



FIGURE 17.1 (A) Stereo view of human SOD1 (PDB code 1AZV 9]). The β -barrel is shown in gray, the disulfide loop (residues 50 to 61) is shown in purple, the zinc loop (residues 62 to 83) is shown in blue, and the electrostatic loop (residues 121 to 142) is shown in red. The disulfide bond between C57 of the disulfide loop and c176 of β -strand 8 is shown as yellow sticks. Cu and Zn ligands are shown as gray and blue sticks and Cu and Zn ions are represented as cyan and magenta spheres, respectively. The α -carbon positions of α -barrel and metal-binding mutants are shown as gray and green spheres, respectively. The $\alpha\beta$ -carbon positions of pathogenic SOD1 mutants for which there are mouse models (see the text) are shown as orange spheres. (B) The possible role of CCS in pathogenic SOD1 toxicity in fALS. A CCS canonical dimer (PDB code 1QUP 72)-to-noncanonical dimer (PDB code 1JK9 75) transition upon the binding of Cu(I) [74]. (C) Updated model of CCS action with selected off-pathway pathogenic SOD1 folding intermediates (see the text).