Probing the thermal stability and X-ray crystal structures of select members of the Verona integron-encoded metallo-β-lactamase 2 family

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Verona integron-encoded metallo-β-lactamase (VIM) is an enzyme that confers antibiotic resistance to bacteria by hydrolyzing antibiotic drugs containing a β-lactam ring, such as penicillin. In order to understand the mechanisms of resistance conferred by bacteria expressing VIM or VIM-like proteins, structural information for these proteins must be determined. The VIM-2 sub-family comprised of 24 VIM variants were characterized using a combination of killing assays and differential scanning fluorimetry (DSF). Select variants from the VIM-2 family were used in crystallization experiments. Crystal structures for both VIM-20 and VIM-31 have been determined. In the structure of VIM-20 the mutation H229R was found to form a salt bridge which may account for the increase in thermal stability. In the structure of VIM-31 the Y201H mutation pinches a loop domain found near active site, which may account for the enhanced resistance profile of VIM-31 as well as a dramatic decrease in thermal stability. Further EPR studies of the loop domain may reveal if this change in resistance is a result of changes in the dynamic motions of the loop.