**About section for BE-FF**

BE-FF (Base Editors Functional Finder) identifies base editors that can repair a given single-nucleotide variation. Currently BE-FF simulates base editing by 26 unique base editors (17 CBEs and 9 ABEs) for all queries:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Base editor** | **Substitution** | **Distance from PAM** | | **PAM** | **Ref. #** |
| **Major activity site** | **Minor activity site** |
| BE1, BE2, BE3, HF-BE3, BE4(max), BE4-Gam | C to T | 13-17 | 10-12, 18-19 | NGG | (1–4) |
| YE1-BE3 | C to T | 14-16 | 17 | NGG | (5) |
| YEE-BE3 | C to T | 15 | 16 | NGG | (5) |
| VQR-BE3 | C to T | 10-17 |  | NGAN | (5) |
| VRER-BE3 | C to T | 11-18 |  | NGCG | (5) |
| SaBE3, SaBE4, SaBE4-Gam  (21nt gRNA) | C to T | 10-19 |  | NNGRRT | (3, 5) |
| Sa(KKH)-BE3 (21nt gRNA) | C to T | 10-19 |  | NNNRRT | (5) |
| Cas12a-BE | C to T | 10-12 downstream | 8-9, 13 downstream | TTTV | (6) |
| Target-AID | C to T | 17-19 | 13-16 | NGG | (7) |
| Target-AID-NG | C to T | 17-19 | 13-16 | NG | (8) |
| xBE3 | C to T | 13-17 | 10-12, 18-19 | NG | (9) |
| eA3A-BE3 | C to T when C comes after T | 13-17 | 10-12, 18-19 | NGG | (10) |
| BE-PLUS | C to T | 7-17 | 5-6 | NGG | (11) |
| CP-CBEmax variants | C to T | 12-17 | 10-11\* may exhibit editing upstream to the protospacer | NGG | (12, 13) |
| evoAPOBEC1-BE4max | C to T | 13-18 | 19-20, 9-12 | NGG | (14) |
| evoFERNY-BE4max | C to T | 13-18 | 19-20 | NGG | (14) |
| evoCDA1-BE4max | C to T | 9-20 | 7-8\* may exhibit editing upstream to the protospacer | NGG | (14) |
| ABE 7.9 | A to G | 13-16 | 12, 17 | NGG | (15) |
| ABE 7.10 | A to G | 14-17 | 13 | NGG | (15) |
| ABE 7.10\* | A to G | 13-17 | 12,18-19 | NGG | (16) |
| xABE, NG-ABEmax | A to G | 14-17 | 13 | NG | (9, 13) |
| ABESa (21nt gRNA) | A to G | 10-16 |  | NNGRRT | (17) |
| VQR-ABE | A to G | 15-17 | 13-14 | NGA | (17, 18) |
| VRER-ABE | A to G | 15-17 | 13-14 | NGCG | (17) |
| Sa(KKH)-ABE (21nt gRNA) | A to G | 10-16 |  | NNNRRT | (17, 18) |
| CP-ABEmax variants | A to G | 14-17 | 7-13 | NGG | (12, 13) |

**For additional questions and suggestions please contact** [**royr2@mail.tau.ac.il**](mailto:royr2@mail.tau.ac.il)

Related references:

**For CRISPR:**

* Jinek,M., Chylinski,K., Fonfara,I., Hauer,M., Doudna,J.A. and Charpentier,E. (2012) A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. Science. 337, 816–21.
* Cong,L., Ran,F.A., Cox,D., Lin,S., Barretto,R., Habib,N., Hsu,P.D., Wu,X., Jiang,W., Marraffini,L.A., et al. (2013) Multiplex genome engineering using CRISPR/Cas systems. Science. 339, 819–23.

**For Base editing:**

* For all base editors:  
  Komor,A.C., Kim,Y.B., Packer,M.S., Zuris,J.A. and Liu,D.R. (2016) Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage. Nature, 533, 420–424.
* For ABEs:  
  Gaudelli,N.M., Komor,A.C., Rees,H.A., Packer,M.S., Badran,A.H., Bryson,D.I. and Liu,D.R. (2017) Programmable base editing of A•T to G•C in genomic DNA without DNA cleavage. Nature, 551, 464–471.

**References for specific base editors: (according to the BEs table)**

1. Komor,A.C., Kim,Y.B., Packer,M.S., Zuris,J.A. and Liu,D.R. (2016) Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage. *Nature*, **533**, 420–424.

2. Rees,H.A., Komor,A.C., Yeh,W.-H., Caetano-Lopes,J., Warman,M., Edge,A.S.B. and Liu,D.R. (2017) Improving the DNA specificity and applicability of base editing through protein engineering and protein delivery. *Nat. Commun.*, **8**, 15790.

3. Komor,A.C., Zhao,K.T., Packer,M.S., Gaudelli,N.M., Waterbury,A.L., Koblan,L.W., Kim,Y.B., Badran,A.H. and Liu,D.R. (2017) Improved base excision repair inhibition and bacteriophage Mu Gam protein yields C:G-to-T:A base editors with higher efficiency and product purity. *Sci. Adv.*, **3**, eaao4774.

