Supplementary Figure S1

Sequence alignment of AdcA and other zinc-binding proteins. Multiple sequence alignment of *Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus suis, Enterococcus faecalis and Staphylococcus haemolyticus* AdcA two zinc-binding domain proteins was performed with Clustal Omega (https://www.ebi.ac.uk/Tools/msa/clustalo/). Conserved residues of N-terminal (His[67], His[154], His[218], Glu[292]) and C-terminal (His[468], His[477], His[479]) domains involved in metal binding are shown in boxes.

An * (asterisk) indicates positions which have a single, fully conserved residue, A : (colon) indicates conservation between groups of strongly similar properties, A . (dot) semi-conserved substitutions

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S.aureus          MKKKLGMLLLVPAVTLSLAACGNDDGKDK----DGKVTIKTTVYPLQSFAEQIGGKHVKV  56
S.haemolyticus    MKRFLSLTVLLSIILCVLVACGKEDSSNKASKDGDKINVSTTVYPLQSFIEQIGGNHVNV  60
E.faecalis        -MKKFTLPLLAALSLILFGACGKTNTSDKTADGKEKLSIVTTFYPMYDFTKNIVGDEGDV  59
S.pneumoniae      -MKKISLL-LASLCALFLVACSNQ-----K-QADGKLNIVTTFYPVYEFTKQVAGDTANV  52
S.suis            -MKKVGLL-FLSVSALLLGACSNS-----TASEDGKLDIVTTFYPVYEFTKQVAGDEANV  53
                    : . :  :       : **.:            *: : **.**: .* ::: *.  .*

S.aureus          SSIYPAGTDLHGYEPTQKDILSASKSDLFMYTGDNLDPVAKKVASTIKDKDKKLSLEDKL  116
S.haemolyticus    SSIYPAGSDLHDYEPTQKDMLKVNKSDLFVYTGDDLDPVAKKVAATIKDDKKKVSLQDKL  120
E.faecalis        KLLIPAGSEPHDYEPSAKDMATIHDADVFVYHNENMESWVPKAAKGWKKGAPNV--IKGT  117
S.pneumoniae      ELLIGAGTEPHEYEPSAKAVAKIQDADTFVYENENMETWVPKLLDTLDKKKVKT--IKAT  110
S.suis            DLLVKAGTEVHGYEPSAKDIARIQEADAFVYENENMETWVHDVEKSLDTTKVNV--ISAT  111
                  . :  **:: * ***: * :    .:* *:* .::::  . .     .    :    .

S.aureus          DKAKLLTDQHEHGEEHEHEGHDHEKEEHHHHHGGYDPHVWLDPKINQTFAKEIKDELVKK  176
S.haemolyticus    DRSTLLTDQHEHGDEEHAD----AHEHHHHHHGGYDPHVWLDPEKNKIFAKEIKEQLVAK  176
E.faecalis        ENMVLLPGSDEDGHDH-----DHEHGEE-GHHHELDPHTWVSPHRAIQEVTNIKEQLVKL  171
S.pneumoniae      GDMLLLPGGEEEEGDH-------DHGEE-GHHHEFDPHVWLSPVRAIKLVEHIRDSLSAD  162
S.suis            DGMLLLPGSEE-GEEH-------DHSEE-GHSHAYDPHVWLSPERAITLVENIRDSLVAK  162
                      ** . .*   :.        : ..  *    ***.*:.*      . .*::.*

S.aureus          DPKHKDDYEKNYKKLNDDLKKIDNDMKQVTKDKQGNAVFISHESIGYLADCYGFVQKGIQ  236
S.haemolyticus    DPKHKNEYEKNYKKLEKSLDDIDNKLKDITKDKQGNAVFISHESLGYLADRYGFVQKGIQ  236
E.faecalis        YPKKAKTFETNAEKYLTKLTALDKEFQTALKDAKQKSFVTQHAAFGYLALDYGLKQVPIA  231
S.pneumoniae      YPDKKETFEKNAAAYIEKLQSLDKAYAEGLSQAKQKSFVTQHAAFNYLALDYGLKQVAIS  222
S.suis            YPEKKDAFETNAAAYIEKLDALDAKYSETLSAAKQKYFVTQHTAFAYLALDYGLKQVSIT  222
                   *.: . :*.*      .*  :*       .  : : .. .* :: ***  **: *  *

