Role of AP-1/RE-1 Binding Site in Transcriptional Regulation of MMP-2 in Skeletal Muscle Atrophy

+1,2Liu, X; 1Manzano, ... is significantly higher in F8 mice than in F8-del mice at 2 and 4 days after Achilles tendon transection (*, P<0.05).

RESULTS:

Activity of MMP-2 promoter in F8 mice increased within the first week after surgery (Fig. 1). Other candidate transcription factors tested did not bind differentially. This data suggests that Fra-2 and YB-1 may play an important role in MMP-2 transcriptional regulation by binding to AP-1/RE-1 binding site in MMP-2 promoter.

DISCUSSION:

The MMP-2 promoter has been the subject of detailed study in a variety of cultured cells, and there are widely varying MMP-2 promoter sequence requirements for transcription in different cell types. Initial reports described MMP-2 as an AP-1-independent gene because it lacked the canonical AP-1 binding site which is located at approximately −70 bp in the proximal promoter of MMP-1, 3, 7, 9, 10, 12, and 13 [3]. Recent functional studies, however, have demonstrated that binding of Fra-1-JunB and Fos-JunB heterodimers binding to a non-canonical AP-1 site located at −1392 bp relative to the start site of translation, which is essential for hypoxia-induced MMP-2 expression in cardiac fibroblasts [4]. The transcription factors YB-1, AP-2 and p53 bind to a regulatory site designated RE-1 which is located in the 5’ regulatory region of the MMP-2 promoter at −1332 bp. Binding of YB-1, AP-2 and p53 to the RE-1 site is important in cell type specific transcription of MMP-2 in glomerular mesangial cells [5] and tumor cells [6].

In our study, we demonstrated that this AP-1/RE-1 binding site is critical for MMP-2 transcriptional regulation in skeletal muscle atrophy. Transcription factors of Fra-2 and YB-1 may play a role in MMP-2 transcriptional regulation by binding to this region in atrophic muscle. This novel information will significantly improve our understanding of in vivo MMP-2 transcriptional regulation in muscle atrophy.

REFERENCES:


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