CdiA toxins induce the formation of antibiotic persisters

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There are many different toxin-antitoxin systems. Contact-dependent growth inhibition (CDI) is a system that acts only when cells are in direct contact with each other. The system was discovered when an *E. coli* isolate derived from the intestinal tract of rats inhibited the growth of other laboratory *E.coli* strains. Inhibitor cells containing the toxin (CdiA) for the CDI system inhibit target cells by delivering their toxin to the target cell. If the target cell expresses the immunity protein specific to that toxin, the cells will be protected and will not be inhibited.

Antibiotics function by inhibiting growing of cells as they target essential active processes within the cell. If the cells are in a metabolically inactive state (persisters) then they cannot be affected by the antibiotic. These cells randomly in time switch back into growing cells that can multiply and increase in number.

During amino acid starvation the level of ppGpp alarmone goes up and ppGpp binds to RNA polymerase. RNA synthesis is inhibited and the remaining amino acids are maintained i.e. kept in the cell. Maisonneuve E. et al have successfully shown that a high level of ppGpp is associated with increased persister formation.

The first goal of this project was to see if cells expressing the CdiA toxin form more antibiotic persisters than the cells containing no toxin. The second goal was to see if target cells inhibited by strains containing the toxin form antibiotic persisters. Finally, the third goal was to identify whether ppGpp is an essential factor required for these processes.

The results indicate that presence of the CdiA toxin does lead to an increase in antibiotic persisters. The target cells containing no CdiA toxins were inhibited by the strains expressing the toxin and did form persisters. Whether ppGpp is a necessary component for these actions or not cannot yet be determined and further investigations must be done.

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