4. Koblan,L.W., Doman,J.L., Wilson,C., Levy,J.M., Tay,T., Newby,G.A., Maianti,J.P., Raguram,A. and Liu,D.R. (2018) Improving cytidine and adenine base editors by expression optimization and ancestral reconstruction. *Nat. Biotechnol.*, **36**, 843–846.

5. Kim,Y.B., Komor,A.C., Levy,J.M., Packer,M.S., Zhao,K.T. and Liu,D.R. (2017) Increasing the genome-targeting scope and precision of base editing with engineered Cas9-cytidine deaminase fusions. *Nat. Biotechnol.*, **35**, 371–376.

6. Li,X., Wang,Y., Liu,Y., Yang,B., Wang,X., Wei,J., Lu,Z., Zhang,Y., Wu,J., Huang,X., *et al.* (2018) Base editing with a Cpf1-cytidine deaminase fusion. *Nat. Biotechnol.*, **36**, 324–327.

7. Nishida,K., Arazoe,T., Yachie,N., Banno,S., Kakimoto,M., Tabata,M., Mochizuki,M., Miyabe,A., Araki,M., Hara,K.Y., *et al.* (2016) Targeted nucleotide editing using hybrid prokaryotic and vertebrate adaptive immune systems. *Science*, **353**, aaf8729–aaf8729.

8. Nishimasu,H., Shi,X., Ishiguro,S., Gao,L., Hirano,S., Okazaki,S., Noda,T., Abudayyeh,O.O., Gootenberg,J.S., Mori,H., *et al.* (2018) Engineered CRISPR-Cas9 nuclease with expanded targeting space. *Science*, **361**, 1259–1262.

9. Hu,J.H., Miller,S.M., Geurts,M.H., Tang,W., Chen,L., Sun,N., Zeina,C.M., Gao,X., Rees,H.A., Lin,Z., *et al.* (2018) Evolved Cas9 variants with broad PAM compatibility and high DNA specificity. *Nature*, **556**, 57–63.

10. Gehrke,J.M., Cervantes,O., Clement,M.K., Wu,Y., Zeng,J., Bauer,D.E., Pinello,L. and Joung,J.K. (2018) An APOBEC3A-Cas9 base editor with minimized bystander and off-target activities. *Nat. Biotechnol.*, **36**, 977–982.

11. Jiang,W., Feng,S., Huang,S., Yu,W., Li,G., Yang,G., Liu,Y., Zhang,Y., Zhang,L., Hou,Y., *et al.* (2018) BE-PLUS: a new base editing tool with broadened editing window and enhanced fidelity. *Cell Res.*, **28**, 855–861.

12. Oakes,B.L., Fellmann,C., Rishi,H., Taylor,K.L., Ren,S.M., Nadler,D.C., Yokoo,R., Arkin,A.P., Doudna,J.A. and Savage,D.F. (2019) CRISPR-Cas9 Circular Permutants as Programmable Scaffolds for Genome Modification. *Cell*, **176**, 254-267.e16.

13. Huang,T.P., Zhao,K.T., Miller,S.M., Gaudelli,N.M., Oakes,B.L., Fellmann,C., Savage,D.F. and Liu,D.R. (2019) Circularly permuted and PAM-modified Cas9 variants broaden the targeting scope of base editors. *Nat. Biotechnol.*, **37**, 626–631.

14. Thuronyi,B.W., Koblan,L.W., Levy,J.M., Yeh,W.-H., Zheng,C., Newby,G.A., Wilson,C., Bhaumik,M., Shubina-Oleinik,O., Holt,J.R., *et al.* (2019) Continuous evolution of base editors with expanded target compatibility and improved activity. *Nat. Biotechnol.*, **37**, 1070–1079.

15. Gaudelli,N.M., Komor,A.C., Rees,H.A., Packer,M.S., Badran,A.H., Bryson,D.I. and Liu,D.R. (2017) Programmable base editing of A•T to G•C in genomic DNA without DNA cleavage. *Nature*, **551**, 464–471.

16. Ryu,S.-M., Koo,T., Kim,K., Lim,K., Baek,G., Kim,S.-T., Kim,H.S., Kim,D.-E., Lee,H., Chung,E., *et al.* (2018) Adenine base editing in mouse embryos and an adult mouse model of Duchenne muscular dystrophy. *Nat. Biotechnol.*, **36**, 536–539.

17. Hua,K., Tao,X. and Zhu,J.-K. (2019) Expanding the base editing scope in rice by using Cas9 variants. *Plant Biotechnol. J.*, **17**, 499–504.

18. Yang,L., Zhang,X., Wang,L., Yin,S., Zhu,B., Xie,L., Duan,Q., Hu,H., Zheng,R., Wei,Y., *et al.* (2018) Increasing targeting scope of adenosine base editors in mouse and rat embryos through fusion of TadA deaminase with Cas9 variants. *Protein Cell*, **9**, 814–819.