Bacterial persistence based on epigenetically correlated stochastic gene expression

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Abstract

Recent progresses of single-cell measurement and analysis have accumulated the evidences on phenotypic heterogeneity at the individual cell level in clonal populations, which is manifested by, for examples, gene expression and growth rate fluctuations. Several lines of research suggest that such phenotypic heterogeneity is beneficial for the survival of cell population under certain conditions. Bacterial persistence is a great model phenomenon for understanding the roles of phenotypic heterogeneity in the survival of cell population. It is the phenomenon in which a subset of clonal population survive lethal environments such as antibiotic exposures without genetic mutations. It is usually assumed that persistence relies on keeping non- or slow-growing "dormant" cells in a population that could circumvent unbalanced growth provoked by stress. Here we report that this picture is only a part of the story of bacterial persistence; our single-cell measurement on the persistence of M. smegmatis against isoniazid shows that growth state before drug exposure is not correlated with the survival of individual cells. Also, we reveal that the persistence phase, in which the number of cells in a population is nearly leveled off, is in fact dynamic with balanced division and killing rates. A quantitative analysis suggests that the epigenetically correlated stochastic gene expression of catalase-peroxidase drives the cell population to exhibit persistence. We present a simple mathematical model and derive a general relation between persistence efficiency and the properties of fitness fluctuation.

Keywords: Bacterial persistence, stochastic gene expression, cell lineage analysis, microfluidics

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