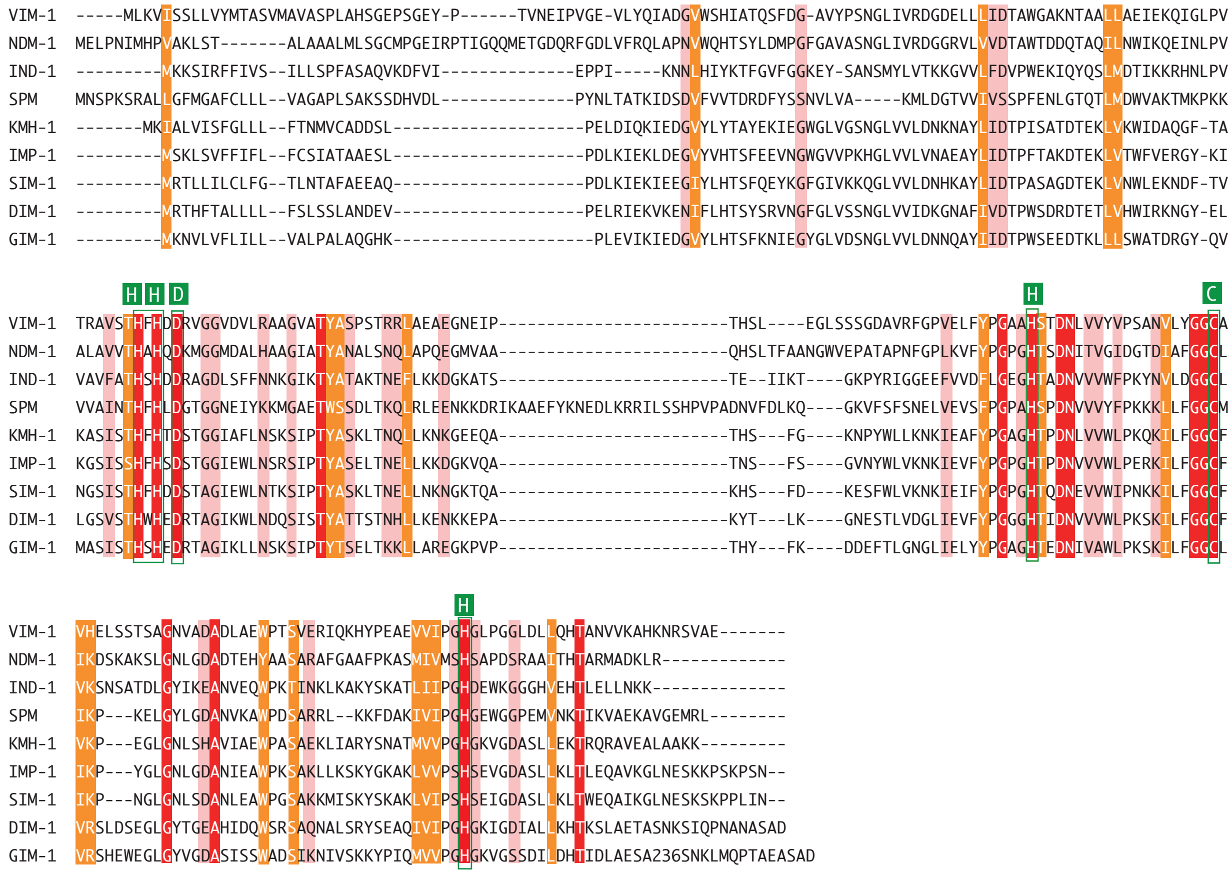
🟩 conserved key motif
🟥 indicates positions which have a single, fully conserved residue
🟧 indicates that one of the following 'strong' groups is fully conserved (>0.5 Gonnet Pam250 matrix)
▨ indicates that one of the following 'weaker' groups is fully conserved (=<0.5 Gonnet Pam250 matrix)



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VIM-1  -----MLKVISSLLVYMTASVMAVASPLAHSGEPSGEY-P------TVNEIPVGE-VLYQIADGVWSHIATQSFDG-AVYPSNGLIVRDGDELLLIDTAWGAKNTAALLAEIEKQIGLPV
NDM-1  MELPNIMHPVAKLST-------ALAAALMLSGCMPGEIRPTIGQQMETGDQRFGDLVFRQLAPNVWQHTSYLDMPGFGAVASNGLIVRDGGRVLVVDTAWTDDQTAQILNWIKQEINLPV
IND-1  ---------MKKSIRFFIVS--ILLSPFASAQVKDFVI--------------EPPI-----KNNLHIYKTFGVFGGKEY-SANSMYLVTKKGVVLFDVPWEKIQYQSLMDTIKKRHNLPV
SPM    MNSPKSRALLGFMGAFCLLL--VAGAPLSAKSSDHVDL--------------PYNLTATKIDSDVFVVTDRDFYSSNVLVA-----KMLDGTVVIVSSPFENLGTQTLMDWVAKTMKPKK
KMH-1  -------MKIALVISFGLLL--FTNMVCADDSL--------------------PELDIQKIEDGVYLYTAYEKIEGWGLVGSNGLVVLDNKNAYLIDTPISATDTEKLVKWIDAQGF-TA
IMP-1  ---------MSKLSVFFIFL--FCSIATAAESL--------------------PDLKIEKLDEGVYVHTSFEEVNGWGVVPKHGLVVLVNAEAYLIDTPFTAKDTEKLVTWFVERGY-KI
SIM-1  ---------MRTLLILCLFG--TLNTAFAEEAQ--------------------PDLKIEKIEEGIYLHTSFQEYKGFGIVKKQGLVVLDNHKAYLIDTPASAGDTEKLVNWLEKNDF-TV
DIM-1  ---------MRTHFTALLLL--FSLSSLANDEV--------------------PELRIEKVKENIFLHTSYSRVNGFGLVSSNGLVVIDKGNAFIVDTPWSDRDTETLVHWIRKNGY-EL
GIM-1  ---------MKNVLVFLILL--VALPALAQGHK---------------------PLEVIKIEDGVYLHTSFKNIEGYGLVDSNGLVVLDNNQAYIIDTPWSEEDTKLLLSWATDRGY-QV

