

TGF beta family members function in uterine healthy and fibrotic smooth muscle cells

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Uterine leiomyomas are the most common benign tumors of fertile women and the most common indication for hysterectomy. Despite the high prevalence, significant health problems, and huge economical impact on the healthcare system, relatively little is understood about the etiology and pathophysiology of uterine leiomyoma (1). Consequently, medical treatments are still limited (2). The role of the growth factors as ultimate mediators of the steroids hormone is evident in the modulation of the cell proliferation and the morphological cells appearance (3).

Activin-A and myostatin are growth factors belonging to TGF- β super family expressed and acting in myometrial (4,5) and leiomyoma cells (6)

We aimed to explore the functions of activin and myostatin in human myometrial and leiomyoma cells. First we tested both Smad and non-Smad signaling pathways by western blot. We found that activin-A and myostatin can activate only Smad signaling pathway in both myometrial and leiomyoma cells. Next we explored the effect on cell proliferation and on fibrotic phenotype.

We found that activin-A and myostatin are able to suppress primary myometrial cell proliferation but they cannot alter the proliferation of leiomyoma cells. In the next step, we found that activin-A can significantly increase fibronectin expression in leiomyoma cells. Those above results suggest that activin-A and myostatin may express antiproliferative and/or fibrotic effects depending on the cell types by activating Smad signaling pathway.

References

- [1] Islam et al. (2013) *Fertil & Steril*, S0015-0282-13 00408-1 [Epub].
- [2] Islam et al. (2013) *JCE&M* 98: 921-934.
- [3] Ciarmela et al. (2011) *Human Reproduction Update* 17: 772-790.
- [4] Ciarmela et al. (2008) *Endocrinology* 149: 2506-2516.
- [5] Ciarmela et al. (2009) *Endocrinology* 150: 906-914.
- [6] Ciarmela et al (2011) *JCE&M* 96: 755-765.