SECTION 6 POST-TRANSLATIONAL CONTROL

PROTEIN FOLDING

All proteins undergo folding to attain a more thermodynamically favorable configuration. This happens even as the polypeptide is still growing during the process of protein synthesis. Proper folding is essential for these molecules to achieve stability in an aqueous environment. Improperly folded proteins are not only unable to perform their functions but are prone to form aggregates as malpositioned hydrophobic residues seek out other hydrophobic residues from other polypeptide chains to interact with. This process of correct folding needs to happen quickly or else many of these proteins would end up as nonfunctional and would need to be degraded and replaced, a remarkable waste of the cell's energy.

In vitro, protein folding is an inefficient process, proceeding not only slowly but with many misfolded and unfolded proteins. In vivo however, this process is remarkably efficient, with an overwhelming majority of polypeptides folded correctly and very few left to form aggregates. This efficiency is in large part due to molecular chaperones, a class of molecules that have ATPase activity and bind and stabilize target proteins and facilitate proper folding. Notable among the molecular chaperones is the Hsp70 family of proteins. When bound to ATP, hydrophobic pockets within Hsp70 bind to exposed hydrophobic regions of the growing, as yet unfolded protein. When the polypeptide has lengthened to a point where intrachain hydrophobic interactions are possible, these Hsp70 are released from the polypeptide, accompanied by the hydrolysis of ATP, and the protein can assume its native conformation. This process may sometimes involve a subgroup of molecular chaperones known as chaperonins which are members of the Hsp60 family, an example of which is the *TCiP.* These chaperonins form multimeric barrel-shaped complexes where the nascent polypeptide is inserted and wherein folding is achieved.