```
                                 ↓ ↓                         ↓         ↓                 ↓ ↓
                                 b b                         b         b                 b b            pos
CthedisCuZnSOD1.      :  GMHIHAFGDN-------TNG-CTSAGPH-FNPHGKTHGAPTD---ENR----HVGDL----G  :  86
CtheCuZnSOD1.         :  GMHTHTFGDN-------TNG-CTSAGPH-FNPHGKTHGAPTD---ENR----HVGDL----G  :  86
CgloCuZnSOD1.         :  GMHIHTFGDN-------TNG-CTSAGPH-FNPHGKTHGAPVD---ENR----HVGDL----G  :  86
CcochCuZnSOD1.        :  GMHIHTFGDN-------TNG-CTSAGPH-FNPHGKTHGAPVD---ENR----HVGDL----G  :  86
SalkCuZnSOD1.         :  GMHIHTFGDN-------TNG-CTSAGPH-FNPHGKQHGAPSD---ENR----HVGDL----G  :  86
NcCuZnSOD1.           :  GFHIHTFGDN-------TNG-CTSAGPH-FNPHGTTHGDRTA---EVR----HVGDL----G  :  86
PanCuZnSOD1.          :  GMHIHTFGDN-------TNG-CTSAGPH-FNPHGKTHGNRTD---ENR----HVGDL----G  :  86
CthedisCuZnSOD2.      :  PYHLHVDPVP-------EDGNCTKTLAH-LDPFIRGEATPCD---PEQPATCQVGDLSGKWG  : 142
CtheCuZnSOD2.         :  PYHLHVDPVP-------SDGNCTKTLAH-LDPFIRGEATPCD---PEQPATCQVGDLSGKWG  : 142
TtheCuZnSOD2.         :  PYHLHVAPVP-------EDGNCTETLAH-LDPYIRGEDTPCN---ADAPATCQVGDLSGKHG  : 143
TterCuZnSOD2.         :  PYHIHVDPVP-------ADGNCTATLAH-LDPFIRGETPPCD---KNAPATCQVGDLSGKHG  : 166
SalkCuZnSOD2.         :  SYHLHAAPVP-------EDGNCTQTLAH-LDPYIRRGSPPCD---ASAPETCEVGDLSGKHG  : 146
CgloCuZnSOD2.         :  SYHLHVDPVP-------ENGNCTATLAH-LDPYIRGEATPCE---KSSPATCQVGDLSGKHG  : 107
PansCuZnSOD2.         :  PYHLHVAPVP-------ADGNCTVTLAH-LDPFIRGENTSCN---PFAPQTCQVGDLSGKFG  : 145
PpatCuZnSOD1.         :  GFHLHEFGDT-------TNG-CMSTGPH-FNPEGKTHGAPED---DNR----HAGDL----G  : 137
PpatCuZnSOD2.         :  TISIHLEGAPWGNVAAFSDGPVGSSGGTPFFYLSRMDPTPNDITLDSRCSLTLSEASLGTCG  : 112
NtabCuZnSOD1.         :  GFHLHEFGDT-------TNG-CMSTGPH-FNPDGKTHGAPED---EIR----HAGDL----G  : 151
BoldCuZnSOD1.         :  GFHVHALGDT-------TNG-CMSTGPH-FNPAGKEHGAPED---ENR----HAGDL----G  :  84
CannCuZnSOD1.         :  GFHVHALGDT-------TNG-CMSTGPH-YNPAGKEHGAPED---ENR----HAGDL----G  :  84
QsubCuZnSOD1.         :  GFHVHALGDT-------TNG-CMSTGPH-FNPANKEHGAPED---ENR----HAGDL----G  :  84
BfloCuZnSOD1.         :  GFHIHEFGDT-------TNG-CTSAGSH-FNPAKKNHGGPQD---AER----HVGDL----G  :  86
BbeCuZnSOD1.          :  GFHIHEFGDT-------TNG-CTSAGGH-FNPAKKNHGGPQD---EER----HVGDL----G  :  86
CintCuZnSOD1.         :  GFHIHEFGDH-------TNG-CTSTGGH-FNPQKCDHGAPEA---EVR----HFGDL----G  :  86
HsCuZnSOD1.           :  GFHVHEFGDN-------TAG-CTSAGPH-FNPLSRKHGGPKD---EER----HVGDL----G  :  86
Consensus             :    H6H             1G Ct     H  1P       p             GDL    G
```

Suppl. Figure 2. Multiple sequence alignment showing essential regions of CuZnSOD obtained with Muscle implemented in MEGA X package [14]. Highly conserved regions responsible for metal binding are shown above the alignment. Color scheme: blue - highly conserved positions (above 95% of all aligned sequences), green - moderately conserved (between 75-95%), yellow - weakly conserved positions (between 50-75%). Numbers on the right represent corresponding amino acid position of each sequence.

