

Supplementary Information

SPIN-dvEvo: Exploration of vast functional sequence space by directed virtual evolution from a local sequence cluster

In the format provided by the authors and unedited

Content

Supplemental information Table S1-8, Figure S1-4.

Supplementary Information

Supplementary Table 1. TadA/ABE deaminase protein sequences for LoRA fine-tuning model

Name	Sequence
ABE7.10	MSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRRAIGL HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECAALLCYFFRMMPRQVF NAQKKAQSSTD
ABE7.9	MSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGR HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECNALLCYFFRMMPRQVF NAQKKAQSSTD
ABE7.4	MSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGR HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECAALLCYFFRMRRQV FNAQKKAQSSTD
ABE6.4	MSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGR HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECNALLCYFFRMRRQV FNAQKKAQSSTD
ABE5.3	MSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGR HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECAALLCYFFRMRRQV FNAQKKAQSSTD
ABE3.1	MSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGR HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECAALLSYFFRMRRQVF KAQKKAQSSTD
ABE2.9	MSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPIGR HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTLEPCVMCAGAMIHSRIGRVV FGVRNAKTGAAGSLMDVLHYPGMNHRVEITEGILADECAALLSYFFRMRRQV IKAQKKAQSSTD
TadA8e	MSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRRAIGL HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRNSKRGGAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRMMPRQV FNAQKKAQSSIN
TadA8e_ V106W	MSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRRAIGL HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GWRNSKRGGAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRMMPRQV FNAQKKAQSSIN
TadA8e_ N108Q	MSEVEFSHEYWMRHALTLAKRARDEREVPVGAVLVLNNRVIGEGWNRRAIGL HDPTAHAEIMALRQGGLVMQNYRLIDATLYVTFEPCVMCAGAMIHSRIGRVVF GVRQSKRGGAAGSLMNVLNYPGMNHRVEITEGILADECAALLCDFYRMMPRQV FNAQKKAQSSIN

Supplementary Table 2. CcdA family antitoxin protein sequences for LoRA fine-tuning model

Uniport ID	Sequence
P62552	RRLRAERWKAENQEGMAEVARFIEMNGSFADENRDW
A0AAX1M1G6	RRLRAERWKAENQEGMVEVARFIEMNGSFADENRNW
A0A6N9SHB8	RRLRAERWQAENQEGMAEVARFIEMNGSFAEENRDW
A0A0B0VNF4	RRLRAERWKAENQEGMAEVARFIEMNGSFADENREW
A0AAN5UII2	RRLRAERWKAENQEGMAEVARFIEMNSSFADENRDW
A0A8S7BM37	RRLRAGRWKAENQEGMAEVARFIEMNGSFADENRDW
A0A828UFP5	RRLRAERWKVENQEGMVEVARFIEMNGSFADENRDW
A0A1W1EMI8	RRLRAERWKAENREGMAEVARFIEMNGSFADENRDW
A0A6D0XUY0	RRLRAERWLAENQEGMAEVARFIEMNGSFADENRDW
A0A0F6YRL5	RRLRAERWRAENQEGMAEVARFIEMNGSFADENRDW
Q46995	RRLRPERWKVANQEGMAEVARFIEMNGSFADENRDW
Q99Q95	RRLRAERWQAENQQGMAEIARFIEMNGSFADENRDW
A0A2X4T6S6	RRLRAKRWQAENQEGMAEVALFIETNGSFADENRDW
A0A0G4JQF2	RRIKAEQWKKENREGMEEVARFITQNGSFADENRNW
Q6D9V2	RRIKAEWKKENRERMEDIARFIAKNVFFADENRNW
A0A0L7T4A9	RRIKAEQWKTENREGMEEVARFIAQNGSFADENRNW
A0A2I5TNW4	RRIKAEAWKKENREGMEEVARFITQNGSFADENRNW
A0A3D9UGR6	RRIKAEKWKADNHEGMTEVANFIAQHGSFAEENRNW
A0A4R3XSF1	RRIKAERWLAENQSALDEYNRRIEMRGTFSDGLRNW
B2TT52	RRLRAERWQAENQQGMAEIARFIEMNGSFADENRDW
D2TV55	RRLRAERWQEENREGMAEVASFIEANGSFADENRDW
A0A4R1NF65	RRIKAEQWKKENHEGMEEVARFIAQNGSFADENRNW

Supplementary Table 3. TadA variant sequences from the SPIN-dvEvo first-round evolved sequences (n = 60) and SPIN-dvEvo second-round evolved sequences (n=60) for experimental test.

Index	Protein Sequence
ecTadA	MLSEVEFSHEYWMRHALTLAKRAWDEREVPVGAVLVHNNRVIGEGWNRPI GRHDPTAHAEIMALRQGGLVMQNYRLIDATLYVTLEPCVMCAGAMIHSRIG RVVFGARDAKTGAAGSLMDVLHHPGMNHRVEITEGILADECAALLSDFFRM RRQEIKAQKKAQSSTD
dvTadA-1	MAYTPEDERWMRLAIEEAAAAQRGEVPVGCVIVRNGQVIARAPNAVEATL KATQHAEILALESASRELISWRLQDTTCYVTLEPCAMCAGAMVLARIPRVF GVVNPBKAGAAGSVVNLLWPHLNHRVEVHRGVLEEEARQLLMEFFKQRR QKKARG
dvTadA-2	MAYTPEDERWMRLAIEEARAAMQRGEVPVGCVIVRNGQVIARAPNAVEAD LKATQHAEWLALELASRELNSWRLPDTTSYVTLEPCACCAGAIALARIPRVV FGVGNPKAGAAGSVVNLLDWPGLNHRVEVMRGVLEGEARQILMEFFKQRR AEKKARG
dvTadA-3	MAYTPEDERWMRLAIEEARAAMQRGEVPVGCVIVRNGQVIARAPNAVEAD LKATQHAEWLALELASRELNSWRSPDTTNYVTLEPCACCAGAIVLARIPRYV FGVNPBKAGAAGSVVNLLDWPGLNHRVEVHRGVLEEEARTLLMEFFKQRR AQKAARG
dvTadA-4	MAYTPEDERWMFLDIEEAAAAQRGEVPVGCVIVRNGQVIARAPNAVEATL KATQHAEILALELASRELNSWRLPDTTCYVTLEPCAMCAGAMVLARIPRVF GVVNPBKAGAAGSVVNLLWPHLNHRVEVHRGVLEEEARQLLMEFFKQRR QKKARG
dvTadA-5	MAYHPEDERWMRLAIEEARAAMQRGEVPVGCVIVRNGQVIARAPNAVEAD LKATQHAEWLALDLASRQLNSWRLDDTTNYVTLEPCAMCAGAMVLARIPR VVFGVNPBKAGAAGMVVNLLDWPGLNHRVEVHRGVLEEEARQILMEFFKQ RRAQKCARG
dvTadA-6	MAYTPEDERWMRLAIEEAYAAKQRGEVPVGCVIVRNGQVIARGPNAEEETL KATMHAEWLAIELASRELGSWRLPETTMYVTLEPCAMCAGAMVSARIPRVV FGVNPBKAGAAGSVVNLLDWPQLNHRVQVHRGVLEEEARNLLMEFFKQRR AQKKAQL
dvTadA-7	MAYTPEDERWMRLAIEEARAAMQRGEVPVGCVIVRNNQVIARAPNAVATL SATQHAEWLAIELASRELNSWRLPDTTCYVTLEPCAMCAGAMVLARIPRVV FGVNPBKAGAAGSVVNILDWPGLNHRVEYHRGVLEEEARQILMEFFKQRR QKKAQG

dvTadA-8	MSEQAQPTDWMQLALEEAKRAMANGEVPVGAVIVRNGEVIARGFNAPEER KNATLHAEVWAIQAAAEKYRSWRLLLECTGFVTVEPCIMCMGAVQMARIPRII FGVANEKGGAAGSYYNLHQVDWFNQRITVEKGVVEERARELLAQFFRDRR AAKRGQA
dvTadA-9	MSEQAQPDWDMQLALEEAKRAMANGEVPVGAVIVRNGEVIARGFNAPEER KNATLHAEVQAIASAAAEKYRSWRLLDCTGFVTVEPCIMCMGAIQIARIPRIIF GVANPKAGAAGSYYNLHQVDWFNHRVTVEKGVMAERARELLAQFFRDRRA AKRGTA
dvTadA-10	MSEQAQPTDWMQLALEEAKRAMANGEVPVGAVIVRNGEVIARGFNAPEER KNATLHAEVWAIQAAAEKYRSWRLLDCTGFVTVEPCIMCMGAVQMARIPRI IFGVANEKGGAAGSYYNLHQVDWFNQRITVEKGVVEERARELLAQFFRDRR AAKRGQA
dvTadA-11	MSEQAQPTDWMRLALEEAKRAMANGEVPVGAVIVRNGEVIARGFNAPEER KNATLHAEVWAIQAAAEKYRSWRLLDCTGFVTEPCIMCMGAVQMARIPRR IFGVANEKGGAAGSYNLHQIDWFNHRVTVEKGVVERERAKELLAQFFRDRR AAKRGQA
dvTadA-12	MAYTEHDLRWMRLAIEQAREAAARRWEVPVGAVIVRDGRVIATAFNEREAE NAYAHAEILAIQRASREWQDWRLWDATWYVALEPCVMCAGALVQAREKRV VNGVRNPKAGAAGSLVDLPQQPWFNHRVEIERGVAQEEAAEILRAFFRERR AQKRAQS
dvTadA-13	MAYTEHDERWMRLAIEQAREAAARRWEVPVGAVIVRDGRVIATAFNEREAE NAYAHAEILAIQRASREWQDWRLWDATWYVTLEPCIMCAGALVQAREKRV VFGVYNPKAGAAGSLVDLPQQPWFNHRVEIERGVAPEEAAEILRAFFRERRA QKRAQS
dvTadA-14	MAYTEHDERWMRLAIEQAREAAARRWEVPVGAVIVRDGRVIATAFNEREAE NAYAHAEILAIQRASREWQDWRLWDATWYVTLEPCVMCAGALVAAREKRV VFGVYNPKAGAAGSLVDLPQQPWFNHRVEIERGVAPEEAAEILRAFFRERRA QKRAQS
dvTadA-15	MAYTAEDERWMRLAIELARRAMERFEVPVGAVIVRDGKLVATAFNEVEELL HPTKQAELLNIEEASKAYNSWRLYGCDDYVTLFPCVMCAGAIVNAWIPRVV FGVPNPKDGAAGFVVRLHDIPEINHRVTVERGVREQECDLLTQFFRERRAQ KRAQR
dvTadA-16	MQHSAQDLQWMQRALELAKRAAAQGEVPVGAVLVRDNQKIGDGFNAVEQ DAQPTGHAEQMAIQAGARAQSWRLQGYTLFVMLEPCPMCMGAIHNARIA RNVFGVHNEKGGADGSYYRLADDARFNHVELHKGVADEAARAQLSDFFK AQRKAKRGDA
dvTadA-17	MSHSAQDLQWMQRALELAKRAAAQGEVPVGAVLVRDNTLIGDSFNAYEQD AQPTGHAEQMAIQAGLAAQQSWRLQGYTLFVMLEPCPMCMGAIHNARIAR NVFGVHNEKGGADVSYRRLADDARFNHQVELHSGVADEAARAQLSDFFKA QRAAKRGKA

