Biological outcomes of CDI-system-delivered DNase toxins

Popular Science Summary

There are different mechanisms of inter-bacterial competition, but one of the systems that was characterized recently is known as Contact-dependent growth inhibition (CDI). As the name suggests, this system helps a bacteria to inhibit the growth of another bacteria upon direct cell-to-cell contact. The system itself is species specific meaning, that *E. coli* can only inhibit *E. coli* and other species their own respective counterparts. The cells which are carrying CDI system have three additional genes on their DNA, which code for three-part system, helping the bacteria to inhibit or kill other bacterial cells around it and to become a dominant in the particular environment. Inhibitory process takes place once the toxin (DNase, RNase etc.), produced and delivered by CDI^+ cells using a protein so called stick (due to its long, rod-like shape), is delivered to the neighboring bacterial cell's surface.

There are different genes switched on or upregulated once the bacterial DNA is damaged. Major factor in initiating the DNA repair is called SOS DNA-damage response during which various genes are induced to help the process of DNA repair or to inhibit the process of proliferation of the cell, so the damaged DNA content does not pass on to the daughter cells. In addition there are other systems taking part into these complex DNA repair processes, referred to as Toxin-Antitoxin systems (TA systems). Different types of TA systems do different tasks. The two members of this, Type I toxin-antitoxin (TA) system, are TisB-IstR and DinQ-AgrB and overexpression of these proteins results in cell membrane depolarisation.

For example, TisB was shown to increase persister formation in bacterial populations, when induced with Ciprofloxacin treatment. As previous findings suggested that cells carrying a CDI system had an increased persister formation, we were wondering if the CDI system delivered DNase toxin activates SOS DNA-damage response and if this results in type I TA system dependent depolarisation of the membrane and if this in turn results in an increased persister formation in the cells.

We find that target cells co-cultured with CDI^+ inhibitor expressing DNase toxin, showed upregulation of the SOS DNA-damage response and the TisB type I TA system. This induction resulted in membrane depolarisation in wild type cells, but whether this was through the action of the TisB and DinQ type I TA systems might be debatable. We think there might be other factors involved in addition to TisB and DinQ expression in the cell that upon SOS response induces membrane depolarization. We believe that further research should be conducted to receive answers about this matter.

In addition we show that cells carrying and delivering DNase formed more persisters compared to W.T, after 3 hours of treatment with Ciprofloxacin (Ciprofloxacin targets DNA, thus induces SOS response). We believe that the increase in persister cell formation was dependent on the TisB and DinQ type I TA systems, confirming our hypothesis that the CDI system expressing DNase toxin contributes to increased persister formation in bacterial culture through an SOS mediated induction of TA systems.

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