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Poster #66: Tin: A Minimalist Abortive PD-(D/E)XK Nuclease Fusing Sensor and Effector Functions for Anti-Phage Defense

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Bacterial abortive infection (Abi) systems typically require multi-component complexes to detect phages and execute cell death. We characterize Tin, a 253-amino-acid protein encoded by prophage P2, as one of the smallest known Abi proteins that mediate phage sensing and abortive response. We demonstrate that Tin protects against T4-like phages by directly recognizing the phage SSB protein gp32. Structural studies reveal that gp32 binds a dimeric core of Tin, stabilizing an activated conformation of the PD-(D/E)XK catalytic motif. Notably, Tin sensory loop integrates into and completes a nuclease domain after gp32 binding - a unique mechanism enabling sensor–effector fusion in such a compact protein. Upon activation, Tin non-discriminately degrades host and phage DNA, and demonstrates an activity against glucosyl-hydroxymethylcytosine-modified T4 genome, challenging the paradigm that such modifications universally block nucleases. Bioinformatic analysis links Tin to type I restriction-modification systems and NucC, underscoring its place among defense systems. This work explains how a regulation of the abortive nuclease can emerge via insertion of a short sensory loop interacting with the phage trigger.

Reference #1

Reference #2

Reference #3

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