



Supplementary Fig. S1. A gallery of histone-fold proteins. Structural representatives of archaeal, bacterial, and eukaryotic histone-fold proteins as well as their distant homologs are shown in cartoon representation. In all structures, α -helices are colored in yellow, β -strands in green, and regions not part of or homologous to the histone fold are colored in grey. In homodimeric and heterodimeric structures, α -helices and β -strands in one of the subunits are shown in lighter shades of yellow and green, respectively. Accession information for the shown structures is provided in Supplementary Data S1.

Supplementary Data S1: accession information for representatives used for the analyses shown in Figs. 1 and 2 as well as for the structures shown in the Supplementary Fig. S1. In sequences of pseudodimers, the two halves are underlined.

Eukaryotic histone-fold proteins

>SCOPE d2cv5c1 a.22.1.1 (C:11-118) Histone H2A {Human (Homo sapiens), H2A.a [TaxId: 9606]}

RAKAKTRSSRAGLQFPVGRVHRLLRKGNYSERVGAGAPVYLAADVLEYLTAEILELAGNAARDNKKTRIIP
RHLQLAIRNDEELNKLGRVTIAQGGVLPNIQAVLLPK

>SCOPE d2cv5d1 a.22.1.1 (D:27-122) Histone H2B {Human (Homo sapiens), H2B.k [TaxId: 9606]}

KRSRKESYSVYVYKVLKQVHPDTGISSKAMGIMNSFVNDIFERIAGEASRLAHYNKRSTITSREIQTAVR
LLLPGELAKHAVSEGTKAVTKYTSK

>SCOPE d2cv5a_ a.22.1.1 (A:) Histone H3 {Human (Homo sapiens) [TaxId: 9606]}

PHRYRPGTVALREIRRYQKSTELLIRKLPFQRLVREIAQDFKTDLRFQSSAVMALQEACEAYLVGLFEDT
NLCAIHAKRVTIMPKDIQLARRIRGER

>SCOPE d2cv5b_ a.22.1.1 (B:) Histone H4 {Human (Homo sapiens) [TaxId: 9606]}

NIQGITKPAIRRLARRGGVKRISGLIYEETRGLKVFLENVIRDAVITYTEHAKRKTVTAMDVVYALKRQG
RTLYGFGG

>ECOD e3vh5A1 A:5-104 000148505; CENP-S

AGGEQRELLIQLRLAAVHYTTGALAQDVAEDKGVLFQSKQTVAAISEITFRQAENFARDLEMFARHA
KRSTITSEDVKLLARRSNSLLKYITQKSDELASS

>ECOD e3vh5D2 D:7-81 001273187; CENP-X

GGFRKETVERLLRLHFRDGRTRVNGDALLLMAELLKVFVREAAAAARAARQAQAEDEKVDIEHVEKVLPL
LLDFV

>ECOD e3vh5T1 T:1-91 000985373; CENP-T

GSTREPEIASSLIKQIFSHYVKTPTVTRDAYKIVEKASERYFKQISSDLEAYSQHAGRKTVMADVELLMR
RQGLVTDKMPHLVHLVERHLPL

>ECOD e3vh5W1 W:3-77 000148506; CENP-W

RRTVPRGTLRKIIKHKHPLRLAANTDLLVHLSFLLFLHRLAEEARTNAFENKSKIIPKPEHTIAAAKVIL
KKSRRG

>SCOPE d2bykb1 a.22.1.3 (B:11-99) Chrac-14 {Fruit fly (Drosophila melanogaster) [TaxId: 7227]}

MVERIEDLNLNPNVIGRLIKEALPESASVSKEARAAIARAASVFAIFVTSSSTALAHKQNHKTITAKDIL
QTLTELDFESFVPSLTQDLEVYRKVVKEKESKASKKDSNTAENANASATATAEEEAPE

>SCOPE d2byka1 a.22.1.3 (A:29-100) Chrac-16 {Fruit fly (Drosophila melanogaster) [TaxId: 7227]}

MGEPRSQPPVERPPTAETFLPLSRVRTIMKSSMDTGLITNEVLFLMTKCTELFVRHLGAAAYTEEFQRP
GEALKYEHLQVNVNKNKLEFLLQIVPQKIRVHQFQEMRLNRSAGSDDDDDDDDDDDEESESSESSE

