Structural insights into the bacterial antiviral defense system Thoeris

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To survive bacteriophage (phage) infections, bacteria have evolved numerous antiphage defense systems. In addition to the well-known gene and genome "scissors" - restriction-modification and CRISPR-Cas systems - more than 200 different bacterial antiviral defense systems have recently been discovered. Some bacterial antiviral defense systems share components and mechanisms with eukaryotic immune system.

Thoeris is a bacterial antiviral defense system, consisting of two components [1]. The first one is a sensor, the TIR (Toll/interleukin-1 receptor)-domain protein ThsB, TIR domains are widely found in animals and plants, where they are essential components of the innate immune system. The second component of Thoeris is an effector ThsA protein, which contains SIR2, Macro or Caspase domains, distinct for three characterized Thoeris types. During phage infection ThsB recognizes a phage protein and synthesizes a unique signaling molecule which is then bound by the ThsA effector and induces cell death [2-4].

Cryo-EM studies of type I Thoeris system revealed activation of ThsA effector by filament assembly [5]. Structural studies of the type II Thoeris Macro domain protein lead to discovery of a novel signaling molecule [6]. Chemical inhibition of the type II Thoeris defense system improved the efficacy of a model phage therapy against a phage-resistant bacterial strain in a mouse infection, suggesting a therapeutic potential [7].

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