Supplementary Information

Figure S1. Superimposition of the fourteen MetRS-inhibitor complexes.

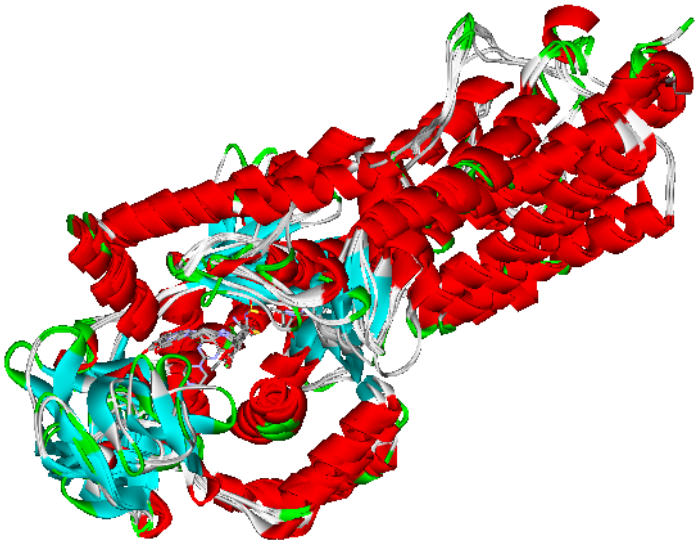

Figure S2. (**A**) All the chemical features of the structure-based comprehensive pharmacophore map; (**B**) View looking into the binding site of MetRS with a comprehensive map from the *N*-terminal domain. Screenshots were taken from Discovery Studio. Features of the pharmacophore models are color-coded as follows: Hydrogen bond acceptor (HBA), green; hydrogen bond donor (HBD), violet; hydrophobic (H), light blue; positive ionizable (pos), red; negative ionizable (neg), blue.

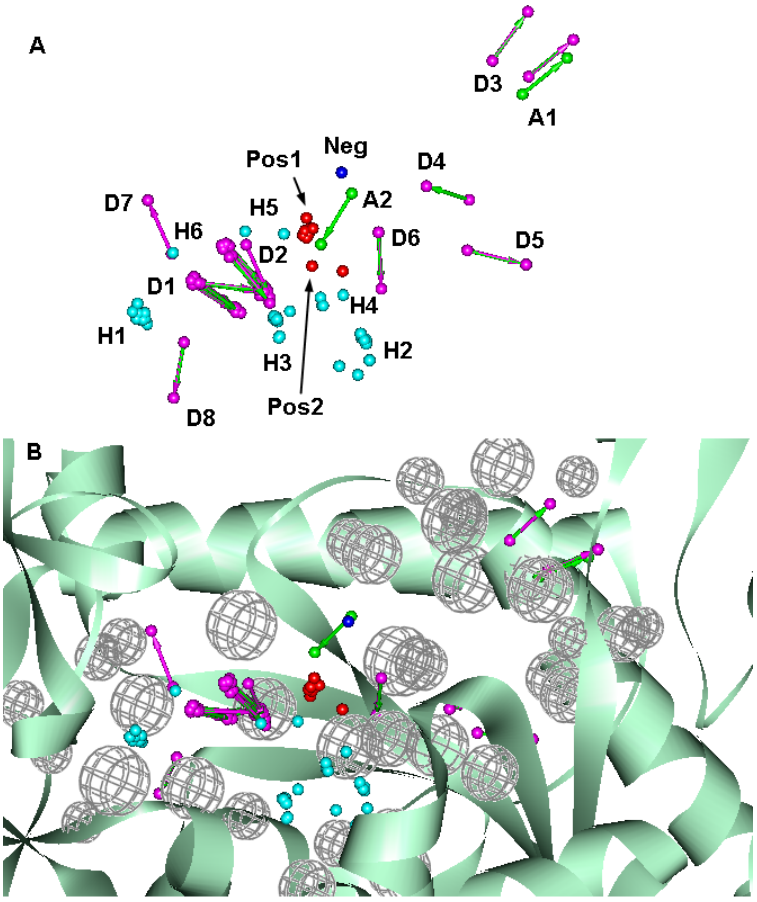

Figure S3. Sequence alignment result between the template protein (MetRS of *E. coli* with PDB ID: 1PFY) and the target protein, MetRS, of *S. aureus* and Human (*Homo sapiens*) represented as the subject. The blue and light blue color residues indicate the conserved residues between the template and target proteins.

Figure S4. (**A**) Ramachandran plot of SaMetRS homology model; (**B**) Profile-3D verify scores per residue for the SaMetRS homology model.

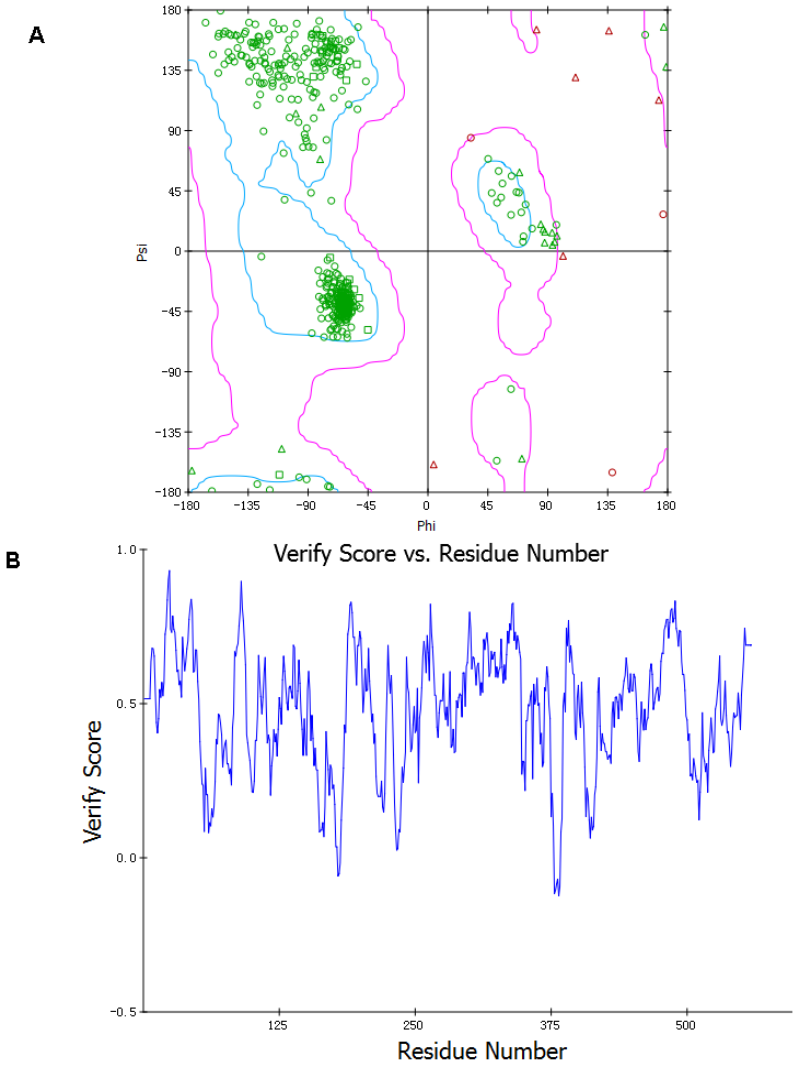

Figure S5. (**A**) Ramachandran plot of hMetRS homology model; (**B**) Profile-3D verify scores per residue for the hMetRS homology model.