effective drugs, leading to decreased efficacy. Additional details of the impact of Pgps on drug discovery will be described in Chapter 6.

Transporters with fewer than 12 transmembrane domains are less common, but still account for a significant portion of this class of proteins. Members of the small multidrug transporter (SMR) family such as EmrE, a multidrug transporter from *E. coli*, for example, have only four transmembrane domains and require oligomerization for functional activity.[95a,95b] The mitochondrial carrier family of transporters, which are responsible for facilitating the transfer of material into and out of the mitochondria, on the other hand typically contain six transmembrane units and do not generally require oligomerization for activity (Figure 3.40(a)).[96] At the other end of the spectrum, NADH: ubiquinone oxidoreductase (also known as respiratory complex I), one of the largest known membrane-protein complexes, contains multiple transporter proteins that contain as many as 14 transmembrane domains (Figure 3.40(b)).[97]

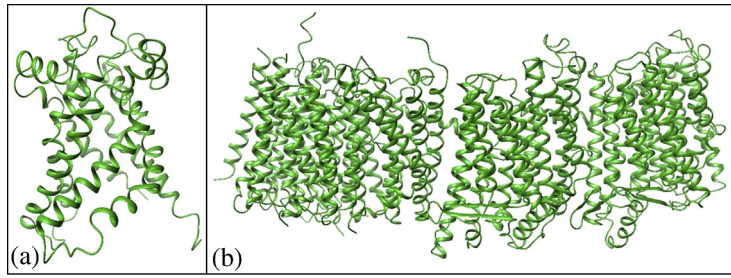

FIGURE 3.40 (a) The mitochondrial ADP/ATP carrier was one of the first mitochondrial carrier family (MCF) transporter to be characterized. It is the most abundant MCF transporter and is responsible for shuttling nucleotides across the inner mitochondrial membrane (RCSB 2C3E). (b) Respiratory complex I is the first protein system in respiratory chain that couples electron transfer between NADH and ubiquinone. It is comprised of six subunits, NuoL, NuoM, NuoN, NuoA, NuoJ, and NuoK, with a total of 55 transmembrane helices (RCSB 3RKO).

Irrespective of their size and shape, membrane transporters share the same basic function, the movement of material across cellular boundaries that would otherwise be impenetrable to the substrate. In a sense, their function is similar to that of ion channels, but there are some key differences. While ion channels form a tunnel for passage of material, membrane transporters employ a binding site that is only available on one side of a cellular membrane at a time. Conformational changes induced by the binding of a solute molecule lead to the transfer of the solute molecule from one side of the membrane to another. There are three basic types of membrane transporters, uniporter, symporters, and antiporters (Figure 3.41). As the name implies, uniporters move a single compound across a barrier. Symporters and antiporters, on the other hand, coordinate the transfer