STV1 is one of two yeast genes encoding isoforms of the a subunit of the yeast V-ATPase V0 domain. Vacuolar-ATPasesare ATP-dependent proton pumps that acidify intracellular vacuolar compartments. Vacuolar acidification is important for many cellular processes, including endocytosis, targeting of newly synthesized lysosomal enzymes, and other molecular targeting processes. The V-ATPase consists of two separable domains. The V1 domain has eight known subunits, is peripherally associated with the vacuolar membrane, and catalyzes ATP hydrolysis. The V0 domain is an integral membrane structure of five subunits, and transports protons across the membrane. The structure, function, and assembly of V-ATPases are reviewed in references 5, 3, 6 and 7. Deletion of STV1 has little effect on cell growth, but deletion of both STV1 and VPH1, which encodes the second a subunit isoform, causes a more severe growth defect at neutral pH or in the presence of excess calcium. Overproduction of Stv1p partially complements a defect in vacuolar acidification in the vph1 null mutant. Stv1p and Vph1p show different localization patterns in indirect immunofluorescence assays, suggesting that they may be equivalent subunits for V-ATPases located on different organelles.Stv1p and Vph1p are 55% identical and proteins similar to Vph1p have also been identified in rat, mouse, C. elegans and humans. Mutations in the isoforms of human V-ATPase most similar to Vph1p, a3 and a4, result in osteopetrosis and distal renal tubular acidosis, respectively.