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Poster #86: A widespread protein family inhibits both restriction-modification and CRISPR-Cas defenses

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Mobile genetic elements and their bacterial hosts are in a never-ending evolution dance, giving rise to a multitude of defense and evasion systems. For one given defense system, it is possible to find multiple escape effector encoded by the bacteriophages, blocking, hiding or mimicking a crucial element for an efficient immune response. Some of those effectors can even block multiple defense system at once, but no anti-defense protein has been shown so far to be able to inhibit two evolutionary unrelated defense systems. Recently, an anti-CRISPR protein called AcrIC11, has been characterized as a type I-C CRISPR-Cas system. Interestingly, by sequence and structural prediction analysis, AcrIc11 have similarities to the broadly distributed anti-restriction protein ArdB, raising the question whether these anti-defense proteins can cross inhibit both defenses.
A set of ArdB orthologues has been determined by sequence similarities, to be tested against different type I CRISPR systems and type I restriction modification (RM) systems. So far, we have shown that ArdB orthologues inhibits also different RM systems, but also type I-C CRISPR system under TXTL condition. Mutational analysis of both ArdB and Cas3 revealed that the C-terminal region of ArdB is needed for inhibition, and that mutating close to the nuclease pocket of Cas3 restore degradation activity in the presence of ArdB. Finally, pull downs of ArdB indicate interaction with the HsdR subunit of type I RM system. These results highlight for the first time the existence of a crosstalk between anti-CRISPR and anti-restriction.

Reference #1

Tesson, F., Huiting, E., Wei, L., Ren, J., Johnson, M., Planel, R., et al. (2025) Exploring the diversity

Reference #2

Wimmer, F., Englert, F., Wandera, K.G., Alkhnbashi, O.S., Collins, S.P., Backofen, R., and Beisel, C.L. (2

Reference #3

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