its genetic material under antibiotic stress. This resistance becomes more serious when bacterial population exposes to antibiotic stress for longer periods via transferring genetic modifications through survived persister cells. Persister cells are resistant to almost any antibiotic and cannot be cleared from the body even with heavy antibiotic treatments. Even though their ratios are only 0.01% or less in bacterial population, this is enough to re-emergence of the next round of infection. Therefore controlling persister cells in chronic diseases might stop further genetic changes of the next generations. To better understand the physiology of persister wake-up process, we have investigated the epigenetic level changes under different antibiotic regimes by using microarray and Q-PCR analysis method. Specifically, transcription profile of E. coli persister cells under the infection mimicking conditions was studied. We have observed that elevated level of aminoacids can change the expression level of some DNA repair related genes during persister wake-up. This might indicate that under the stress conditions persister cells go into a stage which is more convenient for modifications on bacterial genome. Therefore, co-treatment of antibiotics and DNA repair blocking agents might be a good strategy to fight with chronic infections to stop their recurrence. Besides, this data can be used to understand the persister cells physiology better and develop antimicrobial agents to target these preventative measurements of bacteria before they develop further resistance.

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