A nuclease-hypersensitive element of the human c-myc promoter interacts with a transcription initiation factor

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Transcription of the human c-myc oncogene is elaborately regulated, but the relevant molecular mechanisms are not yet understood. To begin to define elements and enzyme systems responsible for c-myc transcription in vitro, we partially purified a transcription factor essential for efficient and accurate in vitro initiation from the principal myc promoter, P2. DNA mobility shift assays located the factor binding domain at -142 to -115 with respect to the P1 promoter. This region contains pur/pyr sequences (predominantly purines in one strand), nuclease-hypersensitive sites (U. Siebenlist, L. Henninghausen, J. Battey, and P. Leder, Cell 37:381-391, 1984; C. Boles and M. Hogan, Biochemistry 26:367-376, 1987), and a triple-helix-forming element (M. Cooney, G. Czernuszewicz, E. Postel, S. Flint, and M. Hogan, Science 241:456-459, 1988). Methylation interference mapping established that the factor, termed PuF, directly contacts the repeated palindromic sequence GGGTGGG of the -142/-115 element. The interaction of PuF with this cis-acting element is necessary for P2 transcription in vitro, for (i) deletion of this 5' region from the myc promoter greatly reduced transcription efficiency and (ii) a synthetic duplex oligonucleotide corresponding to the -142/-115 sequence completely repressed c-myc transcription in the presence of the partially purified factor. These observations lend support to the hypothesis that pur/pyr sequences perform important biological roles in the regulation of c-myc gene expression, most likely by serving as transcription factor binding sites.
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