[MS8 - 05] Structure of the *Legionella* Effector AnkX, an Enzyme that Diverts the Small GTPase Rab1.

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The intracellular pathogen Legionella pneumophila (Lp), the causative agent of Legionnaires' disease, escapes destruction by the infected cell by hiding in a specialized compartment, the Legionellacontaining vacuole (LCV), where it replicates [1].
In order to establish the LCV, the bacterium injects proteins in the host cytoplasm that take command of the trafficking machinery of the cell, thereby bypassing the sophisticated signaling networks that steer intracellular traffic [2]. Notably, Lp injects an arsenal of effectors that intercept the small GTPase Rab1, which is a major regulator of vesicular traffic at the endoplasmic reticulum, and recruit it to function on the LCV.
One of these effectors, AnkX, modulates the activity of Rab1 by covalently attaching a phosphocholine moiety to a serine residue in its switch 2 [3]. This post-translational modification prevents the binding of the GDP dissociation inhibitor to Rab1 and leads to the incorporation of Rab1 into membranes [4]. AnkX is an ankyrin repeat-containing protein with a FIC domain.
Unlike most bacterial FIC domains, which typically bind ATP and transfer an adenosine monophosphate moiety onto target proteins, AnkX utilizes CDP-choline as a substrate to phosphocholinate Rab1 [3]. We solved the crystal structures of AnkX in the apo form, bound to CDPcholine and bound to CMP/phosphocholine [6]. The structures reveal that the ankyrin repeats scaffold constrains the FIC and substrate binding domains.
They also explain why AnkX functions as a phosphocholine transferase rather than a nucleotidyl transferase. Our structures unify a general phosphoryl transferase mechanism common to all FIC enzymes, suggesting that FIC-containing toxins and regulatory eukaryotic proteins have probably evolved to process diverse diphosphate-containing substrates.

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