The role of cytokines in the regulation of connective tissue metabolism has been increasingly emphasized by elucidation of their specific effects using recombinant gene products. Recent studies have demonstrated that tumor necrosis factor-α (TNF-α) decreases α1 (I) collagen gene expression in cultured human dermal fibroblasts. The purpose of this study was to analyze transcriptional control of the α1 (I) collagen gene by TNF-α by means of DNA mediated transfection experiments using recombinant plasmids in which the promoter region of the human α1 (I) collagen had been fused to the chloramphenicol acetyltransferase (CAT) gene, in human dermal fibroblasts. Human dermal fibroblast monolayer cultures were preincubated for 24 hours with recombinant TNF-α ranging from 1-100 ng/ml. Cells were transfected with 20 µg of the chimeric collagen CAT gene by the calcium phosphate technique. pBLCAT (thymidine kinase promoter fused to the CAT gene) was used as the control. We measured the levels of CAT activity 48 hours after transfection. Approximately 5-fold decreased levels of CAT activity were observed in fibroblasts treated with 1 ng/ml of TNF-α, when 2300 bp of the α1 (I) collagen promoter gene fused to the CAT gene was transfected. Similar results were also obtained in the fibroblasts, when both 800 and 330 bp of the α1 (I) collagen promoter fused to the CAT gene were transfected. On the other hand, the levels of CAT activity were unaltered in fibroblasts transfected with the control gene. Our data show that the expression of chimeric collagen CAT gene is strongly inhibited by TNF-α in human dermal fibroblasts, suggesting that a common mechanism inhibits both transfected and endogenous α1 (I) collagen promoters. It is also suggested that TNF-α reduces α1 (I) collagen transcription through at least up to 330 bp upstream of the α1 (I) collagen promoter. Work is in progress to analyze regions further downstream to determine which elements are responsible for decreased transcription with TNF-α.