

Studies on the Variability of Class B (Metallo) *beta*-Lactamases

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The Class B family of *beta*-lactamases contains over 500 enzymes whose three-dimensional structures have been solved either by X-ray crystallography or nuclear magnetic resonance. We have examined the enzymes structurally related to the NDM-1 as presented in the VAST structure alignment system. For those enzymes with over 200 residues aligned with those of NDM-1, the variability of the sequence identity to NDM-1 ranges from 25% or higher, and the root mean square deviation of the structure is 1.7 Å or lower. Thus, at least 75% of the amino acid residues of NDM-1 can be changed in a single enzyme, without a significant change in the three-dimensional structure of the enzyme. This presentation shows the locations and effects for some of this variability.

For this poster, we chose the 5ZGE.pdb structure for NDM-1, derived from *Klebsiella pneumoniae*, and the 5N51.pdb structure of NDM-1, derived from *Pseudomonas aeruginosa*. According to VAST, these two have a 34 % identical amino acid sequence, a 213 amino acid overlap, and 1.40Å RMSD positional deviation.

References:
5ZGE.pdb: H Zhang G Ma Y Zhu L Zeng A Ahmad C Wang B Pang H Fang L Zhao Q Hao
Antimicrob Agents Chemother. . 2018 Oct 24;62(11):e01579-18.
5N51.pdb: Salimraj R, Hinchliffe P, Kosmopoulou M, Tyrrell JM, Brem J, van Berkel SS, Verma A, Owens RJ,
McDonough MA, Walsh TR, Schofield CJ, Spencer J, FEBS J (2019) 286 p.169-183

The VAST Structural Database: see <https://www.ncbi.nlm.nih.gov/Structure/vastplus/vastplus.cgi?uid=5ZGE>
Clustal Omega, Protein Sequence Alignment, see <https://www.ebi.ac.uk/Tools/msa/clustalo/>
Swiss PDB Viewer, see <https://spdbv.vital-it.ch/>
PDB Databases: <https://www.rcsb.org/> and <https://www.ncbi.nlm.nih.gov/Structure/index.shtml>
Blast Sequence Alignment: <https://blast.ncbi.nlm.nih.gov/BlastAlign.cgi>

Blast Sequence Comparison of NDM-1 from 5N51.pdb and 5ZGE.pdb

NW Score	Identities	Positives	Gaps
375	87/258(34%)	131/258(50%)	10/258(3%)
Query 1	GEIRPT---IGQQMETGQDRFGDLVFRQLAPNVWQHTSYLDMPGFGAVASNGLIVRDGGR	57	
Sbjct 1	SPLAHSGEPSGEYPTVNEIPVGEVRLYQIADGVWSHIATQSFQDQ- AVYPSNGLIVRDGDE	59	
Query 58	VLVVDTAWTDQTAQILNWKQEIPLPVALAVVTHAHQDKMGMDALHAAGIATYANALS	117	
Sbjct 60	+L++DTAW TA +L I+++I LPV AV TH H D++GG+D L AAG+ATYA+ +	119	
Query 118	NQLAPQEGMVAAQHSLTFAANGWVEPATAPNFGPLKVFPYGPQHTSDNITVGIDGTDIAF	177	
Sbjct 120	+LA EG HSL G A FGP+++FYPG H++DN+ V + ++ +	175	
Query 178	GGCLIKDSKAKSLGNLGDADTEHYAASARAFGAAPKASIMVMSHSAPODRAAITHTARM	237	
Sbjct 176	GGCAVHELSSTSAGNVADADLAEWPTSVRIQKHYPEAEVVPIGHGLPGGLDLLQHTANV	235	
Query 238	--ADKLR	242	
Sbjct 236	A K R	253	

Ribbon Structure of 5N5I showing Sequence Identities to 5ZGE.pdb