S.aureus          NMNA-EDPSQKELTKIVKEIRDSNAKYILYEDNVANKVTETIRKETDAKPLKFYNMESLN  295
S.haemolyticus    NMNA-EDPSQKALTQLVKEINDKNVKYILYEDNVANKVTETIRKETNAKPLKFYNMESLN  295
E.faecalis        GLTPEQEPTAGRLAELKKYVTDNQIRYIYFEKNANDKIAKTLADEANVQLEVLNPLESLT  291
S.pneumoniae      GLSPDAEPSAARLAELTEYVKKNKIAYIYFEENASQALANTLSKEAGVKTDVLNPLESLT  282
S.suis            GVAADEDPTPSRLAELTEYINKYGIKYIYFEENASKSVAETLAKETGVQLDVLNPLESLT  282
                  .:    :*:   *::: : : .    ** :*.*. . :::*: .*:..:   :  :***.

S.aureus          KEQQKKDNITYQSLMKSNIENIGKALDSGVKVKDDKAESKHDKAISDGYFKDEQVKDREL  355
S.haemolyticus    KEQSKDTSINYQTLMNKNIEALDKALDSNIKVQDDKAEHKHDKAISDGYFKDEQVKDRAL  355
E.faecalis        QKQM-DNGEDYLSVMKENLTALKKTTDTAGKEVQPETSEKTEKTVANGYFKDSEVAERTL  350
S.pneumoniae      EEDT-KAGENYISVMEKNLKALKQTTDQEGPAIEPEKA-EDTKTVQNGYFEDAAVKDRTL  340
S.suis            DEDM-KNGKDYISVMEDNLTALEKTTSQEGSEILPEEGAETAQTVYNGYFEDSAVKDRTL  341
                  .::  . .  * ::*:.*:  : :: .        :   :  ::: :***:*  * :* *

S.aureus          SDYAGEWQSVYPYLKDGTLDEVMEHKAENDPKKSAKDLKAYYDKGYKTDITNIDIKGNEI  415
S.haemolyticus    SDYEGEWQSVYPYLKNGDLDDVMKHKSEEDSSMTAKEYKAYYEKGYKTDISNIHIEGDNI  415
E.faecalis        TDYAGNWQSVYPLLKDGTLDQVFDYKAKLKKDKTPAEYKTYYDAGYQTDVDHINITDSTI  410
S.pneumoniae      SDYAGNWQSVYPFLEDGTFDQVFDYKAKLTGKMTQAEYKAYYTKGYQTDVTKINITDNTM  400
S.suis            SDYVGEWQSVYPYLLDGTLDQVWDYKAKIKGGMTAEEYKAYYDTGYKTDVDQINITDNTM  401
                  :** *:****** * :* :*:* .:*::     :  : *:**  **:**: :*.* .. :

S.aureus          TFTKDGKKHTGKYEYNGKKTLKYPKGNRGVRFMFKLVDGNDKDLPKFIQFSDHNIAPKKA  475
S.haemolyticus    TFEKNGNKVTGTYEYVGKKILDYKKGNRGVRFIYKLKNNDTPSLPKYVQFSDHNIAPKKA  475
E.faecalis        EFLVDGKPQKFTYKAAGYKILNYAKGNRGVRFLFETDDANAG-RFKYVQFSDHNIAPTKA  469
S.pneumoniae      EFVQGGQSKKYTYKYVGKKILTYKKGNRGVRFLFEATDADAG-QFKYVQFSDHNIAPVKA  459
S.suis            EFVVGDKKEKFTYKYVGYKILTYKKGNRGVRFLFEATDANAG-NYKYVQFSDHNIAPVKT  460
                   *  ..:  . .*:  * * * * ********:::  : :     *::******* *:

