MET28, a member of the basic leucine zipper DNA binding factor family, encodes a transcription factor that participates in the regulation of sulfur metabolism. Transcriptional activation of the MET gene network, which includes MET28, requires at least five positive trans-acting factors: Cbf1p, Met4p, Met28p, Met31p, and Met32p. Of these five factors, Met4p is the only one endowed with transcription activation function, while the other four act by promoting the recruitment of Met4p to the DNA.Cbf1p, Met4p, and Met28p form a heteromeric complex that binds to the 5'-TCACGTG-3' motif found in the 5' upstream regions of the structural and regulatory genes of the sulfur network. The leucine zippers of Met4p and Met28p, along with the basic helix-loop-helix domain of Met28p, provide the protein surfaces mediating these interactions. Within the complex, Met4p is responsible for transcriptional activation, and Cbf1p is required for DNA recognition and binding. Met28p regulates the formation of the complex, and functions by stimulating the DNA-binding activity of Cbf1p. Both Met4p and Met28p bind to DNA only in the presence of Cbf1p, and the presence of Cbf1p and Met4p stimulates the binding of Met28p to DNA.As for the structural genes involved in sulfur amino acid metabolism, the transcription of MET28 is repressed by increases in the intracellular concentration of S-adenosylmethionine, the end product of the sulfur amino acid biosynthesis pathway. Transcription of MET28 also strictly depends on Met4p, which is recruited to the promoter region of MET28 through its association with Met28p and either Met31p or Met32p in high molecular weight complexes. Both Met31p and Met32p bind to the 5'-AAACTGTGG-3' sequence, which is present at position -145 upstream of MET28. Met28p may be required to stabilize the interaction established between Met4p and both Met31p and Met32p, but it is not essential for such protein-protein interactions. Taken together, the dual functions of Met28p and the mechanism underlying the regulation of MET28 reveal the existence of a positive regulatory loop within the sulfur network. This loop is expected to increase dynamically the response of the sulfur network when the intracellular concentration of AdoMet is low.