The CRISPR Journal Volume 1, Number 5, 2018 © Mary Ann Liebert, Inc. DOI: 10.1089/crispr.2018.0043



CORRESPONDENCE

A Unified Resource for Tracking Anti-CRISPR Names

Joseph Bondy-Denomy,^{1,*} Alan R. Davidson,^{2,*} Jennifer A. Doudna,^{3–9} Peter C. Fineran,¹⁰ Karen L. Maxwell,¹¹ Sylvain Moineau,¹² Xu Peng,¹³ Eric J. Sontheimer,¹⁴ and Blake Wiedenheft¹⁵

Dear editors

In the battle between CRISPR-Cas* prokaryotic immune systems and the elements that they target, a diverse array of "anti-CRISPR" proteins have evolved. These proteins appear to have arisen independently multiple times in evolution and function through diverse mechanisms to inhibit CRISPR-Cas immunity. For comprehensive reviews on anti-CRISPRs, we direct readers to recent publications. 1,2

Due to the increasing interest in anti-CRISPRs, many new families of these proteins have been discovered in the past year or so. There are now 36 distinct families of anti-CRISPRs described in the literature that block seven subtypes of CRISPR-Cas systems. ^{3–12} In 2015, a naming system for anti-CRISPR genes and proteins was introduced. ^{6,13} To date, this system has been followed in all subsequent publications describing newly discovered anti-CRISPRs. However, as the rate of anti-CRISPR discovery will likely accelerate in the coming years, we feel that it would be advantageous to establish a database for the registration and tracking of anti-CRISPR names.

The primary goal of this database will be to prevent redundant names being used in publications, thus avoiding confusion in the literature. Anti-CRISPR proteins are named according to the subtype they inhibit and the order in which they were discovered—for example, AcrIF1 was the first anti-CRISPR protein identified to inhibit the type I-F system. The database (a Google document) can be found here: https://tinyurl.com/anti-CRISPR

We propose that this document be updated when researchers have had a manuscript accepted for publication in which new anti-CRISPRs are described. We suggest that the authors upload relevant data to the spreadsheet, including the name, CRISPR-Cas subtype inhibited, reference, and amino-acid sequence of the anti-CRISPR (Table 1). This spreadsheet may also be utilized by those preparing a manuscript for submission to ensure that they use anti-CRISPR names that are still available.

*Clustered Regularly Interspaced Short Palindromic Repeats.

Departments of ¹Microbiology and Immunology, and ⁶Biochemistry and Biophysics, University of California, San Francisco, California; ²Departments of Biochemistry and Molecular Genetics, University of Toronto, Toronto, Ontario, Canada; Departments of ³Molecular and Cell Biology, and ⁴Chemistry, University of California, Berkeley, California; ⁵Molecular Biophysics and Integrated Bioimaging Division, Lawrence Berkeley National Laboratory, Berkeley, California; ⁷Gladstone Institutes, San Francisco, California; ⁸Howard Hughes Medical Institute and ⁹Innovative Genomics Institute, University of California, Berkeley, California; ¹⁰Department of Microbiology and Immunology, University of Orago, Dunedin, New Zealand; ¹¹Department of Biochemistry, University of Toronto, Toronto, Ontario, Canada; ¹²Department of Biochemistry, Microbiology, and Bioinformatics, Faculty of Sciences and Engineering, Université Laval, Québec City, Quebec, Canada; ¹³Danish Archaea Centre, Department of Biology, University of Copenhagen, Copenhagen, Denmark; ¹⁴RNA Therapeutics Institute, University of Massachusetts Medical School, Worcester, Massachusetts; ¹⁵Department of Microbiology and Immunology, Montana State University, Bozeman, Montana.
*Co-corresponding authors.

Address correspondence to: Joseph Bondy-Denomy or Alan R. Davidson, E-mail: joseph.bondy-denomy@ucsf.edu or alan.davidson@utoronto.ca

CORRESPONDENCE 305

Table 1. A "Screenshot"	from the Database,	Depicting the Organization
of Anti-CRISPR Entries		

Acr name	Type Inhibited	Species of origin	Type of genomic element	Reference (First author, year, journal)	Sequence
AcrIF1	I-F	Pseudomonas aeruginosa	Phage	Bondy-Denomy, 2013, Nature	MKFIKYLSTAHLNYMNIAVYENGS
AcrIF2	I-F	Pseudomonas aeruginosa	Phage	Bondy-Denomy, 2013, Nature	MIAQQHKDTVAACEAAEAIAIAKD
AcrIF3	I-F	Pseudomonas aeruginosa	Phage	Bondy-Denomy, 2013, Nature	MSSTISDRIISRSVIEAARFIQSWE