>SCOPE dlq9ca_ a.22.1.3 (A:) Histone domain of Son of sevenless protein {Human (Homo sapiens)}

MQAQQLPYEFFSEENAPKWRGLLVPAKVKVQGVHPTLESNDDALQYVEELILQLLNMLCQAQPRASADV
EERVQKSFPHPIDKWAIAADAQSAIEKRKRNRNPLSLPVEKIHPLLKEVLYGKIDHQVSVYIVAVLEYISAD
ILKLVGNYVRNIRHYEITKQDIKIVAMCADKVLMDMFHQDVEDINILSLTDE

>SCOPE dljfia_ a.22.1.3 (A:) Negative cofactor 2, NC2, alpha chain {Human (Homo sapiens) [TaxId: 9606]}

ARFPPARIKKIMQTDDEEIGKVAAAVPVIIISRALELFLESLLKKACQVTQSRNAKTMTTSHLKQCIE

>SCOPE dljfib_ a.22.1.3 (B:) Negative cofactor 2, NC2, beta chain {Human (Homo sapiens) [TaxId: 9606]}

DDLTIPRAAINKMIKETLPNVRVANDARELVVNCCTEFIHLLISSEANEICNKSEKKTISPETHVIAQALESL
GFGSYISEVKEVLQECKTVALKRRKASSRLENLGIPEEELLRQQQELFAKARQQQAELAQQEWLQ

>SCOPE dlnlja_ a.22.1.3 (A:) Nuclear transcription factor Y subunit beta (Nf-Yb3) {Human (Homo sapiens) [TaxId: 9606]}

IYLPANVARIMKNAIPQTGKIAKDAKECVQECVSEFISFITSEASERCHQEKRKTINGEDILFAMSTLG
FDSYVEPLKLYLQKFRE

>SCOPE dlnljb_ a.22.1.3 (B:) Nuclear transcription factor Y subunit gamma (Nf-Yc2) {Human (Homo sapiens) [TaxId: 9606]}

LPLARIKKIMKLDEEDVKMISAEAPVLFAKAAQIFITELTLRAWIHTEDNKRRRTLQRNDIAMAITKFDQFD
FLIDIVPR

>SCOPE dlh3oa_ a.22.1.3 (A:) TAF(II)-135, (TAF(II)-130, hTAF4), histone fold domain {Human (Homo sapiens) [TaxId: 9606]}

MFLQLQAPLQRRILEIGKKHGITELHPDVVSYSVSHATQQRQLQNLVEKISETAQQKNFSYKDDDRYEQASDV
RAQLK

>SCOPE dlh3ob1 a.22.1.3 (B:57-128) TAF 12, TAF(II)-20, (TAF(II)-15, hTAF12), histone fold domain {Human (Homo sapiens) [TaxId: 9606]}

VLTKKKLQDLVREVPNEQLDEEDVEEMLLQIADDFIESVVTAAACQLARHRKSSTLEVKDVLHLERQWNM
WI

>SCOPE dlbh8a_ a.22.1.3 (A:) TAF13, TAF(II)18 {Human (Homo sapiens) [TaxId: 9606]}

MADEEEDPTFEENEENEIGGGAEGGQGRKRLFSKELRCMMYGFQDDQNPYTESVDILEDLVIEFITEMTH
KAMSIGRQGRAQVEDIVFLIRKDPKRFARVKDLLTMNEELKRARKAFDEANYGS

>SCOPE dlbh8b_ a.22.1.3 (B:) TAF11, TAF(II)28 {Human (Homo sapiens) [TaxId: 9606]}

FSEEQLNRYEMYRRSAFPKAAIKRLIQSITGTSVSNVVIAMSGISKVVFVGEVVEEALDVCEKWGEMPPPL
QPKHMREAVRRLKSKGQIP

>SCOPE dltafa_ a.22.1.3 (A:) TAF9, TAF(II)42 {Fruit fly (Drosophila melanogaster) [TaxId: 7227]}

PKDAQVIMSILKELNVQYEYEPVVNQLEFFRYVTSILDDAKVYANHARKKTIDLDDVRLATEVTLD

>SCOPE dltafb_ a.22.1.3 (B:) TAF6, TAF(II)62 {Fruit fly (Drosophila melanogaster) [TaxId: 7227]}