dvTadA-18	MSHSAQDLQWMSRALELAKRAAAQGEVPVGAVLVKDNTLIGDGFNAVEQD AQPTGHAEQMAIQAGARAQQSWRLQDYTLFVMLEPCPMCWGAIHNARIAR NVFGVHNEKGGADGSYYRLADDARFDHQVELHKGVADEAARAQLSDFFK AQRKAKRGKA
dvTadA-19	MSHSAQDLQWMSRALELAKRAAAQGEVPVGAVLVRDNTLIGDHFNAVEQD SQPTGHAEQMAIQAGARAQQSWRLQGYTLFVMLEPCPMCWGAIHNARIAR VVMGVHNEKGGADGSYYRLADDARFNHQVELHNGVADEAARAQLSDFFK AQRKAKRGKA
dvTadA-20	MSHSAQDLQWWQRALELAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEQ DAQPGGHAEQMAIQAGARAQQSWRLQGYTLFVMLEPCPMCGLGAIHNARK ARVVFGVHNEKGGADGSYYRVADDARFNHQIELHNGVADEAARAQLSDFF KAQRAAKRGKA
dvTadA-21	MSHSAQDLQWMQRALELAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEQD AQPTGHAEQNAIQHGQRAQQSWRLQGYTLFVMLEPCPMCWGAIHNARIAR VVFGVHNEKGGADGSYYRLADDARFNHQVELHKGVADEAARAQLSDFFK AQRKAKRGKA
dvTadA-22	MSHSAQDLQWMQRALELAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEQD AQPTGHAEQMAIQAGARAQQSWRLQGYTLFVMLEPCPMCWGAIHNARIAR VVFGVHNEKGGADGSYYRLADDARFNHQVELHKGVADEAARAQLSDFFK AQRKAKRGKA
dvTadA-23	MSHSAQDLQWMQRALELAKRAAAQGEVPVGAVLVRDNTLIGDSFNAYEQD AQPTGHAEQMAIQAGARAQQSWRLQGYTLFVMLEPCPMCWGAAHNARAA RVVFGVHNEKGGADVSYRLADDAHFNHQVELHSGVADEAARAQLSDFFK AQRAAKRGKA
dvTadA-24	MSHSAQDLQWMSRALELAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEHD SQPTGHAEAMAIQAGARAQQSWRLQGYTLFVTLEPCPMCWGAIHNARIAR VVFGVHNEKGGSDGSYLRLADDARFNHQVEWHKGVADEAARAQLSDFFK AQRAAKRGKA
dvTadA-25	MSHSAQDLQWMSRALELAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEQD SQPTGHAEQMACCAGARAQQSWRLQGYTLFVTLEPCPMCWGAIHNARIAR NVFGVHNEKGGADGSYYRLADDARFNHKVELHNGVADEAARAALSDDFFK AQRKAKRGKA
dvTadA-26	MSHSAQDLQWMQRALELAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEQD AQPSGHAEQMAIQAGARAQQSWRLMGYTLFVTLEPCPMCWGAIHNARIAR PVFGVHNEKGGADGSYYRLADDARFNHQVELHNGVADEAARAYLSDDFFKA QRAAKRGKA
dvTadA-27	MSHSAQDLTWMQRALELAKRAAAQGEVPSGAVLVRDNTLIGDGFNAVEQD AQPTGHAEQMAIQAGKRAQQSWRLQGYTLFVMLEPCPMCWGAIHNARIAR NVFGVHNEKGGADGSYYRLADDARFNHQVELHKGVAEEAARAQLSDFFKA QRKAKRGKA

dvTadA-28	MSHSAQDLQWMSHALNLAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEQD AHPTGHAEQMAIQRGDRCCQSWRLQGYTLGVTLEPCPMCWGAVHNARIAR VVFGVHNEKGGADGSYYRLADDARFNHQVELHAGVADEAARAQLSDFFK AQRAAKRGKA
dvTadA-29	MSHSAQDLQWMSRALELAKRAAAQGEVPVGAVLVRDNTLIGDGFNAVEQD AQMTGHAELMAIQAGARAQQSWRLQGYHLFVTLEPCPMCWGAIHNARIGR VVFGVFNEKGGADGSYYRLADDARFNHQVELHKGVSDEFARAQLSDFFKA QRTAKRGKA
dvTadA-30	MSDTALPQHWLQHAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQL AEPCGHAEMVAKQQACKALNSWRLLDCHWFVSVEPCNMCAGALINSRIAQ LHFGVPNDKMWAAGSYIDLAQGEWYNHRVQVHSGVNAEQCAELLKGFFKS QRAAKKAKG
dvTadA-31	MSDTALPQHMLQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQL AEPTGHAEMVAIQWACKALESWRLLDCHWFVSIIEPCAMCAGALINSRIAQL HFGVWNDKMGAAGSLIDLAQGEWYNHRVQTHSGVQAEQCAELLKGFFKS QRAAKKAKG
dvTadA-32	MSDTALPQHWLQQAIEQAKLAADNWEVPVGHVIVQDGKVLATGFNAVEQH AEPTGHAEMVAIQWACKALNSWRLLDCHMFVTLEPCAMCAGALINSRIKQC HFGVRNDKMGAAGSLIPLAQGEWYNHRVQTHSGEQAEQCAELLKGFFKSQ RAAKKAKG
dvTadA-33	MSDTALPAHWLQQACEQAKLAADNWEVPVGCVIVQDGKTLATGFNAVEQA REPTGHAEMVAIQWATKALESWRLLDCHIFVSIIEPCAMCAGALINSRIAQLHF GVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGQQAEQCAELLKGFFKGQR AARKAKG
dvTadA-34	MSDTALPAHWLQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQL AEPTGHAEMVAIQWSCKALNSWRLLDCHMFVTVEPCAMCAGALINSRIASL HFGVPNDKMGAAGSLDDLAQGEWNNHRAQTHSGVQAEQCAELLKGFFKS QRAAKKAKG
dvTadA-35	MSQTAVPAHWLQQAIELAKLAADNWEVPVGCVIVQDGKVLATGFYAVEQL AEPTSHAEMVAIQWACKALNSWRLLDCHMFVTVEPCAMCAGALINSRIADL HFGVPNDKMGAAGSLIDLLQGEWYNHRVQTHSGVQAEQCAELLKGFFKSQ RAAKKAKG
dvTadA-36	MSATALPAHWLQQAIEQAKLAYDNWEVPVGCVIVQDGKVLAGGFNAVEQL REPTGHAEMVAIQWACKALNSWRLKECHWFVQVEGCAMCAGALINSRIAQ LHFGVQNDKMGAAGSFIDLAQGEWYNHRVQTHSGVQAEQCAELLKGFFKS QRAAKKAKG
dvTadA-37	MSDTALPQHWIQQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQA REPTGHAEMVADQWACKALNSWRLLDCHWFVSIIEPCAMCAGALICSRIAQL HFGVINDKMGAAGSLIDLAQGEWYNHRVQTHSGWQAEQCAELNKGFFKSQ RAAKKAKG

dvTadA-38	MSDTALPAHWLQQACEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQ AREPTGHAEMVAIQWACKALESWRLLDCHIFVSIIEPCAMCAGALINSRIAQL HFGVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGQQAEQCAELLKGFFKGQ RAARKAKG
dvTadA-39	MSDTALPQHWLQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQL AEPTGHAEMVAIQWACKALNSWRLLDCHWFVSIIEPCAVCAGALINSRIAQL HFGVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGVQEEQCAELLKGFFKSQ RAAKKAKG
dvTadA-40	MSDTALPAHWLQQACEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQ AREPTGHAEMVAIQWACKALESWRLLDCHIFVSIIEPCAMCAGGLINSRIAQL HFGVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGQQAEQCAELLKGFFKGQ RAARKAKG
dvTadA-41	MSDTALPQHWLQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQL AEPTGHAEMVAIQWACKALESWRLLDCHWFVSIIEPCAMCAGALINSRIAQL HFGVWNDKMGAAGSLIDLAQGEWYNHRVQTHSGVQAEQCAELLKGFFKS QRAAKKDKG
dvTadA-42	MSDTQLPQHWLQQAIEQAKLAADNWEVPMGCVIVQDGKQLATGFNAVEQL AEPTGHAEMVAIQWACKALFSWRLLDCHMDVTVEPCAMCAGALINSRIRQ DHFGVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGVQAEQCAELLKGFFKS QRAAKKAKG
dvTadA-43	MSDTALPAHWLQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQA REPTGHAEMVAIQWACKALESWRLLDCHIFVSIIEPCAMCAGALINSRIAQLH FGVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGQQAEQCAELLKGFFKGQR AARKAKG
dvTadA-44	MSDTALPAHWLQQAIETAKLAADNWEVPVGCVIVQEGKVLATGFNAVEQLA EPCGHAEMPPQQACKHLNSWRLLDCHMFVSVEPCAMCAGALINSRIAQLH FGVGNDKMGAAGSLIDLAQGEWYNHRVQTHVGVQAEQCAELLKGFFKSQ RAAKKAKG
dvTadA-45	MSDTALPQHWLQQAIEQAKLAADNWEVPVGHVIVQDGKVLATGFNAVEQL AEPTGHAEMVAIQWACKALESWRLLDCHWFVSIIEPCAMCAGALINSRIAQL HFGVPNDKMGAAGSLIDLCQGEWYNHRVQTHSGWQAEQCAELNKGFFKS QRAAKKAKG
dvTadA-46	MSDTALPAHWLQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQA REPTGHAECVAIQWACKALESWRLLDCHIFVSIIEPCAMCAGALINSRIAQLHF GVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGQQAEQCAELLKGFFKGQR AARKAKG
dvTadA-47	MSDTQLPQHWLQQAIEQAKLAADNWEVPMGCVIVQDGKQLATGFNAVEQL AEPTGHAEMVAIQWACKALNSWRLLDCHMDVTVEPCAMCAGALINSRIRQ DHFGVPNDKMGAAGSLIDLAQGEWYNHRVQTHSGVQAEQCAELLKGFFKS QRAAKKAKG

