The ATP binding cassette (ABC) is the largest protein family known and many of its members are membrane proteins (ABC transporters) active in the transport of a wide variety of substances across membranes. ABC proteins are identified by the presence of one or two cytosolically oriented ATP-binding cassettes or nucleotide-binding domains (NBD) of about 200 amino acid residues. Each NBD contains three typical motifs: the Walker A motif, GX4GK(ST), the Walker B motif and the ABC signature or C motif. Walker A and B motifs are found in other nucleotide-binding proteins, including P-, F- and V-ATPases, G proteins, adenylate kinase, myosin, phosphofructokinase and ATP/ADP exchangers. Although the overall similarity between ABC proteins can be very low, their NBDs share an average of 30-40% similarity.