Contribution ID: **75** Type: **Poster only**

Poster #75: Who starts, who follows: reading assembly grammar in bacterial and metazoan death domains

Monday, 5 October 2026 21:22 (1 minute)

Accurate cell signaling requires information to be moved through a cascade of signaling effectors in a directional and controlled manner. Death domains orchestrate metazoan signalosome formation through ordered, often heterotypic assembly.
However, whether these assembly rules are universal has remained unclear. The recent discovery of bacterial death domain homologs provides a valuable opportunity and we find that bacterial and metazoan death domains share the same assembly and directionality grammar: Each system has a nucleator to start complex formation and a dependent domain that requires the base created by its seeding partner. Recent work shows that bacterial death domains (bDDs) indeed mediate phage defense in various systems featuring TIR, PNP, and CHAT domains as effectors (in collaboration with Gideon Cummings, Wein Lab). Using TIRF microscopy at single molecule resolution, we characterize 11 bDDs from single- and dual-bDD systems regarding which domains can self-assemble and recruit their partner domains. One example is a dual-bDD system from *Ca. Magnetaquicoccus inordinatus*: The effector-associated bDDs assemble on a base of receptor-associated bDDs and only this direction enables the complex to form. Notably, bDD systems appear to differ in how they restrain constitutive activation, pointing to distinct regulatory architectures.

Reference #1

Reference #2

Reference #3

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Session Classification: Poster-Session