dvTadA-48	MSDTALPQHWMQQAIEQAKLAADNWEVPVGCVIVQDGKVLATGFNAVEQL AEPTGHAEMVAIQWACKALESWRLLDCHWFVSIIEPCAMCAGALINSRIAQP HFGVGNDKMGAAGSLIDLAQGEWYNHRVQTHSGVQAEQCAELLKGFFKSQ RAAKKAKG
dvTadA-49	MSTETWDERWMRLALEQARLAMDSWEVPVGAVIVRNNQVVATSFNEREQ RNPTAHAEMLAFERAARELGSWRCTDTTSYVTLEPCIMCAGAAHLARLDRI VFGVMNPKAGGVESWINIADEPRHNHRIEVRRGVLEEEARELLKAFFRQRR AEKARQS
dvTadA-50	MATETWDERWMRLALEQARLAMDSWEVPVGAVIVRNNQVVATCFNDREQ LDNPTAHAEMLAFERAARELGSWRCVDTTSYVTLEPCIMCAGAAHLARLDR IVFGVPNPKAGGVESWINITDEPRWNHRIEVRRGVLEEEAREPLKAFFRQRR AEKARQS
dvTadA-51	MSEYEYMRHALTLAHDARDEFEPVVGAVNVWNNRTHNAGWNRLVGLDDP FTHAEIMALRYS GPVKTGHTLMWATLYMTFPCVMCAGAMVTSRIGDVVFG VRNAKGSAAQGEMDVLHRPWYGARVIITEGKLDQECARSLCRFFISQRRRST A
dvTadA-52	MYEHEYWMRHALTLAHDAGDEFEPVVGAVQVMNTRTDRSSVFRTKGLDDL TTHAEIMALRQQGQVATGITLIWAHLATFPCVMCAGQTIASRLGDVVFGV RNAKGSAAQSEMDVLHRPQMGARVIITEGRLDQECARLLCRFFSRHRRVSK A
dvTadA-53	MSEHEWMRHALTLAHDAAATEFEIPVVGAVNVWNNRTINS GWNDLKGLDDPT YHAEIMADRQSWDVMFGHTLMWATLYMTFPCVMCAGAMVTSRIGDVVF GVRNAKGSAAQGEMDVLHRPWYGARVIITEGKLDQECARSLCRFFISQRRR STA
dvTadA-54	MGDDEHWRHALTLAKRAHDEEEVPVGCVLVQNNKVIQEFHNNAFGRMDP TAHAEISILNQAQDQEQLTSLDATLYTTLEPCVMCAMEMQLSRIDRVVFGV ANPYTGAAGSLMDILDHPRQNHTVEIHAGILADECAQELAHYFRSKRP GK
dvTadA-55	MADDEEHWRHALTLAKRAHDEAEVPVGCVLVQNNKVIQEFHNNAFGRM DPTAHAEIDILNQCGDVEQNYQLSDATLYTTLEPCVMCAMEMQLSRIDRVVF GVANPKDGAAGSLMDILKHPVMNHRVEIHAGILADECAQALAMYFISKRPV K
dvTadA-56	MADEEHWLSHALTLAKRAHAEAEVPVGCVLVQNNKVIQEFANNAFGRMDP TAHAEIDILNQCCDVEQNTQLSDATLYTTLEPCVMCAMEMQLSRIDRVVFGV ANPKTGAAGSLMDILTHPRQNRVNIHAGILADECAQELAHYFRSKRP GT
dvTadA-57	MADDEHEHWRHALTLAKRAHDEAEVPVGCVLVQNNKVIQEFHNNAFGR MDPTAHAEIDILNQCGDVEQNYQLSDATLYTTLEPCVMCAMEMQLSRIDRV VFGVANPKDGAAGSLMDILKHPVMNHRVEIHAGILADECCQALAHYFQSKR PVK

dvTadA-58	MADDEEYHWRHALTLAKRAHDEAEVPVGCVLVQNNKVIQEFHNNAFGR MDPTAHAEIDILNQCRDVEQNYQLSDATLYTTLEPCVMCAMAQSLRIDRV VFGVANPKTGAAGSLMDILKHPRQNHRVEIHAGILRDECAQVLAHYFDSKRP GK
dvTadA-59	MADDEHWRHALTLAKRAHDIAEVPTGCVLVQNNKVIQEFHNNAFGRMDP TAHAEIDILNQCRDVEQNYQLSDATLYTTLEPCVMCAMAQSLRIDRVVFG VANPKTGAAGSLMDILKHPRQNHRVEIHAGILADECAQVLAHYFDSKRTGK N
dvTadA-60	MYEVEYWMRHALTLAHDAGDEFEGPVGAVQVMNTRTDRSSVFRTKGLDDL TTHAEIMALRQQGQVATGITLIWAHLATFEPVCMCAGQTIASRLGDVVFGV RNAKGSAAQSEMDVLHRPQMGARVIITEGRLDQECARLLCRFFSRHRRVSK A
dvTadA-2-1	MGKRMQNECKFMQKAIDEARKAFALKEVPIGAIICKGDEVIASANNELING MLPSKHAEFIAIEMAAQRLDSWRLEGFDIYVSMEPCMMCADALLHSRIARV VFGVDNIKCGSMGMAQEIFKAPQNNKVVSVEKGVLGDECVNLLKDYFAHV RAKGGVKK
dvTadA-2-2	MGKRMQNECKFMQKAIDEARKAFALKEVPIGAIICKGDEVIASANNELINN MLPSKHAEFIAIEMAAQRLDSWRLEGFDIYVSMEPCMMCADALLHSRIARV VYGVDNIKCGSMGMAQEIFKAPQNNKVVSVEKGVLGDECVNLLKDYFAHV RAKGGVKK
dvTadA-2-3	MRYDMATDKKFMERAIAEAKKAYAGGEFPSGAIIVKNGEVIGTANNSYFTG MKPEMHCEKINIEDAANALHSYRLEGCTVYCTMEPCLMCAGTIVMSRIWRI VYGADDWKGGGAKVAATLIPQEGVNSRVIVEKGIFKDECDFMDFFSAGR DKWKHHY
dvTadA-2-4	MRYDMATDKKFMERAIAEAKKAMAGGEFPSGAILVKNGEVIGAAYNSYRA GNKPEKHAEQICIEEACSM LHSYHLEGCTVYCTMEPCLMCAGTIVMSRI PHI VFGADDWRGGNHKVAANLIPQEGVNHRFMIEKGYKDECDFLNADFFSNG RRKNKHEY
dvTadA-2-5	MRYDMATDKKFMERAIAEAKKAFAMGEFPSGAILVKNGEVIGA AVNSYRAG NKPEKHAEQICIEEAAANALHSYHLEGCTVYCTMEPCAMCAGTIVMSRIWHIV FGVDNWKGGGAKVAANLIPQEGVNHRVMVEKGAYKDECDFLNADFFSNG RRKWMHHS
dvTadA-2-6	MGEEELRDRNYMRLAIEMAKKARELGEVPTGAIITLGDKVIAKSYNMYVGY HAPTAHAEVRTPLEASEVLKSWNLEGCVMYCTLEPCVMCAGAICH SRIKRV VFGVDNFKGGSAGSGMQILQCQNKNHDIIVDKGVMVDECKALLAGFFAGR RANKDYRY
dvTadA-2-7	MGEQELRDRYYMRLAIEEAKKARELGEVPTGAIITLGDKVIAKSMNEYVGG CAPTAHAEVRAPLEASEVLKSWNLEGCVIYWTL EPCVMCAGAVQHSRIK RVI FGYDDFKGMAIGSGMKILSKGNHNHDIIVDKGVMVDECKALLAGFFAGRRA NKTDRY