To avoid the listing of many orthologues, we propose that the database only contain one entry per Acr, which will be considered the "type" Acr for that sequence family. In a case where a paper has investigated proteins that are homologous to an Acr protein, authors should utilize a subscript (e.g., AcrIF6 $_{Pae}$) to denote the species in which the anti-CRISPR is found. When multiple proteins from one species are investigated, we suggest a format of AcrIF6 $_{Pae-1}$, AcrIF6 $_{Pae-2}$, and so on. The established conventions for naming anti-CRISPR proteins and genes will be described as part of the database. We view this as an open repository for the field and as a complementary resource to a previously described anti-CRISPR database. ¹⁴

Two of us (J.B.-D. and A.R.D.) were inspired to establish this database by the success of the CRISPR-Cas classification scheme in bringing order to the naming of Cas proteins. ^{15,16} This work has been tremendously valuable for advancing the CRISPR-Cas field. We hope that our contribution to the anti-CRISPR field as presented here will provide a similar long-term benefit.

References

- 1. Borges AL, Davidson AR, Bondy-Denomy J. The discovery, mechanisms, and evolutionary impact of anti-CRISPRs. *Annu Rev Virol* 2017;4:37–59. DOI: 10.1146/annurev-virology-10141-041616.
- Pawluk A, Davidson AR, Maxwell KL. Anti-CRISPR: discovery, mechanism and function. Nat Rev Micro 2018;16:12–17. DOI: 10.1038/nrmicro.2017.120.
- 3. Bondy-Denomy J, Pawluk A, Maxwell KL, et al. Bacteriophage genes that inactivate the CRISPR/Cas bacterial immune system. *Nature* 2013;493:429–432. DOI: 10.1038/nature11723.
- Pawluk A, Bondy-Denomy J, Cheung VHW, et al. A new group of phage anti-CRISPR genes inhibits the type I-E CRISPR-Cas system of *Pseudomonas aeruginosa*. mBio 2014;5:e00896-14. DOI: 10.1128/ mBio.00896-14.
- 5. Pawluk A, Staals RH, Taylor C, et al. Inactivation of CRISPR-Cas systems by anti-CRISPR proteins in diverse bacterial species. *Nat Microbiol* 2016;1:16085. DOI: 10.1038/nmicrobiol.2016.85.
- Pawluk A, Amrani N, Zhang Y, et al. Naturally occurring off-switches for CRISPR-Cas9. Cell 2016;167:1829– 1838.e9. DOI: 10.1016/j.cell.2016.11.017.
- Rauch BJ, Silvis MR, Hultquist JF, et al. Inhibition of CRISPR-Cas9 with bacteriophage proteins. Cell 2017;168:150–158.e10. DOI: 10.1016/j.cell.2016.12.009.
- 8. Hynes AP, Rousseau GM, Lemay ML, et al. An anti-CRISPR from a virulent streptococcal phage inhibits Streptococcus pyogenes Cas9. Nat Microbiol 2017;2:1315–1380. DOI: 10.1038/s41564-017-0004-7.
- He F, Bhoobalan-Chitty Y, Van LB, et al. Anti-CRISPR proteins encoded by archaeal lytic viruses inhibit subtype I-D immunity. Nat Microbiol 2018;3:461–469. DOI: 10.1038/s41564-018-0120-z.
- 10. Hynes AP, Rousseau GM, Agudelo D, et al. Widespread anti-CRISPR proteins in virulent bacteriophages inhibit a range of Cas9 proteins. *Nat Commun* 2018;9:2919. DOI: 10.1038/s41467-018-05092-w.
- 11. Marino ND, Zhang JY, Borges AL, et al. Discovery of widespread type I and type V CRISPR-Cas inhibitors. *Science* 2018 Sep 6 [Epub ahead of print]; DOI: 10.1126/science.aau5174.
- 12. Watters KE, Fellmann C, Bai HB, et al. Systematic discovery of natural CRISPR-Cas12a inhibitors. *Science* 2018 Sep 6 [Epub ahead of print]; DOI: 10.1126/science.aau5138.
- Bondy-Denomy J, Garcia B, Strum S, et al. Multiple mechanisms for CRISPR-Cas inhibition by anti-CRISPR proteins. Nature 2015;526:136–139. DOI: 10.1038/nature15254.
- 14. Dong C, Hao GF, Hua HL, et al. Anti-CRISPRdb: a comprehensive online resource for anti-CRISPR proteins. *Nucleic Acids Res* 2018;46:D393–D398. DOI: 10.1093/nar/glxx835.
- Makarova KS, Haft DH, Barrangou R, et al. Evolution and classification of the CRISPR-Cas systems. Nat Rev Micro 2011;9:467–477. DOI: 10.1038/nrmicro2577.
- Makarova KS, Wolf YI, Alkhnbashi OS, et al. An updated evolutionary classification of CRISPR-Cas systems. Nat Rev Micro 2015;13:722–736. DOI: 10.1038/nrmicro3569.