Paf1p is a nuclear RNA polymerase II-associated factor important for cell growth and required for full expression of a subset of cell cycle-regulated genes. Yeast contains at least two complex forms of RNA polymerase II, one including the SRBpsand a second biochemically distinct form defined by the presence of Paf1p and Cdc73p. The Cdc73p-Paf1p-Pol II-containing complexalso includes Ctr9p, Rtf1p, Leo1p, Gal11p, Ccr4p, Hpr1p, and the general initiation factors TFIIB and TFIIF, but lacks Tbp1p, TFIIH, and transcription elongation factor TFIIS, as well as the SRBps. It appears to function during elongation in conjunction with Spt4p-Spt5p and Spt16p-Pob3p. The human homolog of yeast Paf1p is hPaf1, a pancreatic differentiation 2gene that has been shown to be associated with tumorigenesis. The Paf1p complex acts in the same pathway as the Pkc1p-Slt2p MAP kinase cascade and is required for full expression of many cell wall biosynthetic genes. The complex is also required for the interaction of Rad6p and COMPASS with RNA polymerase II and for monoubiquitination of histone H2B at promoters. Further, the Paf1p complex is required for histone H3 methylation at lysines 4 and 79, thereby linking transcriptional elongation to chromatin methylation. Disruption of PAF1 leads to pleiotropic phenotypic traits, including slow growth, temperature sensitivity, and abnormal cell morphology, as well as decreased induction of the galactose-regulated genes, and greatly increased induction of MAK16. Deletion leads to elevated recombination between direct repeats, a defective Paf1p complex, and a block in transcription, which is relieved by removal of Leo1p or Rtf1p. Loss of Paf1p is lethal in combination with loss of Swi4p or Swi6p, and overexpression of either Swi4p or Mbp1p suppresses some paf1 phenotypes.