dvTadA-2-8	MGEELRDRNYMRLAIEMAKKARELGEVPTGAIITLGDKVIAKSYNEYVGY HAPTAHAEVRTPLEASEVLKSWNLEGCVMYCTLEPCVMCAGAICHSRIKRV VFGVDNFKGGSAGSGMQILQCQNKNHDIIVDKGVMVDECKALLAGFFAGR RANKTDRY
dvTadA-2-9	MGYDMAKECEFMEFGIKEAASAMQNNDVPTGGVIFRGNKVIAMGHNAYEE DGIPSMHAEANIIKECTNALGNVDLEGCINVITLEPCPMCAGTIVHSRIAKVIY GCDDVKYGWAGVASELYRIKGNNKSKVIVEKGIARDACERLLTGFFKKRRAD KNGRY
dvTadA-2-10	MGKAMAEDKYFMQLALENAKKAMINGDVPIGAIIVKNGEVIADVGNAYATG MAPMGHAEFIAIKKAQNELKSWRLEGCTLYVSLEPCVMCAGATVQSRIERV VFGVDNAKGGALGCAMKIYEYAGANRKVMVEKGFLKDECDALLHAAFVS RRRYFKRNE
dvTadA-2-11	RIPQGSDEYWMKKALELAKQARAAGERPYGAVLIKKGEEVGRGYNTRITER DPTAHAEIKALREAGRRLDDWLLDGATLKVTEQPCVMCAGALIHARVKRVV YGAPNIEFGAAVSYMDVLNHPGLGHRVEVVKGVYAAECAALIDDYKAVKE ALKAADK
dvTadA-2-12	EIDPGSDEYWMKQAIELAKIALQRGELPIGFVVVKNGEVVGKGFNERMTLN DPTAHAEIRLCLREAGERLGNPVLEDCTDYITPEPCVMCAGALINAKVARVVY GLRNEDFGASGSLMRVLDFPGNSHRVEVVRGVLAEECKALLEEYKAGHRK KKERLA
dvTadA-2-13	VIDENSDEYWMRKALELAREAYKAGEYPVGAVFVKNEIIGTGYNARIRHN DAPAHAEISAIREEAAKKMENPFLEGATLYITLEPCVMCAGAMINKKIAKVYVY GAPNVKHGACGSFMDVLNHPKNPWKTEVVKGVLADECAALLRTEFFKYKQ MKGRN
dvTadA-2-14	SYDDNSAEYWMLKALELAKIAYKLGEYPVGAVLVKDGQVIFEGYNAEVTLN DPTAHCEIIALREAGKKMKNFCLEGATLYITLEPCVMCAGAMIAAKIAYVVY GADNISSGAAGNYMTVLDHPGNHHRVAVRRGVLAEEAAELLRKYKEDKAK AKKGSA
dvTadA-2-15	ACDEGSDERWMQKAIELAKISLKKGEYPIGAVLVENGKVIGEGYPNRKVSND PTAHDEIIALRKIGKSKGNYRLKGCTLYITEEPCVMCSGAMIAAKVDRVIYGA DDPLHGALGTAMDVLHHPGNDNRVAVRRGVCADECALREKYFRLIREKK LVS
dvTadA-2-16	RKDIDLDA AFLRRAKELAEKAYEAGEVPVGAVVVKDG VIVAEGYNQVVATR DTTAHNEVEAIREAAKHLGSHRIEGTVLYVTLEPCAMCCGWVQARVARLIF GAPDPRAGAVGNVNLCEDDSLNHQADVVGVL ENEASELLKKFFAKRRK KKAAEE
dvTadA-2-17	EFPKNSDAYWMQRALDLAKQALAAGEYPVGRVLVKGNEVVGTMFNMRITE KDPTGHAEIKALREGGKTLKSPYLEDCVLYITREPCVMCAGALNNAKIASVV YGAVNNASGAAGSTMDVLNTPGNPFTVAVKRGVLADEAAALEAAYFAKKS KKKELFK

	REDIDLDEAYMERAISIAEQAYEAEVPIGAIVVKDDMIVAEGYNQYIETNDP
dvTadA-2-18	TAMAE DLADTEAAAKLDNHRLEGT VLFVTLEPCIMCAGAKLQARVKKIVYG APDPKAGATGTVVNLLQDDRLNHKAENAGGVLKEDASELLKKFFCKRRKK KERFK
	EISKNSDEYWMSVAIEEAKKALADGEGPRGAVLIKDNKIIGRGYNARRKEND
dvTadA-2-19	PTAHAEIIAYREDGKNLKNFELKDCTLYITQEPCVMCAGAMINAKIAKVVG APNPNHGAVGSFMDVLNRPGNNHKVEVVRGVLAEECQALLDEYFVRKYAK YLRAR
	KNPADSDEYWMKKALEMARKALAAGEYPIGAVLVLDNEVIGEGYYSPTTK
dvTadA-2-20	NDPYAHAEIENLRAAGQKRNDWRLEGATLYVTCEPCFMCAGAMNAAKIGR VVYGAENPRRGATGDYMDVLCHPGNPHRVEGVVRGVLAEE SKALLDYYFTK ESQDKARQR
	MRD TDLDKEFMERAIAQAEKAYEAGEVPVGAIVVHDNEILAEGYNQFISTN
dvTadA-2-21	DPTAHGQVEAMRMAAQALGNYRIENCVLVVTLEPCSMCTGAIVQARVARLI YGAPDPRAGAVGTVVNLVND DSLNHHADVYCGVLEERASDLLKKFFKKLR KKKEGAH
	LKYE GSDAYYMKMALELANEALKAREYPVGAILCKDNELVGRGYNN TIVS
dvTadA-2-22	M DATAHAEINALREGGKILKSWMLKNCTLYITCEPCVMCAGALIHWKIGKV YGAPNPSWGAAGSLMDVLHMPGNDIQVEVVS GPYAEQCKALKDEFLAKRR KKKRELK
	MKDADLDAAFMERAIELAEKAYQAGEVPTGAVVVKDDKIVAEGYNQPVAT
dvTadA-2-23	NEPTAHEEIIAIREAAMALNNHRIEGTVLYVTLEPCIMCAGAITQARVKRLVY GAPDPRAGVVGTVVNLLNDPSLNHKATVIGGVLEERAREMLKAFFQTLRKK KAASK
	ATPEESDAYWMQLAFEEAEKARAGGEYPVFAVLVKDGEVVG TGWNNRVTR
dvTadA-2-24	NDPTAHAEIVALREGGKSLKRWELNGCTLFITEEPCVMCAGALINAKVAKVV YGAPNPATGALGVYMDVLQHPGNPHRVEVVGVLAEACAALKNAYKEAK AGAKYEAL
	MEDIA LDEKFLFRAVEQARKAYEAGEVPIGRLIVHDGKELAE GYNQTVHTR
dvTadA-2-25	DPTAF AEVEAPREAAAHLNFRLEGT VLYVTLEPCIMCTGALVQARVKKVIY GCPDPRAGAVGTVQNLVDDPRLNHQAQVIGGVLAEEASELLKKFFKKRRKK KAASE
	KIPDGSDEAWMDQALELA AVALQNGEHPVGAVLVKDNKVIGKGYNAKKILN
dvTadA-2-26	DATAHAEIIALREAGKNMKSYWLEDATLYITEEQCVMCAGACINAKVKKVV YGAPNPKQGACGEFMDVLSHPGNMHKIETVKGVLAEKAAKLLEEFK KKR KAKRAIA
	DIPEGSDEYWMCRALALA QKAYEAGELPIGAVLVKNGEVIGEGFNAITTLND
dvTadA-2-27	PTAHAEIMAIRKGGKTCKNPMLQGSTLYITREPCVMCAGAMIAAQIARVVY GAPDPASGAAGSAMDVYMAPGNKHKVEVVKGVLAEE SAALIARYLKEKRN AKRRKA

	REDCDLDRAFLERAIAQARQAYEAGEVPIGALVVHDGEILATGYNQTVIND
dvTadA-2-28	PTWHAEVLAHRENARVLGNHRLEGTVLYVTLEPCIMCAGAIVQCRVARLIY GMPDPRAGAVGTVVKLVEDESLNHKAEVVGMLVEEEAMDLLKKFFQQRK KKAASE
dvTadA-2-29	MNDAELDDRFLARAIEHAEKAYIAWEVPVGAVVVKDGEKYAEGYNQTVAT RDPTAHAEVLQIREAAAALGSHRLEGCVLYVTLEPCAMNTGALVQARIERLI YGAPDPKAGASGTVVKLVADERLNHKADVIGGVRAEEASELLKKFFKCLRK KKAASE
dvTadA-2-30	MEDKKKDEEFMERAIEQAEKAYAAGEVPVGAIVVKDGGKIVAEGYNKLIETR DPTAHAYVEAIREAAAALGNHRLEGTVLYTTLEPCIMCSGALMQQRVARLVF GARDPRAGAVGTAVNLVEDDRLNHKTDVVEGVLEEEASDLLKAFFKKRRIK KYASE
dvTadA-2-31	PIPMNSDEYWMKKALEYAKKAYEEGERPIGAVLVKNGEIIGVGYNARVTENF PTAHAEIKAIAREAGKRLGNFVLEGATLYITQEPCVMCAGAMIAAKVKRVCFG ARNPRYGAAGSYMMDVLMHPGNPWRVEIVDGVLADECKALLRNYFKEKRK GKPALK
dvTadA-2-32	QGDYDLDDKFMEERAIEQAEKAYEAKEVPIGAIVVKDGENLAYGYNQTVETR DCTAHAEMLAIREAAAKLGNHRLEGTVLYVTLEPCIMCTGAIVQARVARVV YGCPDTKAGAVGTVVNLVDNPSLNHQATVVGGVLEERASKLLKAFFAGRRK KYAASE
dvTadA-2-33	EIDEGSDAYYMQKAIELAMKAKAAGEYPVGLVLVKNKEIIGEGYNAVSVLN DPTAHGEIVALRAAGKATYNPKLEGATLYITEEPCVMCAMAMINAKVARVV YGAPNADSGAAGGAMQVLHHPNPHKVEVVKGVLADQCKHLRDEYFAKL EKKAEQVL
dvTadA-2-34	RIDIGSDEYWMSKAIELAREAYRAKEIPVGAVLVKDGEVIGRGYNNFFTEND PTKHAEINALREAMKTSKNPFLNATLYITQEPCVMCAGALVAAKVKRVVFG ATQPQTGATGSFMDVLHNPNGNTHRVEVYRGVLADECAALMEIYFVGRKQD CLARK
dvTadA-2-35	FNDIALDDDFMEKAISQAEKAYEAGEVPVGRVVVKDGEIVAEAYNQTIMTN DATAHAEIGAIRNAAAKLGNRYRIEGCVLYVTLEPCIMCAGAIVQARVARLVF GAADPKAGAVGTVVNLFNPKLNHQAKVIGGCREAEASEILKKFFKKLRKK KGAEQ
dvTadA-2-36	LKDEDLDEEFMKRAIEFAEKAYEAGEVPIGAIVVKDGRVVATGYNQIAEYKD HTAHAEVEADREAAAALENHRLEGCVLYVTLEPCYMCAGAIVQARVARVV YGAADPRAGAVGTVVNLTNDESLNHQADVGGVLEERASDLLKKFFKRLR KKKAESY
dvTadA-2-37	KNDFDADDDFMRRAIAMAEEKAYEAGEVPIGAVVVKDGMIVASGYNQTIENH DATYHAENEAIREEAAAALGNHRLPGYMLYVTLEPCIMCAGALVQARVKHV VYGAADPRAGAVGTVLDLVEDLRLNNKVDVVGGVLEEDASNLLKKFFKKR RKLSEDA

