Adenylylation of Gyrase and Topo IV by FicT Toxins Disrupts Bacterial DNA Topology

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Toxin-antitoxin (TA) modules are ubiquitous molecular switches controlling bacterial growth via the release of toxins that inhibit cell proliferation. Most of these toxins interfere with protein translation, but a growing variety of other mechanisms hints at a diversity that is not yet fully appreciated. Here, we characterize a group of FIC domain proteins as toxins of the conserved and abundant FicTA family of TA modules, and we reveal that they act by suspending control of cellular DNA topology. We show that FicTs are enzymes that adenylylate DNA gyrase and topoisomerase IV, the essential bacterial type IIA topoisomerases, at their ATP-binding site. This modification inactivates both targets by blocking their ATPase activity, and, consequently, causes reversible growth arrest due to the knotting, catenation, and relaxation of cellular DNA. Our results give insight into the regulation of DNA topology and highlight the remarkable plasticity of FIC domain proteins.
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