MLYGSSISAESMKVIAESIGVGLSDDAAKELAEDVSIKLRIVQDAAKFMNHAKRQKLSVRDIDMSLKV

>ECOD e4wv4A1 A:3-102 001492373; TAF10
STPLVDFLMQLEDYTPPTIPDAVTGYLNRAGFEASDPRIIRLISLAAQKFISDIANDALQHCKMKGTSAG
SSRSKSKDRKYTLTMEDLTPALSEYGINVK

>ECOD e4wv4B1 B:5-76 001492374; TAF8
NYHLARRRTLQVVVSSLLTEAGFESA EKASVETLTEM LQSYISEIGRS AKSYCEHTARTQPTLS DIVVTL
VE

Archaeal HMfB-like

>SCOPE d1b67a_ a.22.1.2 (A:) Archaeal histone HMfA {Methanothermus
fervidus, histone A [TaxId: 2180]}
MGELPIAPIGRIIKNAGAERVSDDARIALAKVLEEMGEEIASEAVKLAKHAGRKTIKAEDIELARKMFK

>SCOPE d1a7wa_ a.22.1.2 (A:) Archaeal histone HMfB {Methanothermus
fervidus, histone B [TaxId: 2180]}
MELPIAPIGRIIKDAGAERVSDDARITLAKILEEMGRDIASEAIKLARHAGRKTIKAEDIELAVRRFKK

>SCOPE d1f1ea_ a.22.1.2 (A:) Archaeal histone HMk {Methanopyrus kandleri
[TaxId: 2320]}
MAVELPKAAIERIFRQIGERRLSQDAKDTIYDFVPTMAEYVANAAKSVLDASGKKTLMEEHLKALADVL
MVEGVEDYDGE LFG RATVRRILKRAGIERASSDAVDLYNKLICRATEELGEKAAEYADEDGRKTVQGEDV
EKAITYSMPKGGEL

Bacterial single histone fold-like proteins

>NP_712639.2 hypothetical protein LA_2458 [Leptospira interrogans serovar
Lai str. 56601]
MAGKNVERETLIVTSKVKAYIKSKGFMTSGDAIDGLNEKIHQLIDDAVKRTE SNKRSTVRPTDF

>WP_011162677.1 hypothetical protein [Bdellovibrio bacteriovorus]
MAEVLVVTSKVKLIKEKGMNTSAETIDVLSKAIEQLCLKGVESAKADGRKTVMARDIVIDHL

>WP_006975389.1 hypothetical protein [Plesiocystis pacifica]
MARKSTKQEILVVGSKVKAIVRDAGLRSDGELVAALSGRVHAMLEGAIVRCTRNM RSTVRPQDL

Bacterial pseudodimeric histone-fold proteins

>SCOPE d1r4va_ a.22.1.4 (A:) Hypothetical protein Aq_328 {Aquifex aeolicus
[TaxId: 63363]}
MQEKYNFGKVSSQHKNYSKIETMLRPKGFDKLDHYFRTELDIDDLTDETI ELLLSVKA AAFGKLFYGAEQR
ARWNGRDFIALADLNITKALEEHIKNFQKIEQDMGVDELLEYIAFIPPVEMNVGEDLKSEYRNIMGLLLL
MHADVIKKATGERKPSREAMEFVAQIVDKVF

>SCOPE dlwwia1 a.22.1.4 (A:1-148) Hypothetical protein TTHA1479 {Thermus
thermophilus [TaxId: 274]}
MLMKVAEFERLFRQAAGLDVDKNDLKRVSDFLRNKLYDLLAVAERNAKYNGRD LIFEPDLP IAKGLQETL
QEFRMDTALELKPVLDALAALPPLDLEVAEDVRNLLPELAGALVVAYARVLKELDPALKNPQTEHHERA
ERVFNLLL

Distant homologs

>ECOD e1in4A2 A:180-254 000003427; AAA+ C-domain
YTVKELKEIIKRAASLMDVEIEDAAAEMIAKRSRGTPRIAIRLTKRVRDMLTVVKADRINTDIVLKTMEV
LNIDD

>ECOD e1k6kA1 A:1-142 000003424; Clp N-domain
MLNQELELSLNMAFARAREHRHEFMTVEHLLLALLSNPSAREALEACSVDLVALRQELEAFIEQTTPVLP
ASEEEERDTQPTLSFQRVLQRAVFHVQSSGRNEVTGANVLVAIFSEQESQAAYLLRKHEVSRLDVVNFISH
GT

>ECOD e2v6zM1 M:25-99 000168577; Dpoe2NT
MAPERLRSRALSAFKLRGLLLRGEAIKYLTEALQSISELELEDKLEKI INAVEKQPLSSNMIERSVVEAA
VQESS

>ECOD e2kruA1 A:2-55 000138180; PCP_red
MGELSWTAEAEKMLGKVPPFFVRKKVVRKNTDNYAREIGEPVVTADVFRKAKEHLGGLEHHHHHH

Supplementary Data S2: Accession information for sequences shown in Fig. 3.