S.aureus          EHFHIFMGN-DNDALLKEMDNWPTYYPSKLNKDQIKEEMLAH         516
S.haemolyticus    EHFHIFMGD-NNETLLKEMDHWPTYYPASLDKDDIKEEMLAH         516
E.faecalis        AHFHIFFGGDSQESLFNEMDNWPTYYPNDLSKQEIAQEMIAH         511
S.pneumoniae      EHFHIFFGGTSQETLFEEMDNWPTYYPDNLSGQEIAQEMLAH         501
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S.suis          DHFHIYFGGESQEKLLEELENWPTYYPVGLNGLEIGQEMLAH      502
                 ****::*. .:: *::*:::******  *.  :* :**:**
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Staphylococcus aureus AdcA two zinc-binding domain and *Salmonella enterica* ZnuA single zinc-binding domain proteins sequence alignment analysis. Conserved AcdA residues of domain N-terminal (His[67], His[154], His[218], Glu[292]) involved in metal binding present in ZnuA are shown in boxes; an aspartate in ZnuA replaces glutamate [292] in AdcA, groups of strongly similar properties.

```
S.aureus        MKKKLGMLLLVPAVTLSLAACGNDDGKDKDGKVTIKTTVYPLQSFAEQIGGKHVKVSSIY     60
S.enterica      MLQKNTLL--FAA--LSAALWGSAT---QAADAAVVASLKPLGFIASAIADGVTDTQVLL     53
                * :*  :*  . *  ** *  *.     : ...:: ::: **  :*. *..  .... :

S.aureus        PAGTDIHSYEPTQKDILSASKSDLFMYTGDNLDPVAKKVASTIKDKDKKLSLEDKL-DKA     119
S.enterica      PDGASEHDYSLRPSDVKRLQGADLVVWVGPEMEAFMEKSVRNIPDNKQV-TIAQLADVKP     112
                * *:. *.*.   .*:   . :**.::.* ::: . :* . .* *:.:  :: :    *

S.aureus        KLLTDQHEHGEEHEHEGHDHEKEEHHHHHGGYDEHVWLDPKINQTFAKEIKDELVKKDPK     179
S.enterica      LLMKGADDDEDEHAHTGADEEKGDVHHHHGEYNMHLWLSPEIARATAVAIHEKLVELMPQ     172
                 *:.. .:. :** * * *.** : ***** *: *:**.*:* :: *  *:::**:  *:

S.aureus        HKDDYEKNYKKLNDDLKKIDNDMKQVTKDKQGNAVFISHESIGYLADCYGFVQKGIQNMN     239
S.enterica      SRAKLDANLKDFEAQLAATDKQVGNELAPLKGKGYFVFHDAYGYYEKHYGLTPLGHFTVN     232
                 : . : * *.:: :*   *::: :     :*:. *: *:: **  . **:.  *  .:*

S.aureus        AED-PSQKELTKIVKEIRDSNAKYILYEDNVANKVTETIRKETDAKPLKFYNMESLNKEQ     298
S.enterica      PEIQPGAQRLHEIRTQLVEQKATCVFAEPQFRPAVVEAVARGTSV---RMGTLDPLGTN-     288
                 *  *. :.* :* .:: :.:*. :: * :.   *.*:: : *..   :: .:: *..:

S.aureus        QKKDNITYQSLMKSNIENIGKALDSGVKVKDDKAESKHDKAISDGYFKDEQVKDRELSDY     358
S.enterica      IKLGKTSYSAFLSQLANQYASCLKGD--------------------------------     314
                 * .: :*.::::..  :: ...*...

S.aureus        AGEWQSVYPYLKDGTLDEVMEHKAENDPKKSAKDLKAYYDKGYKTDITNIDIKGNEITFT     418
S.enterica      ------------------------------------------------------------     314

S.aureus        KDGKKHTGKYEYNGKKTLKYPKGNRGVRFMFKLVDGNDKDLPKFIQFSDHNIAPKKAEHF     478
S.enterica      ------------------------------------------------------------     314

S.aureus        HIFMGNDNDALLKEMDNWPTYYPSKLNKDQIKEEMLAH       516
S.enterica      -------------------------------------       314
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Staphylococcus aureus AdcA two zinc-binding domain and *Salmonella enterica, Escherichia coli, Bacillus subtilis* ZinT proteins sequence alignment analysis. Conserved AdcA residues of C-terminal domain (His[468], His[477], His[479]) involved in metal binding and present in ZinT are shown in boxes.

