APA1 and APA2 encode diadenosine 5',5'''-P1,P4-tetraphosphatephosphorylases, which catabolize bistetraphosphates. The APA1 gene product also exhibits ADP sulfurylase activity. Ap4A phosphorylases catalyze phosphorolysis of dinucleoside oligophosphates, always cleaving the substrates' alpha,beta-anhydride bond and introducing Pi into the beta-position of the corresponding NDP formed. The enzymatic reaction is dependent on the presence of divalent metal ions; Mn2+ or Mg2+ sustain the greatest rates of reaction. Mn2+, Mg2+, and Ca2+ sustain phosphorolysis by both Apa1p and Apa2p, whereas Co2+ and Cd2+ stimulate only Apa2p activity. Several bistetraphosphatesare substrates of the two enzymes, but Apa2p shows a preference for A-containing substrates. The two enzymes catalyze adenosine 5'-phosphosulfate phosphorolysis or an exchange reaction between Pi and the beta-phosphate of any nucleoside diphosphate. They can also produce Ap4A at the expense of ATP and ADP. APA1 and APA2 are paralogs that arose from the whole genome duplication, and share 60% amino acid sequence identity. Disruption of either APA1 or APA2 shows that neither gene is essential for viability. The apa1 apa2 double mutant exhibits increased concentrations of all bistetraphosphates. Overexpression of APA1 decreases the intracellular glutathione content.