Eukaryotic nucleosome core histones

>AAA63191.1 histone H2A.1 [Homo sapiens]
MSGRGKQGGKARAKAKTRSSRAGLQFPVGRVHRLLRKGNYSERVGAGAPVYLAADVLEYLTAEILELAGNA
ARDNKKTRIIIPRHLQLAIRNDEELNKKLLGRVTTIAQGGVLPNIQAVLLPKKTESHHKAKGK

>CAB02542.1 histone H2B [Homo sapiens]
MPEPAKSAPAPKKGSKKAVTKAQKKDSKKRKRSRKESYSVYVYKVLKQVHPDTGISSKAMGIMNSFVNDI
FERIAGEASRLAHYNKRSTITSREIQTAVRLLLLPGELAKHAVSEGTKAVTKYTSSK

>NP_003520.1 histone H3.1 [Homo sapiens]
MARTKQTARKSTGGKAPRKQLATKAARKSAPATGGVKKPHRYRPGTVALREIRRYQKSTELLIRKLPFQR
LVREIAQDFKTDLRFQSSAVMALQEACEAYLVGLFEDTNLCAIHAKRVTIMPKDIQLARRIRGERA

>NP_003529.1 histone H4 [Homo sapiens]
MSGRGKGGKGLGKGGAKRHRKVLDRNIQGITKPAIRRLARRGGVKRISGLIYEETRGLKVFLENVIRDA
VTTYEHAKRKTVTAMDVVYALKRQGRRTLYGFGG

Archaeal HMfB-like histones

>WP_013413995.1 histone family protein HMfA [Methanothermus fervidus]
MGELPIAPIGRIIKNAGAERVSDDARIALAKVLEEMGEEIASEAVKLA KHAGRKTIKAEDIELARKMFK

>sp|P19267.1|HMFB_METFE RecName: Full=DNA-binding protein HMf-2; AltName:
Full=Archaeal histone B
MELPIAPIGRIIKDAGAERVSDDARITLAKILEEMGRDIASEAIKLARHAGRKTIKAEDIELAVRRFVK

>WP_048053612.1 histone [Pyrococcus horikoshii]
MGELPIAPVDRLIRKAGAERVSEQAQKVLAEYLEEYAEIETIAKKAVEFARHAGRKTIVKVEDIKLAIS

>WP_011012868.1 histone [Pyrococcus furiosus]
MGELPIAPVDRLIRKAGAQRVSEQAQKVLAEHLLEEKAEIETIAKKAVDLAKHAGRKTIVKVEDIKLAIS

Prokaryotic single histone fold-like proteins

Bacteria

>WP_006975389.1 hypothetical protein [Plesiocystis pacifica]
MARKSTKQEILVVGSKVKAIVRDAGLRSDGELVAALSGRVHAMLEGAIVRCTRNMNRSTVVRPQDL

>WP_052547863.1 hypothetical protein [Enhygromyxa salina]
MAAKKKTAKTKKAREIVVVGSKVKDVVRAAGYRSDGELVQAVSEKVVHEMLEAAIKRAESNKRGTVVRPYDL

>WP_096326703.1 hypothetical protein [Nannocystis exedens]
MATKNKAPKEILVVGSKVKDVIRDAGLRSDGELIQAVSDKVHELLGAAIERCKSNRSTVVRPYDL

>KPJ56806.1 hypothetical protein AMS16_01810 [Planctomycetes bacterium
DG_58]
MAKDMLVVGSKVKAYLKSSGMKTAGDTLAAVSDKVYAMLDAAVERTKANKRATVVRPQDL

Archaea

>WP_099254152.1 DUF1931 domain-containing protein [Halorubrum persicum]
MSDLIVKAAVKDALSDHNVSADFYDALNEEVAELLDAAERAETNGRKTVQPRDL