	REYADTDEEFMEKAIELAEKAMEADEIPIGAIVVKDGTIVAEGYNQTIATRDP
dvTadA-2-38	TAHAEVEAIRAAAAHLGRHRIEGTVIYVTLEPCIMCAGALCQARVKRLIFGA PDPRAGAAGTGVNLMEDPSLNRQAFVVGGVLEEEPRELLMKFFKKLRKKK AAAE
dvTadA-2-39	LEDYDLDMDFMKRAIEIAEKAKEAGEVPIGEIVVKDGRIVATGYNQRIENND CTAHAEVLAIREAAAAHLGNHKLEGTVIYVTLEPCIMCSGACVQARVARVIYG APDPRAGAAGTVVNLVNDRLNTQAEVVGGVLEEQAHELLKAFFKSKRKK KPAEE
dvTadA-2-40	REDIKEDQTFMRRAICQPEKAYEAGEVPIGAIVCRDGEIVAEGYNQTIETNDA WAHAEVLADREAALALGNHRLEETVLYTTLEPCIMCTGAIVQARVKRIVYG AYDPRAGAVGTVVNLTEDESLNHMADVVGGVYEEEEISELLKKFFKTKRKKK AVSW
dvTadA-2-41	GQAERDDLRYARMAYEEARKAYAMKEMPIGAIVVKDGAVIGAAHNDSFMQ CTPHMHAELNVISQASAMLQDWRLEGCTLYVVAEPCAMCAGVIHMSRIPRV IYGIDDGKYGAVGSCYSLLQQNGVNHVRVDVLKGVMRDAAMDNMRYYFAV RRAQNKAYI
dvTadA-2-42	GQDMLDDLKYMKLAIEEAKFAAQNGEFPIGAIIVKDGKVIARAHNKN- FNGSPNAHQEIECIEEAAKVLMSWDLNGVTNYVTTEPCLMCAGCIVHNRK RVVYGCDDVKHGCMSGMALYQCANVNHDVIVDKGYAKEACMALLAEAF AKRRAMKKRVF
dvTadA-2-43	GFDMANEKRFMELAIEEAKKAMQNGELPIGAITCNGKVIARNNNARIGDGQ MFKHAHEYELIEMA AKELGSRLEGTTLYVTNEPCMMCAGTIYMSRIERVY GCDDFKGGCSGKAFNILQAPNANHRAQVCKGVLKEECEHLLRDYFKARRK NVKSVH
dvTadA-2-44	GFDMANDEKFMATAIEEAKRAMQNGEVPAGAIIVKNNEIIRCDNAFYTSGD MTGHCEHIAPLRAKEAKNDWKLYDCTLYVTVEPCVMCAAFICNSRIPRNVF GMDTPVKGAAGSCYNILNIHDNNHRVDVVKGYTKDECEHLLSAYFKGIRNG KYLKF
dvTadA-2-45	GDRMKDDKRFM TLAYELAKKAFSEGEMPMGAIVVKNGCVIGEGLNFGMFN SDPSQHA EHNAPERASAVLGSKLDGCDIYVTAEP CALCMGTIAMSRI SRVV YGIDNETNGGAGSIIALAQLRDLNHRVQVDCGMLRADAYALMADYFKRRR KRFGKAI
dvTadA-2-46	AEDDIRDARFMQMAYEEAMKAWEGGDNPAGAIIVKDDKVIARTFNYKELA NNPIKHGEHIAVEMAAKELGNFYLDGCTLYVTLEPCVGCAGTIINSRIKRIYY GFDDDKGGCAGSVYNVLKDKNANHEVIVKKGMLSEACRALCENFFKRKRA MKKYNV
dvTadA-2-47	GYDIRNEAEFMEKAIAQAEKAYEAGEVWIGAIVVKNDEIVATGYNQTVATND PTAHAEVN AIREAAAAALKNYRLEGT VLFVTLEPCIMCAGAI VQARVARVIFG APEPRAGAVGSVVNLVNDPQLNHIADVIGGVLEE CIDLLKKFFKGRRKKKA GAE

dvTadA-2-48 GEEELRDRNYMRLAIEMAKKARELGEVPTGAIITLGDKVIAKSYNEYVGYH
APTAHAEVRTPLEASEVLKSWNLEGCVMYCTLEPCVNCAGAICHSRIKRVV
YGYDCFKGGSAGSGMQILQCQKNHDIIVDKGVMVDECKALLAGFFAGRR
ANKTDRY

dvTadA-2-49 GYDMENDERYLNLAIENAEKAFRNRDFPMGAIVVKDGAVIASAENYYECTH
KPNVPAEYECIERAGEALNSWRLEGCVLVYVTLEPCVMCAGTIVMSRIPRIY
GIDDDKMGCVSSAVNILQSKDNNHKIFIDRGVLKGRCEELLRSFFRNVRGQK
YNHR

dvTadA-2-50 GFDMAADDRKYMERAIEIAKKAQAQNGEVPIGRIIVKDGAVIAEAFNNNEMTSS
PCAHAECEQIELAAKVLGKWTLLEGCTMYVTLEPCVMCAGTIHMRRIQRIVY
GVDDMKGGCAGSVMNLFKNKGINREAIVEKCVLKHACETLLRDFFKAKRK
EYKYIR

dvTadA-2-51 GYDMAEDERFAHDAIEEAKKAFAQGEVPIGAIICRDGKVIIRAFNNAETDAKP
TAHPEYLMIERAKEELHSWRLEGCTLYVTIEPCVQCAGIIIMSRIERIVFGCDD
DKYGCIGSIVKLLAQKHMNHRVKVDKGVLKDECMTLLKDDFFVRLRSGKIYI
R

dvTadA-2-52 GEAMKDDKRFMMLALEEAEKARQNGDFPVGAIICKDGAVLVKANNAQYEN
AKPTKHAECEIQDEAANVLGMYALEGCTLYVTHEPCPMCAGIFHWSRIGKVI
YGMDDIKNGCVGCVVNLLNDAKANHRVDVYKVDLKEANMALLSAYFAAK
RAGKKKTF

dvTadA-2-53 GDDMLADKRYMELAIEESKRAFAKGEVPTGAVIVKGKEVIARAENLCYEDGI
PAKHAENIELETASKALNEFHLEGTTIYVTLEPCVQCAGAIMSRIDRIVYGL
DDEKGGAYGQTMNLL-
KANRCNRREVIHGYLCDAGKDLIKAYFAMRRRNYKHHY

dvTadA-2-54 GFDMANDEQFMKLAIENAKRGKARPEVPIGAIIVKNNELIMSADNYCEGNT
DPTRPAEHIAIEEAAKRLNNWRLEGCTNYVTQEPCVMCAGTIVMSRIERIIYG
ADNIKMGAGSVMALLQAKNANHRVQVIKGVLKEACEHLLADYFRGLRKN
KDRNR

dvTadA-2-55 VYDMANDERFCRKAIEEAEKAFALGETPQGAIIVKWNELICGAYNGNCDNG
CPTAHADMRHIELAKKALGCYALEGCTLFVTTEPCVMCAGTIMQSKIGRVV
YGCDDVKVGAVGKCVNLLQFANVNNRIEVKKGYAQDKCRDLCKRYFANIR
KDKYGHK

dvTadA-2-56 GEFKESDAYWMARALEMARRAFACGEYPIGAVLVKDGEVVGEGYNCRISSH
DPTAHAEQIDLREAGARLRSPELTGAVLYVTKEPCVMCAGALIAARVARVVY
GAPDPLYGAVGSAMDVLHHPGNPHRVNVVKGVLADESIALLKAYAKYERRR
LLGLE

dvTadA-2-57 RNDLDLDRTFLEAREQAEQAYELGEVPIGAIIVRDGEIVATGYNQVVTTND
PTAHAIVEAIREAARRLGKHRLEGTVLYVTLEPCIMCAGALVQARVKRVVFG
APDPRAGAWGTVVNLLNDESLNHQADVVKGVLEEEAFALLKKFFAVRRKQ
EAASE

MYDIDNDACFMERAIEQAEKAYRAGENPIGAIMVKGDEIVGTGYNQTMATN
dvTadA-2-58 DPTVHAEVEAIREAAAALGNHRLEGTVLFTLEPCIMCAGAIVQARVARVIF
GLPEPRAGAYGSVYNLVNQPLNHMADVIGGVLEERASDLLKKFFANIRKD
KYGHK
REDTDLDMEFMERAIALSEKAYEAREVPVGAIVVHDNEILAEGYNNNTIYTND
dvTadA-2-59 PTAHREVEAIREAAQALGNHRIENCVLVYVLEPCIMCTGAIVQARVRRLIYGA
PDPRAGAVGTVVNLVRDDSLNHIADVIRGVLEEDASDLLKKFFKQLRKKKE
GAE
NYPKDSDEYWMSKAIELALKALAANEYPVGAVNAKDNQVVGEGYNARTG
dvTadA-2-60 LNDATEHAEIRCLRQAGKTLNNMFLEDTTLYITEEPCVMCAGAMIEWKIKRV
VYGADNPLRGAAGSFMDVLNHPGNPHKVEVKRGVLAEKCRGLIEEYFARE
RKKRLAEK

Supplementary Table 4. First-round TadA variants: mean colony counts, activity, and enzyme-catalyzed base-substitution rates (μ)

Index	Mean colony count (10 mL)	Activity (resistant plate colonies / colony count)	Enzyme-catalyzed base-substitution rate, $\mu_{s.p.b.}$
ecTadA	4.00E+09	6.39E-08	1.42E-8
dvTadA-1	2.40E+10	3.70E-09	8.222E-10
dvTadA-2	1.15E+11	4.83E-10	1.073E-10
dvTadA-5	1.35E+10	3.29E-09	7.311E-10
dvTadA-6	1.00E+12	4.11E-10	9.133E-11
dvTadA-7	1.30E+10	3.42E-09	7.600E-10
dvTadA-10	6.00E+09	1.11E-08	2.467E-09
dvTadA-15	7.50E+09	1.93E-08	4.289E-09
dvTadA-16	1.20E+10	4.63E-09	1.029E-09
dvTadA-17	2.05E+10	2.17E-09	4.822E-10
dvTadA-18	4.50E+11	5.68E-10	1.262E-10
dvTadA-21	1.65E+10	2.69E-09	5.978E-10
dvTadA-22	2.50E+11	1.33E-10	2.956E-11
dvTadA-23	7.00E+09	4.13E-08	9.178E-09
dvTadA-25	1.05E+10	3.17E-09	7.044E-10
dvTadA-27	1.20E+10	1.02E-08	2.267E-09
dvTadA-43	1.00E+11	7.78E-10	1.729E-10
dvTadA-44	2.50E+11	2.67E-10	5.933E-11
dvTadA-45	2.00E+11	9.44E-10	2.098E-10
dvTadA-49	1.30E+10	2.56E-09	5.689E-10
dvTadA-55	1.75E+9	3.95E-07	8.778E-08
dvTadA-56	1.4E+9	1.14E-07	2.533E-08
dvTadA-59	1.3E+9	1.58E-08	3.511E-09
dvTadA-60	3.25 E+9	5.13E-08	1.140E-08

