Disuse leads to severe muscle atrophy and a slow-to-fast myofiber-type transition. PGC-1α (Peroxisome proliferator-activated receptor γ coactivator 1α) is documented to play an important role in muscle atrophy and slow-twitch myofiber determination. Transcription of atrophy-related Atrogin-1 by FoxO3 can be reduced by PGC-1α. While Smad3 augments FoxO3-induced Atrogin-1 and MuRF1 promoter activity. So PGC-1α, as a transcription co-activator, may regulate hindlimb unloading (HU)-induced myofiber-type transition and muscle atrophy through Smad3. Our results showed that transgenic PGC-1α mice resisted HU-induced muscle loss, atrophy-related genes expression, and slow-to-fast myofiber.type transition. Furthermore, over-expression of PGC-1α resisted the increase in pSmad3 during muscle atrophy *in vivo* and *in vitro*. And, PGC-1α over-expression inhibited the expression of atrogenes via suppressing the phosphorylation of Smad3 *in vitro*. Thus, PGC-1α is effective in regulating myofiber-type transition during HU, and it alleviates skeletal muscle atrophy partially through suppressing the activation of Smad3.

PGC-1α overexpression alleviates HU-induced myofiber-type transition and may attenuate muscle atrophy partially via suppressing pSmad3.