>AAF03226.1 ORF6 [Pyrococcus furiosus]
MEVKEMVELLVKSKVKEFVSSIDKDMRVSPPEFYEALEAEVKALIEKAVKRAQAEGRKTLYARHV

>WP_011249991.1 hypothetical protein [Thermococcus kodakarensis]
MAEMLVKSKVKEFVKSVDPEMRVSPPEFYDALEAEVKALVEKAIKRAQAEGRKTLYARHV

>KHO49746.1 hypothetical protein QT01_C0002G0030 [archaeon GW2011_AR6]
MELVIKSKLKDAVKGLRVSSSELAELNKKVEAMLKEAAERAKANHRGTVMPQDL

Prokaryotic pseudodimeric histone-fold proteins

Bacteria

>NP_213225.1 hypothetical protein aq_328 [Aquifex aeolicus VF5]
MQEKYNFGKVSSQHKYNSKIETMLRPGKGFDKLDHYFRTELDIDLTDETIELLLNSVKAAGFKLFYGAEQR
ARWNGRDFIALADLNITKALEEHKFNQKIEQDMGVDELLEYIAFIPPVEMNVGEDLKSEYRNIMGLLLL
MHADVIKKATGERKPSREAMEFVAQIVDKVF

>YP_144745.1 hypothetical protein TTHA1479 [Thermus thermophilus HB8]
MLMKVAEFERLFRQAAGLDVVDKNDLKRVSDFLRNKLYDLLAVAERNAKYNGRDLIPEPDLPIAKGLQETL
QEFRMDTALELKPVLDALAALPPLDLEVAEDVRNLLPELAGALVVAYARVLKELDPALKNPQTEHHERA
ERVFNLLL

>WP_012409489.1 DUF1931 family protein [Nostoc punctiforme]
MSVISISKFERFFRTVAGLDVVDKNDLKRYSDFVNHKTYDLLLLRGQATAKANGRDIIEPFDVPITKGLEER
IHNFKIEINEEIELKPILEDMYTTTRPLDLLDYSKETEARLSDIVGGLSVALARTFKIIDPALKNPQTMQWER
AFSIFDLLLL

>WP_041939166.1 DUF1931 family protein [Frankia alni]
MPVMGVTRFERFFRIAAGLDMDKNDVKRYGDFVNKVVYDLLLLMAQATAKANVRDVIEPWLDPITKGLQES
IHHRFDLDEEIELRPILEQIAARPPDLLALSDDTAARLPLIVGGLSLALARAFTIIEPELKNPQPSEWER
VSRIFDLLLL

Archaea

>WP_050003266.1 DUF1931 family protein [Thermococcus eurythermalis]
MAEMIIPYPQLQKILERTCELAVIKPRAEEMMEIVEKKLADLFEVAYENAKAERSSTIKMRHIPITKGFK
NSLNLFRAVIEDEKVEIEPIRKYVLRKIPGDIPLLEEDVVNELPIIAGTLFVVLVGRVIKALHPEIKNVYPE
HIEEAKKVLDTL

>WP_011011744.1 DUF1931 family protein [Pyrococcus furiosus]
MAEMVIPYPHLQRILEKTCELAVTKPAERMMEIVERKLADLFEVAYENATAENSETIKMRHIPITKGFR
SSMNLFRAVIEDENIKIEPILDYVLRKIPADKPLEEEVINELPIITGTLFVVLIGRVIKALHPEVRNVYPE
HIEEAEKVLDTL

>WP_012941033.1 DUF1931 family protein [Archaeoglobus profundus]
MAEMIIPYPQLKILEDTCELDVYKAEASKMMDIVERKLADLFEVAYDKARAEGREMIMFRDLPLTKGFL
NSMELFRKAIERQNVVDEPIKKFVLKGLPVDAPLQDELVDLPIITGTLFVVLIGRVIKALHPDVERVKDE
HIDEARRVLDTL

>WP_010871032.1 DUF1931 family protein [Methanocaldococcus jannaschii]
MAEMIIPYPQLKIMKTTCEIDLYKTEAEDIMDVVEKKLADLFEVAHRNAKEENAKI IKMRHIPITKGFL
NSMELFRSVIEEENIVAETIKKYVMKKIPGDLPLDDIVVDNLPLITGTIFIVVGRVIKALHEDIERIRKE
HIEEAKKVLDTL