Supplementary Table 5: Second-round TadA variants: mean colony counts, activity, and enzyme-catalyzed base-substitution rates (μ)

Index	Mean colony count (10 mL)	Activity (resistant plate colonies / colony count)	Enzyme-catalyzed base-substitution rate, μ s.p.b.
ecTadA	4.00E+09	6.39E-08	1.420E-08
dvTadA-2-02	8.00E+08	2.36E-07	5.247E-08
dvTadA-2-04	2.50E+09	3.11E-08	6.914E-09
dvTadA-2-05	2.00E+09	7.22E-08	1.605E-08
dvTadA-2-09	1.50E+09	1.26E-07	2.798E-08
dvTadA-2-11	2.00E+09	2.81E-07	6.173E-08
dvTadA-2-12	3.50E+09	4.23E-08	9.407E-09
dvTadA-2-14	8.00E+08	5.83E-07	1.296E-07
dvTadA-2-15	2.00E+09	1.61E-07	3.580E-08
dvTadA-2-17	3.50E+09	6.19E-08	1.375E-08
dvTadA-2-18	3.50E+08	3.17E-07	7.055E-08
dvTadA-2-19	8.50E+08	1.96E-07	4.347E-08
dvTadA-2-22	3.00E+09	1.11E-07	2.469E-08
dvTadA-2-23	4.00E+09	5.00E-08	1.111E-08
dvTadA-2-26	1.50E+09	6.91E-08	1.535E-08
dvTadA-2-27	6.00E+08	2.96E-07	6.584E-08
dvTadA-2-28	1.50E+09	3.70E-08	8.230E-09
dvTadA-2-29	2.50E+09	2.96E-08	6.584E-09
dvTadA-2-32	2.50E+09	3.70E-08	8.230E-09
dvTadA-2-35	8.00E+08	5.42E-07	1.204E-07
dvTadA-2-36	1.45E+09	1.15E-07	2.556E-08
dvTadA-2-37	8.50E+08	1.70E-07	3.769E-08
dvTadA-2-39	4.50E+08	2.22E-07	4.938E-08
dvTadA-2-43	4.50E+08	6.17E-08	1.371E-08
dvTadA-2-48	1.50E+09	4.94E-08	1.097E-08
dvTadA-2-50	7.50E+08	1.48E-07	3.292E-08
dvTadA-2-51	8.50E+08	2.72E-07	6.035E-08

dvTadA-2-52	4.50E+08	1.98E-07	4.389E-08
dvTadA-2-55	4.00E+08	5.56E-08	1.235E-08
dvTadA-2-56	8.00E+08	6.48E-08	1.440E-08
dvTadA-2-57	1.00E+09	5.19E-08	1.152E-08
dvTadA-2-60	3.00E+09	1.85E-07	4.115E-08

Supplementary Table 6. The sequence of pUC57-Kan-ccdA/B, pUC57-Kan-2BspQI-ccdB and primers

pUC57-Kan-ccdA/B	TGCAGCTCTGGCCCGTGTCTCAAAATCTCTGATGTTACATTGCACAAG ATAAAAATATATCATCATGAACAATAAAACTGTCTGCTTACATAAACAG TAATACAAGGGGTGTTATGAGCCATATTCAACGGGAAACGTCGAGGCC GCGATTAAATTCCAACATGGATGCTGATTTATATGGGTATAAATGGGCTC GCGATAATGTCGGGCAATCAGGTGCGACAATCTATCGCTTGTATGGGA AGCCCGATGCGCCAGAGTTGTTTCTGAAACATGGCAAAGGTAGCGTTG CCAATGATGTTACAGATGAGATGGTCAGACTAAACTGGCTGACGGAAT TTATGCCCTCTCCGACCATCAAGCATTTTATCCGTA CTCTGATGATGCA TGGTTACTCACCCTGCGATCCCCGGA AAAACAGCATTCCAGGTATTA GAAGAATATCCTGATT CAGGTGAAAATATTGTTGATGCGCTGGCAGTGT TCCTGCGCCGGTTGCATTGCTGCTGTTTGTAAATTGTCCTTTTAACAG CGATCGCGTATTTTCGTCTCGCTCAGGCGCAATCACGAATGAATAACGGT TTGGTTGATGCGAGTGATTTTGTATGACGAGCGTAATGGCTGGCCTGTT GAACAAGTCTGGAAAGAAATGCATAAACTTTTGCCATTCTCACC GGAT TCAGTCGTCACTCATGGTGATTCTCACTTGATAACCTTATTTTTGACG AGGGGAAATTAATAGGTTGTATTGATGTTGGACGAGTCGGAATCGCAG ACCGATAACCAGGATCTTGCCATCCTATGGAAC TGCCTCGGTGAGTTTTC TCCTTCATTACAGAAACGGCTTTTTCAAAAATATGGTATTGATAATCCTG ATATGAATAAATTGCAGTTTCATTTGATGCTCGATGAGTTTTTCTAATCA GAATTGGTTAATTGGTTGTAACATTATTCAGATTGGGCTTGATTTAAAA CTTCATTTTAAATTTAAAAGGATCTAGGTGAAGATCCTTTTTTGATAATCT CATGACCAAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGA CCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGC GTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTT TGTTTGCCGGATCAAGAGCTACCAACTCTTTTCCGAAGGTAAC TGGC TTCAGCAGAGCGCAGATACCAAATACTGTTCTTCTAGTGTAGCCGTAGT TAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTC TGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCT TACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTC GGGCTGAACGGGGGGTTTCGTGCACACAGCCAGCTTGAGCGGAACGA CCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCA CGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGG GTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCT GGTATCTTTATAGTCCTGTGCGGTTTCGCCACCTCTGACTTGAGCGTCG ATTTTTGTGATGCTCGTCAGGGGGGGCGAGCCTATGGAAAAACGCCAG CAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCAC ATGTttgacagtagctcagctcaggtataatgctagtactagagaaaggagaaatactagATGCGT CGTCTGCGCGCAGAACGTTGGAAGCAGAAAAATCAGGAAGGCATGGC AGAAGTGGCCCGTTTTATTGAAATGAATGGCAGCTTTGCCGATGAAAA TCGTGATTGGtaaaAGCTTgcacaggtcGTCGACTTAAATGCCCAAACATC AGGTTAATGGCATTCTTAATATCATTTTCACGATGACTCAGATCTGCCAC
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TTCTTCACCAATAACACTAACCGGCACACTTGCCATATCGGTGGTCA TC
 ATACGCCAACTTTCATCGCCAATATGCACAACCGGATACAGTTCACGAC
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 GGCGACCCGGGGTATCAATAATATCGCTCTGCACATCCACAAACAGAC
 GATAACGGCTTTCACGCTTATAGGTGTAAACCTTAAACTGCATactcttcttt
 tcaatattattgaagcatttatcagggtattgtctcatgagcgatacatattgaatgtatttagaaaaataacaaaC
 ATATGGTGC ACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCC
 AGCCCCGACACCCGCCAACACCCGCTGACGCGCCCTGACGGGCTTGT
 CTGCTCCCGGCATCCGCTTACAGACAAGCTGTGACCGTCTCCGGGAGC
 TGCATGTGTCAGAGGTTTTACCGTTCATCACCGAAACGCGCGA

For pUC57-Kan-ccdA/B, the J23119 promoter, ccdA³⁶⁻⁷², ccdB and AmpR promoter sequence are highlighted in red, green, blue, and purple, respectively. The plasmid backbone is pUC57-Kan.

pUC57-Kan-2BspQI-ccdB	TGCAGCTCTGCCCCGTGTCTCAAAATCTCTGATGTTACATTGCACAAG ATAAAAATATATCATCATGAACAATAAAACTGTCTGCTTACATAAACAG TAATACAAGGGGTGTTATGAGCCATATTCAACGGGAAACGTCGAGGCC GCGATTAAATTCCAACATGGATGCTGATTTATATGGGTATAAATGGGCTC GCGATAATGTCGGGCAATCAGGTGCGACAATCTATCGCTTGTATGGGA AGCCCGATGCGCCAGAGTTGTTTCTGAAACATGGCAAAGGTAGCGTTG CCAATGATGTTACAGATGAGATGGTCAGACTAAACTGGCTGACGGAAT TTATGCCTCTTCCGACCATCAAGCATTTTATCCGTACTCCTGATGATGCA TGGTTACTCACCCTGCGATCCCCGAAAAACAGCATTCCAGGTATTA GAAGAATATCCTGATTCAGGTGAAAAATATTGTTGATGCGCTGGCAGTGT TCCTGCGCCGGTTGCATTTCGATTCCTGTTTGTAATTGTCCTTTTAAACAG CGATCGCGTATTTTCGTCTCGCTCAGGCGCAATCACGAATGAATAACGGT TTGGTTGATGCGAGTGATTTTGATGACGAGCGTAATGGCTGGCCTGTT GAACAAGTCTGGAAAGAAATGCATAAACTTTTGCCATTCTCACCGGAT TCAGTCGTCACCTCATGGTGATTCTCACTTGATAACCTTATTTTTGACG AGGGGAAATTAATAGGTTGTATTGATGTTGGACGAGTCGGAATCGCAG ACCGATACCAGGATCTTGCCATCCTATGGAAGTGCCTCGGTGAGTTTTC TCCTTCATTACAGAAACGGCTTTTTCAAAAATATGGTATTGATAATCCTG ATATGAATAAATTGCAGTTTCATTTGATGCTCGATGAGTTTTTCTAATCA GAATTGGTTAATTGGTTGTAACATTATTCAGATTGGGCTTGATTAAAA CTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTTGATAATCT CATGACCAAAAATCCCTTAACGTGAGTTTTTCGTTCCACTGAGCGTCAGA CCCCCTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGC GTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTT TGTTTGCCGGATCAAGAGCTACCAACTCTTTTCCGAAGGTAACGGC TTCAGCAGAGCGCAGATACCAAATACTGTTCTTCTAGTGTAGCCGTAGT TAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTC TGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCT TACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTC GGGCTGAACGGGGGGTTTCGTGCACACAGCCAGCTTGGAGCGAACGA
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CCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCA
CGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGG
GTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAACGCCT
GGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCG
ATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAG
CAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCAC
ATGTttgacagtagctcagtcctaggtataatgctagctactagagaaaggagaaatactagATGAGA
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CTCAGATCTGCCACTTCTTCACCAATAACACTAACCGGCACACTTGCC
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GATACAGTTCACGACTCACTTTATCACTCAGCAGGCGGGCGCTGGCCA
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CCCTGACGGGCTTGTCTGCTCCCGGCATCCGCTTACAGACAAGCTGTG
ACCGTCTCCGGGAGCTGCATGTGTCAGAGGTTTTACCGTCATCACCG
AAACGCGCGA

For pUC57-Kan-2BspQI-ccdB, the J23119 promoter, BspQI site, ccdB and AmpR promoter sequence are highlighted in red, green, blue, and purple, respectively. The plasmid backbone is pUC57-Kan.