```
                                                                                                                                  ↓
                                                                                                                                  b                                                                  pos
CthedisCuZnSOD1.     : NIETDANGNSKGTMTDHLVK-LIGPESVIG-RTVVVHAGT-------------D-------- : 125
CtheCuZnSOD1.        : NIETDANGNSKGTMTDHLVK-LIGPESVIG-RTVVVHAGT-------------D-------- : 125
CgloCuZnSOD1.        : NIETDAQGNSKGTVTDKHIK-IIGPESVIG-RTVVVHAGT-------------D-------- : 125
CcochCuZnSOD1.       : NIETDAQGNSKGSVTDKHIK-IIGPESVIG-RTVVVHAGT-------------D-------- : 125
SalkCuZnSOD1.        : NIETDAQGNSKGEVTDSLIK-LIGPESVIG-RTVVVHAGT-------------D-------- : 125
NcCuZnSOD1.          : NIETDAQGNAKGTVTDNLVK-LIGPESVIG-RTVVVHAGT-------------D-------- : 125
PanCuZnSOD1.         : NIETDAQGNSKGTVTDNLIK-LIGPESVIG-RTVVVHAGT-------------D-------- : 125
CthedisCuZnSOD2.     : DIIPDENGTFEQTYTDLYASTKEGIGAFFGNRSVVVHFPN-------------KTRITCASF : 191
CtheCuZnSOD2.        : DIIPDENGTFEQTYTDLYASTKEGIGAFFGNRSIVVHFPN-------------K-TRITCAN : 190
TtheCuZnSOD2.        : KIPANKT-TFETSYVDLYASTVEGIGAFFGNRSIVFHFPN-------------K-TRITCAN : 190
TterCuZnSOD2.        : AIPTDQD-TWETSYVDLYASTLEGIGAFFGNRSIVVHYPN-------------K-TRITCAS : 213
SalkCuZnSOD2.        : LIDP-AGGAFEAVYVDEFASLIEGQGAFFGNRSFVLHLAS-------------D-------- : 186
CgloCuZnSOD2.        : AITPDAEGAFEATYVDLYASTLEGIGAFFGNRSIVFHHPN-------------K-TRISCAS : 155
PansCuZnSOD2.        : EIRPEEDGTWETTYTDLYSSTLEGLGSFFGNRSIVFHYPN-------------K-TRISCAN : 193
PpatCuZnSOD1.        : NVIAGNDGVVEVTLEDSQIP-LSGPHSVVG-RAFVIHEAE-------------D-------- : 176
PpatCuZnSOD2.        : SVDPENPTCARLTLSGKMMEITDQQELDFAALALFSKHPEMPDWPKWHKWIFYKLDILNIYL : 174
NtabCuZnSOD1.        : NIVANANGVAEATFVDNQIP-LTGPNSVVG-RALVVHELE-------------D-------- : 190
BoldCuZnSOD1.        : NVTAGADGVANVNVVDSQIP-LTGPQSIIG-RAVVVHADP-------------D-------- : 123
CannCuZnSOD1.        : NITVGEDGTASFTITDEQIP-LTGPQSIIG-RAVVVHADP-------------D-------- : 123
QsubCuZnSOD1.        : NVNVGADGTVNFTITDKQIP-LSGPNSIIG-RAVVVHADP-------------D-------- : 123
BfloCuZnSOD1.        : NVEVGDDGVATINITDSQLQ-LTGPNSIVG-RAVVVHAGE-------------D-------- : 125
BbeCuZnSOD1.         : NVEVGEDGEANIKITDSQLQ-LTGPNSIIG-RAVVVHAGE-------------D-------- : 125
CintCuZnSOD1.        : NVTADSSGVAEVNISDKYVT-LTGINSVIG-RAVVVHADV-------------D-------- : 125
HsCuZnSOD1.          : NVTADKDGVADVSIEDSVIS-LSGDHCIIG-RTLVVHEKA-------------D-------- : 125
Consensus            :  6     g       D       G     G R  V H
```

Suppl. Figure 2 continued.