VIM-1  TRAVSTHFHDDRVGGVDVLRAAGVATYASPSTRRLAEAEGNEIP------------------------THSL----EGLSSSGDAVRFGPVELFYPGAAHSTDNLVVYVPSANVLYGGCA
NDM-1  ALAVVTHAHQDKMGGMDALHAAGIATYANALSNQLAPQEGMVAA------------------------QHSLTFAANGWVEPATAPNFGPLKVFYPGPGHTSDNITVGIDGTDIAFGGCL
IND-1  VAVFATHSHDDRAGDLSFFNNKGIKTYATAKTNEFLKKDGKATS------------------------TE--IIKT----GKPYRIGGEEFVVDFLGEGHTADNVVVWFPKYNVLDGGCL
SPM    VVAINTHFHLDGTGGNEIYKKMGAETWSSDLTKQLRLEENKKDRIKAAEFYKNEDLKRRILSSHPVPADNVFDLKQ----GKVFSFSNELVEVSFPGPAHSPDNVVVYFPKKKLLFGGCM
KMH-1  KASISTHFHTDSTGGIAFLNSKSIPTYASKLTNQLLKNKGEEQA------------------------THS---FG----KNPYWLLKNKIEAFYPGAGHTPDNLVVWLPKQKILFGGCF
IMP-1  KGSISSHFHSDSTGGIEWLNSRSIPTYASELTNELLKKDGKVQA------------------------TNS---FS----GVNYWLVKNKIEVFYPGPGHTPDNVVVWLPERKILFGGCF
SIM-1  NGSISTHFHDDSTAGIEWLNTKSIPTYASKLTNELLNKNGKTQA------------------------KHS---FD----KESFWLVKNKIEIFYPGPGHTQDNEVVWIPNKKILFGGCF
DIM-1  LGSVSTHWHEDRTAGIKWLNDQSISTYATTSTNHLLKENKKEPA------------------------KYT---LK----GNESTLVDGLIEVFYPGGGHTIDNVVVWLPKSKILFGGCF
GIM-1  MASISTHSHEDRTAGIKLLNSKSIPTYTSELTKKLLAREGKPVP------------------------THY---FK----DDEFTLGNGLIELYYPGAGHTEDNIVAWLPKSKILFGGCL

VIM-1  VHELSSTSAGNVADADLAEWPTSVERIQKHYPEAEVVIPGHGLPGGLDLLQHTANVVKAHKNRSVAE-------
NDM-1  IKDSKAKSLGNLGDADTEHYAASARAFGAAFPKASMIVMSHSAPDSRAAITHTARMADKLR-------------
IND-1  VKSNSATDLGYIKEANVEQWPKTINKLKAKYSKATLIIPGHDEWKGGGHVEHTLELLNKK--------------
SPM    IKP---KELGYLGDANVKAWPDSARRL--KKFDAKIVIPGHGEWGGPEMVNKTIKVAEKAVGEMRL--------
KMH-1  VKP---EGLGNLSHAVIAEWPASAEKLIARYSNATMVVPGHGKVGDASLLEKTRQRAVEALAAKK---------
IMP-1  IKP---YGLGNLGDANIEAWPKSAKLLKSKYGKAKLVVPSHSEVGDASLLKLTLEQAVKGLNESKKPSKPSN--
SIM-1  IKP---NGLGNLSDANLEAWPGSAKKMISKYSKAKLVIPSHSEIGDASLLKLTWEQAIKGLNESKSKPPLIN--
DIM-1  VRSLDSEGLGYTGEAHIDQWSRSAQNALSRYSEAQIVIPGHGKIGDIALLKHTKSLAETASNKSIQPNANASAD
GIM-1  VRSHEWEGLGYVGDASISSWADSIKNIVSKKYPIQMVVPGHGKVGSSDILDHTIDLAESA236SNKLMQPTAEASAD
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Supplemental Fig. 5. Alignment of the class B metallo-β-lactamase family and their zinc enzymatic active center

The level of amino acid identity between groups was as low as 20% or less. As a feature of class B β-lactamases, the binding site for Zn2+ at the enzymatic active site involves three histidines (His116, His118, and His196). Based on the primary sequences, the alignment was generated using Clustal Omega [32, 33, 34] of GenomeNet at Kyoto University Bioinformatics Center (https://www.genome.jp/tools-bin/clustalw).