BspQI-FP	GATTGCTCTTCGtaaAAGCTTgcacaggtcGTCGACTTAAAT
BspQI-RP	GGACGTGCTCTTCTCATctagtatttcctctttctctagtagtagc

Supplementary Table 7. Cloning and sequence verification of selected CcdA variants.

Nam e	Protein sequence	Log2 F	AF3 ipTM	Sequence identity to WT	DNA sequence
WT	MRRLRAER WKAENQE GMAEVARF IEMNGSFA DENRDW	8.46	0.973	1.0	ATGCGTCGTCTGCGCGCAGAACG TTGGAAAGCAGAAAATCAGGAAG GCATGGCAGAAGTGGCCCGTTTTA TTGAAATGAATGGCAGCTTTGCCG ATGAAAATCGTGATTGGTAA
878	MRRIEAEEF REKNKEGL KEVAEFIKK EGSFAEENR DW	5.31	0.91	0.65	ATGCGTCGTATTGAAGCGGAAGA ATTCGCGGAAAAAACAAGAAG GCCTGAAAGAAGTGGCGGAATTT ATTAAAAAGAAGGCAGCTTTGC GGAAGAAAACCGCGATTGGTAA
854	MRRISAEEF REKNKEGL KEIAEFIKE EGSFAEENR DW	3.28	0.9	0.62	ATGCGTCGTATTAGCGCGGAAGAA TTTCGCGGAAAAAACAAGAAGG CCTGAAAGAAATTGCGGAATTTAT TAAAGAAGAAGGCAGCTTTGCGG AAGAAAACCGCGATTGGTAA
903	MRRISAEEF REKNKEGL EEIARFIEEE GSFAEDNR DW	3.30	0.9	0.65	ATGCGTCGTATTAGCGCGGAAGAA TTTCGCGGAAAAAACAAGAAGG CCTGGAAGAAATTGCGCGCTTTAT TGAAGAAGAAGGCAGCTTTGCGG AAGATAACCGCGATTGGTAA
924	MRRLEAEA FREKNKEG LAEVAKFIE EEGSFSEEN RDW	3.23	0.9	0.68	ATGCGTCGTCTGGAAGCGGAAGC GTTTCGTGAAAAAACAAGAAG GCCTGGCGGAAGTGGCGAAATTT ATTGAAGAAGAAGGCAGCTTTAG CGAAGAAAACCGCGATTGGTAA
1654	MRQARAER WKTENREG MAEVQHFI AENGSCFD ENREW	3.04	0.91	0.73	ATGCGTCAGGCGCGTGCGGAACG TTGGAAAACCGAAAACCGTGAAG GCATGGCGGAAGTGCAGCATTTTA TTGCGGAAAACGGCAGCTTTTGC GATGAAAACCGTGAATGGTAA

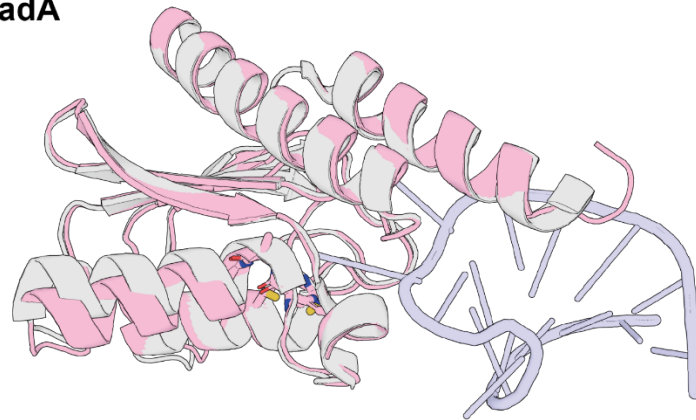
Table S8. Identity-to-reference versus predicted divergence time from TimeTree-calibrated fits

Family	Reference	Identity to reference	Predicted divergence (Ma)
TadA	<i>E. coli</i> TadA (UniProt P68398)	0.8	1.4049
		0.7	231.7360
		0.6	561.3701
		0.5	1148.1288
CcdA	<i>E. coli</i> CcdA (UniProt P62552)	0.9	4.6449
		0.8	20.3885
		0.7	40.2859
		0.6	67.3466
		0.5	109.8419
		0.4	215.5726

Notes: Values are derived from TimeTree-calibrated timetrees and MSA-based identities using a saturating decay fit. They are intended as approximate, order-of-magnitude mappings rather than strict molecular-clock estimates.

Supplementary Fig. 1

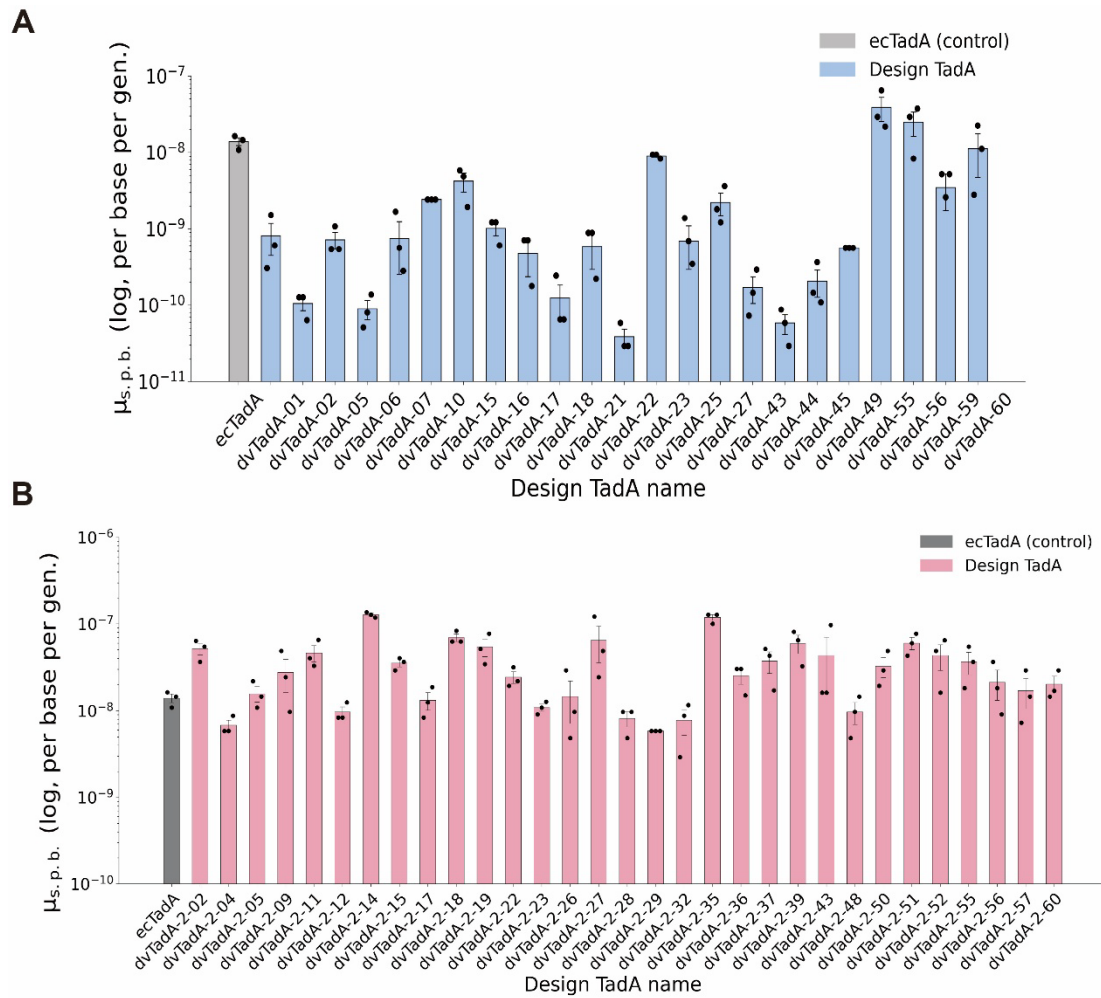
TadA



TM-score : 0.969

Supplementary Fig.1. One illustrative example of the OmegaFold-predicted structure, superimposed on the corresponding wild-type structure (PDB ID: 2B3J). Gray, wild-type; light pink, a SPIN-dvEvo-evolved variant.

