



**Figure 6.1** The secondary structure of  $\beta$ -lactamase TEM-1 (PDB ID 1ERO (Ness et al. 2000)) and the location of catalytic residues and residues whose mutations are the key (ESBL; IRT), and the most common residues whose mutations are secondary.

contains from one to seven single substitutions, and the number of mutating amino acids, found in  $\beta$ -lactamases isolated from clinical strains, incorporates 32% of the residues in the primary sequence.

Protein globule of TEM-type  $\beta$ -lactamases is formed by a single chain of 288 amino acid residues. The secondary structure consists of 11  $\alpha$ -helices, five  $\beta$ -strands, and the loops of irregular structure (Figure 6.1). Structural fold of these  $\beta$ -lactamases is sandwich-like and consists of three domains: the first includes eight  $\alpha$ -helices (H2–H9), the second in the middle five-stranded (S1–S5)  $\beta$ -sheet, and the third three  $\alpha$ -helices (H1, H10, and H11) (Pimenta et al. 2014) (Figure 6.2a). The domains are structured by a network of ionic and hydrogen bonds. By SCOP classification it relates to  $\beta$ -lactamase/D-Ala carboxypeptidase family (SCOP 56602).

The structural feature of TEM-type  $\beta$ -lactamases is a compact core scaffold including the H2  $\alpha$ -helix with catalytic S70 and the S3  $\beta$ -strand located close to each other (Figure 6.2b). The rest of the protein includes regular and mobile elements of the secondary structure (loops). Although the structure of the protein globule is generally quite rigid, its mobility is maintained by the movement of the loops (Fisette et al. 2010). The  $\Omega$ -loop (residues 164–179), located in the lower part at the entrance to the active site of the enzyme, is an important conservative structural element of all serine  $\beta$ -lactamases (Fink 1985). According to the molecular dynamics data, the root mean square deviation (RMSD) of atoms in  $\beta$ -lactamase TEM-1 at 300 K is 1.3–1.4 Å; in the mutant form with substitutions of residues 238 and 240, it increases by 0.5 Å, with the highest mobility observed in the  $\Omega$ -loop (Shcherbinin et al. 2017).