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Molecular mechanisms of progesterone and selective progesterone receptor modulator action in uterine leiomyomas

Introduction

Uterine leiomyomas (ULs) are the most common benign tumors of the female genital tract mainly affecting women in reproductive age. Due to clinical symptoms like lower abdominal pain, excessive menstrual bleeding and anemia, they are the most common indication for hysterectomy worldwide. ULs may cause impaired embryo implantation, recurrent pregnancy loss or infertility. ULs growth is dependent on the ovarian steroid hormones, progesterone and estradiol. Progesterone through its receptors can regulate the proliferation, apoptosis and accumulation of the extracellular matrix. However, data on the pathogenesis of these tumors in the available medical literature are still obscure, which cause a lack of effective and non-invasive medical treatment. At present, among the most promising and effective drugs for ULs are the selective progesterone receptor modulator, such as ulipristal acetate (UA) reduces the clinical symptoms associated with pain and metrorrhagia, but also shrinks significantly the tumor volume. The pathogenesis and precise mechanisms of progesterone and UA action in these tumors are not fully understood and require further analysis.

Objective

This laboratory-based study investigated the molecular mechanisms underlying the action of UA, as well as its distinct effects from the progesterone-induced activation of the signaling cascades involved in uterine leiomyomas in the deposition and growth of extracellular matrix. Among other aims, the mechanisms that explain the therapeutic effects of ulipristal acetate in the control of uterine leiomyomas growth were additionally investigated.

Materials and methods

This study analyzed n=250 ULs tissues. Samples were obtained immediately after surgery from untreated women (n=100) and from women treated with ulipristal acetate before the surgery. Pre-operative therapy with ulipristal acetate lasted 3 months at a dose of 5 mg/day. The control group was normal myometrium (n=100). In addition, experiments were performed on primary ULs cell cultures (n=30) and on ULs (n=30) and normal myometrium explants.