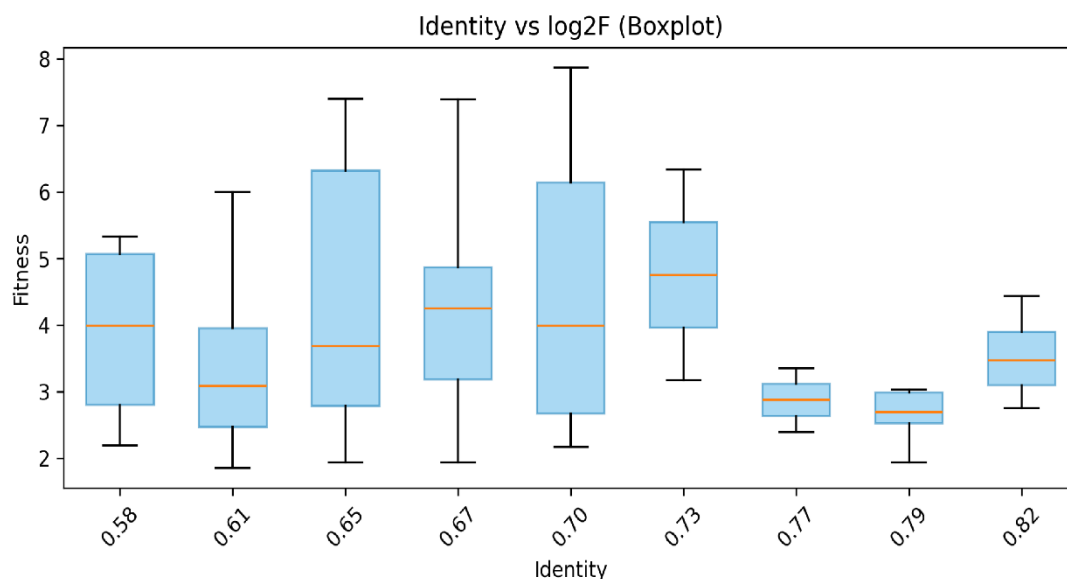
Supplementary Fig. 2



Supplementary Fig.2. DNA-editing activity of SPIN-dvEvo evolved sequences across two rounds.

(A) DNA-editing activity reported as mutation frequency and expressed as $\mu_{s.p.b.}$ for 60 selected variants from SPIN-dvEvo, along with the activity of *E. coli* TadA as a reference. Data are from Table S4 (B) DNA-editing activity reported as mutation frequency and expressed as $\mu_{s.p.b.}$ for 60 second-round dvTadA variants after LoRA retraining on first-round data. Data are from Table S5.

Supplementary Fig. 3



Supplementary Fig.3. Relationship between divergence from wild-type CcdA and activity among functional hits.

Boxplots show the distribution of log₂ fitness for variants with log₂ fitness > 3, grouped by sequence identity bins relative to wild-type CcdA.

Joint phylogenetic analysis of natural homologs and evolved variants

For each target (TadA and CcdA), we constructed a single “mixed” phylogeny containing both natural homologs and experimentally validated positive evolved variants. For TadA, we used 1000 natural homologs from ref.¹ For CcdA, we collected 100 UniProtKB homologs by BLAST against the *E. coli* CcdA sequence (UniProt ID: P62552) as in ref.² Natural homologs and evolved sequences were combined and aligned with MAFFT³. Poorly aligned columns were optionally trimmed to reduce alignment noise. Maximum-likelihood trees were inferred from the trimmed alignments using IQ-TREE⁴ with automated model selection (ModelFinder) and branch-support estimation by bootstrap. Evolved sequences were renamed with a consistent prefix (dvTadA_* or dvCcdA_*) and natural homologs were renamed to compact UniProt-style labels (accession_mnemonic) to enable unambiguous parsing and visualization. Novelty was assessed directly on the resulting tree topology by whether evolved sequences formed evolv-enriched clades distinct from the natural-homolog structure and by identifying the split point of the evolved clade as the parent node of the evolved sequences’ MRCA, with the nearest natural lineage defined as the sister clade at that split.

Identity–time calibration for TadA and CcdA^{5–7}

To provide a rough evolutionary scale for sequence exploration, we performed coarse identity–time calibrations within the TadA and CcdA families using the same procedure. For TadA, the ~1,000 orthologous sequences were taken from Supplementary Data 2 of the referenced study¹. For CcdA, ~100 sequences were collected from UniProtKB by searching the keyword “Antitoxin CcdA” and retaining representative hits.

For each family, we computed identity to the *E. coli* reference from a multiple sequence alignment (MSA), and obtained approximate lineage divergence times by building a TimeTree 5⁵ timetree for the subset of taxa recognized by the database and downloading the resulting Newick tree.

TimeTree branch lengths are in absolute time (Ma), so for each species we estimated its divergence from *Escherichia coli* as

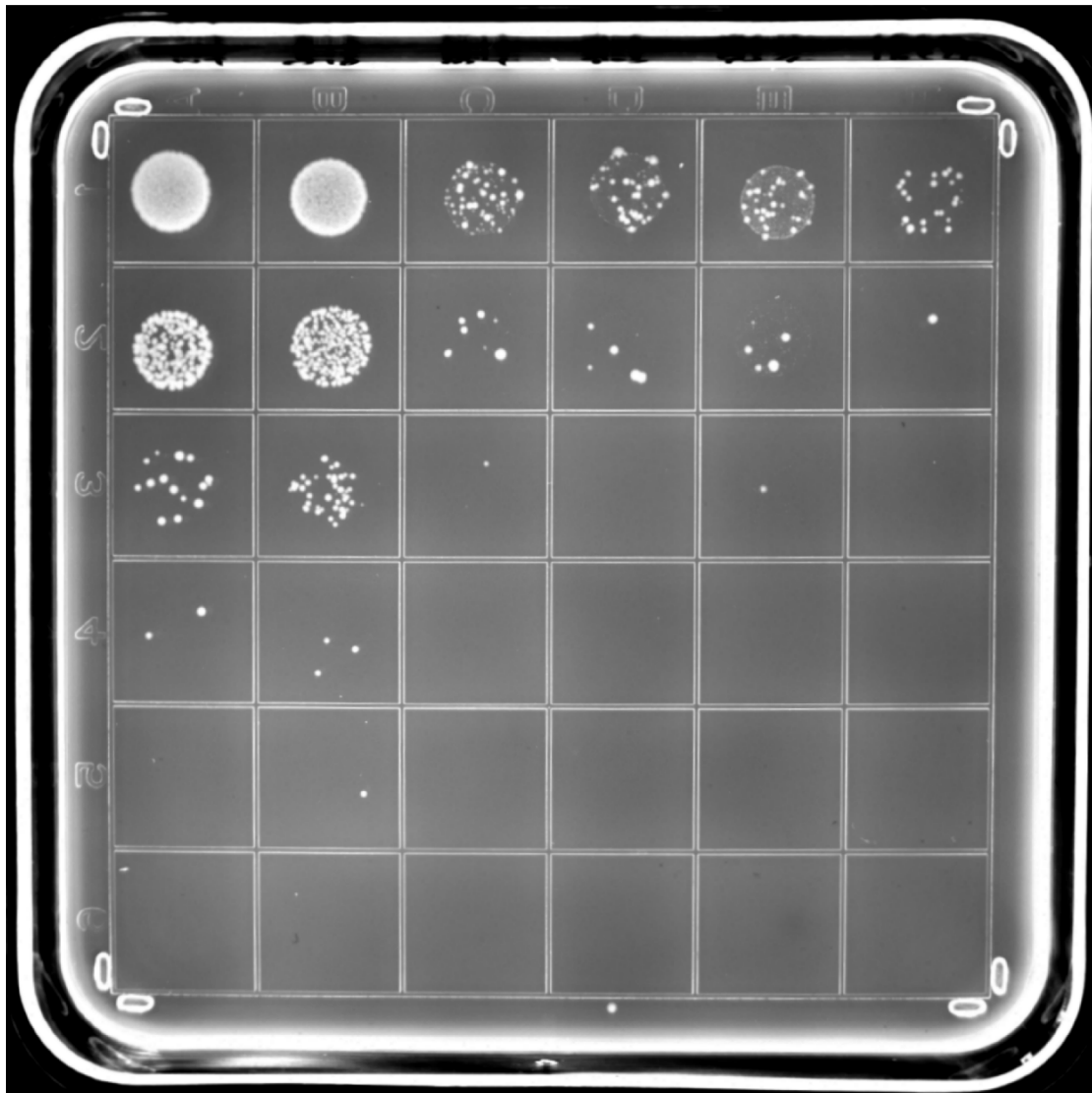
$$T_{div}(species, E. coli) = \frac{1}{2} d_{timetree}(species, E. coli)$$

where $d_{timetree}$ is the patristic distance (sum of branch lengths) between the two leaves in the TimeTree timetree. Species times were mapped onto TadA sequences by matching normalized organism names, and we fit a simple empirical saturating exponential

$$I(T) = I_{\infty} + (I_0 - I_{\infty})e^{-kT}$$

to relate identity I to divergence time T .

Supplementary Fig. 4



Supplementary Fig.4. Full CcdA spot-assay plates.

Uncropped images of the serial 10-fold dilution spot assays for CcdA SPIN-dvEvo-evolved sequences tested in Fig. 3E. Overnight cultures were normalized, serially diluted (10^2 – 10^5), and spotted onto the corresponding selective agar used for the CcdA–CcdB growth assay. Growth across dilutions indicates functional CcdA variants that rescue viability under the assay condition, whereas reduced/no growth is consistent with non-functional variants. Negative and positive controls and variant identities are labeled on the plate.

1. Zhang, S. et al. TadA orthologs enable both cytosine and adenine editing of base editors. *Nat. Commun.* **14**, 414 (2023).
2. Wu, A.Y., Kamruzzaman, M. & Iredell, J.R. Specialised functions of two common plasmid mediated toxin-antitoxin systems, ccdAB and pemIK, in Enterobacteriaceae. *PloS one* **15**, e0230652 (2020).
3. Rozewicki, J., Li, S., Amada, K.M., Standley, D.M. & Katoh, K. MAFFT-DASH: integrated protein sequence and structural alignment. *Nucleic Acids Res.* **47**, W5-W10 (2019).
4. Minh, B.Q. et al. IQ-TREE 2: New Models and Efficient Methods for Phylogenetic Inference in the Genomic Era. *Mol. Biol. Evol.* **37**, 1530-1534 (2020).
5. Kumar, S. et al. TimeTree 5: An Expanded Resource for Species Divergence Times. *Mol. Biol. Evol.* **39** (2022).
6. Feng, D.-F., Cho, G. & Doolittle, R.F. Determining divergence times with a protein clock: Update and reevaluation. *Proc Natl Acad Sci U S A* **94**, 13028-13033 (1997).
7. Konaté, M.M. et al. Molecular function limits divergent protein evolution on planetary timescales. *eLife* **8** (2019).