```
S.aureus        MKKKLGMLLLVPAVTLSLAACGNDDGKDKDGKVTIKTTVYPLQSFAEQIGGKHVKVSSIY      60
B.subtilis      ------------------------------------------------------------      0
E.coli          ------------------------------------------------------------      0
S.enterica      ------------------------------------------------------------      0

S.aureus        PAGTDLHSYEPTQKDILSASKSDLFMYTGDNLDPVAKKVASTIKDKDKKLSLEDKLDKAK      120
B.subtilis      ------------------------------------------------------------      0
E.coli          ------------------------------------------------------------      0
S.enterica      ------------------------------------------------------------      0

S.aureus        LLTDQHEHGEEHEHEGHDHEKEEHHHHHGGYDPHVWLDPKINQTFAKEIKDELVKKDPKH      180
B.subtilis      ------------------------------------------------------------      0
E.coli          ------------------------------------------------------------      0
S.enterica      ------------------------------------------------------------      0

S.aureus        KDDYEKNYKKLNDDLKKIDNDMKQVTKDKQGNAVFISHESIGYLADCYGFVQKGIQNMNA      240
B.subtilis      ------------------------------------------------------------      0
E.coli          ------------------------------------------------------------      0
S.enterica      ------------------------------------------------------------      0

S.aureus        EDPSQKELTKIVKEIRDSNAKYILYEDNVANKVTETIRKETDAKPLKFYNMESLNKEQQK      300
B.subtilis      ----------------------------------MKISFATRLGVLTFGSLLVLAGCQAS      26
E.coli          ----------------------------------MAI---------RLYKLAVALGVFI-      16
S.enterica      ----------------------------------MVI---------HLKKLTMLLGMLL-      16
                                                    *          : .:

S.aureus        -----KDNITYQSLMKSNIENIGKALDSG-VKVKDDKAESKHDKAISDGYFKDEQVKDRE      354
B.subtilis      GSSKGESHKTSSSVAEDASKTQEQSLGSHDHEHDHSHAHDEETEKIYEGYFKNSQVKDRP      86
E.coli          --------------------VSAPAFSHG--HHSHGKPLTEVEQKAANGVFDDANVQNRT      54
S.enterica      --------------------VNSPAFAHG--HHAHGAPMTEVEQKAAAGVFDDANVRDRA      54
                                          ::     .  ..    :  :    * *.: :*::*

S.aureus        LSDYAGEWQSVYPYLKDGTLDEVMEHKAENDPKKSAKDLKAYYDKGYKTDITNIDIKGNE      414
B.subtilis      LTDWEGDWQSVYPYLQDGTLDEVFSYKSKHEGDKTAEEYKEYYKKGYKTDVDRIFIQKDT      146
E.coli          LSDWDGVWQSVYPLLQSGKLDPVFQKKADADKTKTFAEIKDYYHKGYATDIEMIGIEDGI      114
S.enterica      LTDWDGMWQSVYPYLVSGELDPVFRQKAKKDPEKTFEDIKAYYRKGYVTNVETIGIENGV      114
                *:*: * ****** * .* ** *:  *:. :  *:  : * ** *** *::  * *: .

S.aureus        ITFTKDGKKHTGKYEYNGKKTLKYPKGNRGVRFMFKLVDGNDKDLPKFIQFSDHNIAPKK      474
B.subtilis      VTFFKNGKEYSGKYTYDGYEILTYDAGNRGVRYIFKRAK-EAEGLPQYIQFSDHSIDPTK      205
E.coli          VEFHRNNETTSCKYDYDGYKILTYKSGKKGVRYLFECKDP-ESKAPKYIQFSDHIIAPRK      173
S.enterica      IEFHRDNNVASCKYNYAGYKILTYASGKKGVRYLFECKDA-NSKAPKYVQFSDHIIAPRK      173
                : * ::.:  : ** * * : *.*  *::***::*:  .   .  *:::*****  * * *

S.aureus        AEHHHIFMGNDN-DALLKEMDNWPTYYPSKLNKDQIKEEMLAH  516
B.subtilis      AGHYHLYWGDDR-KALLDEVKNWPTYYPSEMDGHDIAHEMMAH  247
E.coli          SSHHHIFMGNDSQQSLLNEMENWPTYYPYQLSSEEVVEEMMSH  216
S.enterica      SAHHHIFMGNTSQQALLQEMENWPTYYPYQLKANEVVDEMLHH  216
                : *:*:: *:   .:**.*:.******* ::. .:: .**: *
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