S. cerevisiae has five genes encoding type 4 P-type ATPases: NEO1, DRS2, DNF1, DNF2, and DNF3. The \"P-type\" designation indicates that these integral membrane proteins form a covalent aspartyl-phosphate catalytic intermediate during ATP hydrolysis. Most P-type ATPases mediate the transport of small cations across biological membranes. However, members of the \"type 4\" subfamily are aminophospholipid translocases, rather than cation transporters, and move phospholipids from one side of a membrane bilayer to the other. Of the five S. cerevisiae type 4 P-type ATPases, only NEO1 is essential. Although the four other genes appear to have substantial functional overlap, they are distinct in their localization, specificity, and cofactor association.Dnf3p localizes to the trans-Golgi network and it is proposed that phospholipid translocation in Golgi vessicles helps create aminophospholipid asymmetry in membranes en route to the cell surface. Although it may contribute to other Golgi-related processes as well, intracellular protein transportis the only process in which Dnf3p has a demonstrated role. Dnf3p is associated with the non-catalytic subunit Ynr048Wp, and is specific for phosphatidylcholine translocation.The P-type ATPase superfamily is evolutionarily conserved, but the type 4 subfamily is found only in eukaryotes. Fourteen type 4 P-type ATPases have been characterized in humans, including the DRS2 homolog, ATP8A1and the DNF1/DNF2 homolog ATP8B1. Mutations in ATP8B1 result in progressive familial intrahepatic cholestasis, benign recurrent intrahepatic cholestasis, and intrahepatic cholestasis of pregnancy.