MS05-P117 LATE | THE BEP1 FIC-DOMAIN: UNRAVELLING THE MECHANISM OF NARROW SELECTIVITY TOWARDS RAC GTPASES

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Small GTPases of the Rho-family are molecular switches that regulate fundamental biological processes in mammalian cells. They thus represent favored targets of pathogens that strive to influence host cell behavior to their advantage. While most virulence factors target a wide range of GTPases, we recently discovered an effector of the gram-negative bacterium Bartonella spp. with unprecedented GTPase selectivity.

Here we show that the FIC-domain of Bartonella effector protein 1 (Bep1) exclusively AMPylates the Rac subfamily of Rho GTPases. Based on a co-crystalized FIC-target complex (IbpAFIC2-Cdc42), we generated an atomic model of the Bep1-Rac interaction and support the model with mutational studies and quantitative enzyme kinetics of wild-type and designed GTPases. This allowed us to pinpoint critical molecular details needed for Bep1-target selectivity.