

**S1 Table.** Whether all known anti-CRISPRs can bind Cas proteins or inhibit their cleavage activity as purified proteins.

Acr	Binds cognate Cas protein?	Inhibit as pure proteins?	References
AcrIIA1	Yes	No	(Osuna et al., 2020)
AcrIIA2	Yes	Yes	(Jiang et al., 2019; Liu et al., 2019)
AcrIIA3	unknown	unknown	(Rauch et al., 2017)
AcrIIA4	Yes	Yes	(Dong et al., 2017; Shin et al., 2017; Yang and Patel, 2017)
AcrIIA5	Yes	Yes	(An et al., 2020; Garcia et al., 2019; Song et al., 2019)
AcrIIA6	Yes	Yes	(Fuchsbaier et al., 2019)
AcrIIA7	No	Yes	(Uribe et al., 2019)
AcrIIA8	Yes	Yes	(Uribe et al., 2019)
AcrIIA9	Yes	Yes	(Uribe et al., 2019)
AcrIIA10	Yes	Yes	(Uribe et al., 2019)
AcrIIA11	Yes	Yes	(Forsberg et al., 2019)
AcrIIA12	probable	Yes	(Eitzinger et al., 2020; Osuna et al., 2020)
AcrIIA13	unknown	Yes	(Watters et al., 2020)
AcrIIA14	unknown	Yes	(Watters et al., 2020)
AcrIIA15	unknown	Yes	(Watters et al., 2020)
AcrIIA16	Yes	Yes	(Mahendra et al., 2020)
AcrIIA17	Yes	No	(Mahendra et al., 2020)
AcrIIA18	Yes	No	(Mahendra et al., 2020)
AcrIIA19	Yes	No	(Mahendra et al., 2020)
AcrIIA20	unknown	Yes	(Eitzinger et al., 2020)
AcrIIA21	unknown	Yes	(Eitzinger et al., 2020)
<b>AcrIIA22</b>	<b>No</b>	<b>No</b>	<b>This study</b>
AcrIIA23	unknown	unknown	(Varble et al., 2020)
AcrIIC1	Yes	Yes	(Pawluk et al., 2016)
AcrIIC2	Yes	Yes	(Pawluk et al., 2016)
AcrIIC3	Yes	Yes	(Pawluk et al., 2016)
AcrIIC4	Yes	Yes	(Lee et al., 2018)
AcrIIC5	Yes	Yes	(Lee et al., 2018)
AcrVA1	Yes	Yes	(Knott et al., 2019b; Watters et al., 2018; Zhang et al., 2019)
AcrVA2	unknown	unknown	(Marino et al., 2018)
AcrVA3	unknown	unknown	(Marino et al., 2018)

AcrVA4	Yes	Yes	(Knott et al., 2019a; Knott et al., 2019b; Watters et al., 2018; Zhang et al., 2019)
AcrVA5	transiently	Yes	(Knott et al., 2019b; Watters et al., 2018; Zhang et al., 2019)
AcrVIA1(Lse)	Yes	Yes	(Meeske et al., 2020)
AcrVIA1(Lwa)	Yes	unknown	(Lin et al., 2020)
AcrVIA2	Yes	unknown	(Lin et al., 2020)
AcrVIA3	Yes	unknown	(Lin et al., 2020)
AcrVIA4	Yes	unknown	(Lin et al., 2020)
AcrVIA5	Yes	unknown	(Lin et al., 2020)
AcrVIA6	Yes	unknown	(Lin et al., 2020)
AcrVIA7	unknown	unknown	(Lin et al., 2020)
AcrlB1	unknown	unknown	(Lin et al., 2020)
AcrlC1	unknown	unknown	(Leon et al., 2020)
AcrlC2	probable	unknown	(Leon et al., 2020)
AcrlC3	unknown	unknown	(Leon et al., 2020)
AcrlC4	probable	unknown	(Leon et al., 2020)
AcrlC5	probable	unknown	(Leon et al., 2020)
AcrlC6	unknown	unknown	(Leon et al., 2020)
AcrlC7	probable	unknown	(Leon et al., 2020)
AcrlC8	probable	unknown	(Leon et al., 2020)
AcrlD1	Yes	unknown	(He et al., 2018)
AcrlE1	Yes	unknown	(Pawluk et al., 2017)
AcrlE2	unknown	unknown	(Pawluk et al., 2014)
AcrlE3	probable	unknown	(Stanley, 2018)
AcrlE4	unknown	unknown	(Pawluk et al., 2014)
AcrlE5	unknown	unknown	(Pawluk et al., 2014)
AcrlE6	unknown	unknown	(Pawluk et al., 2014)
AcrlE7	unknown	unknown	(Pawluk et al., 2014)
AcrlE4-IF7	unknown	unknown	(Marino et al., 2018)
AcrlE8	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF1	Yes	unknown	(Bondy-Denomy et al., 2015; Chowdhury et al., 2017; Guo et al., 2017)
AcrlF2	Yes	unknown	(Bondy-Denomy et al., 2015; Chowdhury et al., 2017; Guo et al., 2017)
AcrlF3	Yes	unknown	(Bondy-Denomy et al., 2015; Wang et al., 2016a; Wang et al., 2016b)
AcrlF4	Yes	unknown	(Bondy-Denomy et al., 2015)
AcrlF5	unknown	unknown	(Bondy-Denomy et al., 2013)

AcrlF6	Yes	Yes	(Zhang et al., 2020)
AcrlF7	Yes	unknown	(Hirschi et al., 2020)
AcrlF8	Yes	Yes	(Zhang et al., 2020)
AcrlF9	Yes	Yes	(Hirschi et al., 2020; Zhang et al., 2020)
AcrlF10	Yes	unknown	(Guo et al., 2017)
AcrlF11	unknown	unknown	(Marino et al., 2018)
AcrlF12	unknown	unknown	(Marino et al., 2018)
AcrlF13	unknown	unknown	(Marino et al., 2018)
AcrlF14	unknown	unknown	(Marino et al., 2018)
AcrlF15	probable	unknown	(Pinilla-Redondo et al., 2020)
AcrlF16	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF17	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF18	probable	unknown	(Pinilla-Redondo et al., 2020)
AcrlF19	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF20	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF21	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF22	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF23	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlF24	unknown	unknown	(Pinilla-Redondo et al., 2020)
AcrlII-1	No (degrades CA4 second messenger)	No	(Athukoralage et al., 2020)
AcrlIIB1	Yes	unknown	(Bhoobalan-Chitty et al., 2019)

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