Implementation of a microfluidic device for real-time monitoring and sorting of E. coli persister cells

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Abstract

Bacterial persistence is a major research topic in modern microbiology. To this day, the underlying mechanisms behind antibiotic persistence are still unclear and controversial. The very low occurrence of this phenomenon among a bacterial population makes observation and analysis of persister cells challenging. Single cell analysis represents the best alternative to classical culture-based methods in order to understand what triggers the differentiation of these elusive persister cells from the vast majority of sensitive cells. We developed a microfluidic device using the submicrometric resolution of the Nanoscribe 3D printer, in order to visualize and sort *E. coli* persister cells. The device uses trapping chambers of the size of bacteria with an iteration rate compatible to the very low occurrence rate of persistent cells (1/1.000-10.000). After inoculation, cells are pushed inside trapping chambers by centrifugation, allowing a fast and stress-free cell capture. Cell growth and filamentation, a characteristic trait of persister cell recovery after an ofloxacin treatment, can be monitored in real-time under the microscope. The design is such that only persistent filamentous cells will be swept by the flow and sorted downstream by deterministic lateral displacement. Methods to recuperate and characterize the persister filaments at the molecular level are currently being investigated.

Keywords: Mother Machine, single, cell, bacteria, persistence, antibiotics

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