

**O-0103****IL-1 $\beta$ /TGF- $\beta$ 1 up-regulation and hypoxia induced in immobilization are related to the molecular mechanisms governing muscle contracture**

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**【Purpose】**

This investigation was conducted to determine the molecular mechanism underlying muscle contracture in immobilized rat soleus muscle.

**【Methods】**

Wistar rats were divided randomly into immobilization groups (n = 25) and control groups (n = 25). In the immobilization group, both ankle joints were fixed in full plantar flexion with plaster casts for 1, 2, 4, 8, and 12 weeks. The right soleus muscle was immunostained for CD-11b, which is a macrophage marker,  $\alpha$ -SMA, which is a myofibroblast marker, and type I and III collagen. Additionally, the left soleus muscle was used to detect the mRNA expression of HIF-1 $\alpha$ , which is a hypoxic marker, IL-1 $\beta$ , TGF- $\beta$ 1,  $\alpha$ -SMA, and type I and III collagen by RT-PCR.

**【Results】**

The levels of CD-11b and  $\alpha$ -SMA protein, IL-1 $\beta$  and TGF- $\beta$ 1 mRNA, and type I and III collagen protein and mRNA were significantly higher in the immobilization group than in the controls at each time point. HIF-1 $\alpha$  mRNA levels were significantly higher in the immobilization group than in the controls at 4 weeks. Moreover, HIF-1 $\alpha$ ,  $\alpha$ -SMA, and type I collagen levels were significantly higher at 4, 8, and 12 weeks than at 1 and 2 weeks in the immobilization group.

**【Discussion】**

In the early stages of immobilization (1 to 2 weeks after immobilization), the up-regulation of IL-1 $\beta$ /TGF- $\beta$ 1 via macrophages may activate fibroblasts and promote their differentiation into myofibroblasts, and that may be associated with the over-expression of type I and III collagen. Additionally, the soleus muscle became hypoxic after 4 weeks of immobilization. Thus, hypoxia accelerates fibrosis and these alterations may influence the progression of muscle contracture in the later stages of immobilization (4, 8, and 12 weeks after immobilization).