ULIPRISTAL ACETATE REDUCE ENDOMETRIAL STROMAL CELLS MIGRATION INDUCE BY 17B-ESTRADIOL AND PROGESTERONE

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Ulipristal acetate (UPA) is a selective progesterone receptor modulator (SPRM); due to it progesterone agonist and antagonist effects in the myometrium and endometrium respectively. Novel studies support the efficacy and safety profile of UPA on long-term medical management of symptomatic myomas. In fact UPA inhibits proliferation and stimulates apoptosis of leiomyoma cells without affecting normal myometrial cells. However, UPA administration is associated with a set of endometrial called PRM-associated endometrial changes (PAECs). Nonetheless, histological and clinical studies conclude that endometrium changes are reversible with the interruption of UPA therapy.

Materials/Patients and methods: This is an *in vitro* study involving the collection of proliferative phase biopsies of woman younger than 45 years old (n = 8). We isolate endometrial stromal cells (ESC) based on adhesion protocol. ESC were treated with UPA, progesterone (P4) and 17β-estradiol (E2) alone or in combination. Cell migration, immunofluorescence and western-blot assays were performed.

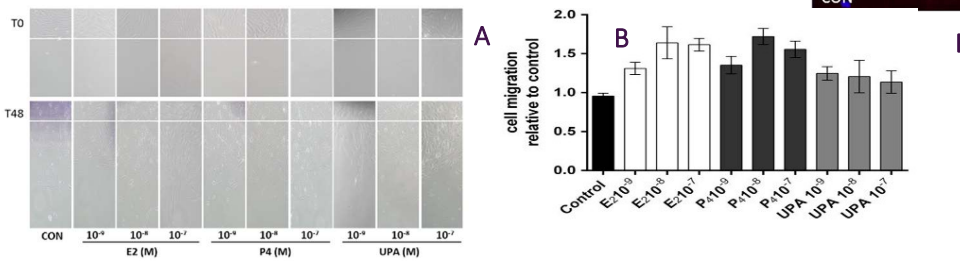

Fig. 1 Concentration-dependence cell migration. ESCs were treated 17β-Estradiol (E2), Progesterone (P4) and Uripristal acetate (UPA) at different concentrations. A) Representative photography at 0 hr and 48 hr. B) Cell migration quantification was measure with image j NHI software and expressed as Media± SD.

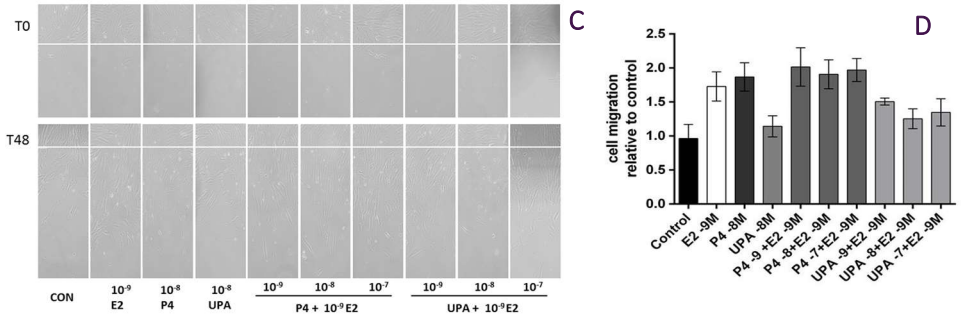

Fig. 2 Cell migration. ESCs were treated E2, P4, UPA and P4 or UPA + E2 at different concentrations. C) Representative photography at 0 hr and 48 hr. D) Cell migration quantification was measure with image j NHI software and expressed as Media± SD.

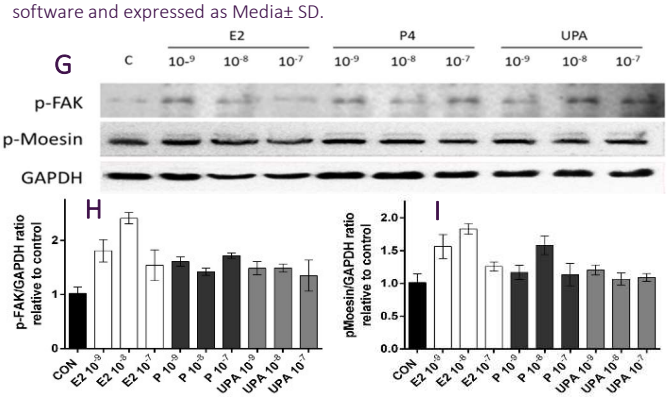

Fig. 4 Western blot. G) Representative blot of p-FAK, p-Moesin and GAPDH. H) Optical densitometry of p-FAK/GAPDH. I) Optical densitometry of p-Moesin/GAPDH. All graph are expresed as Media±SD.

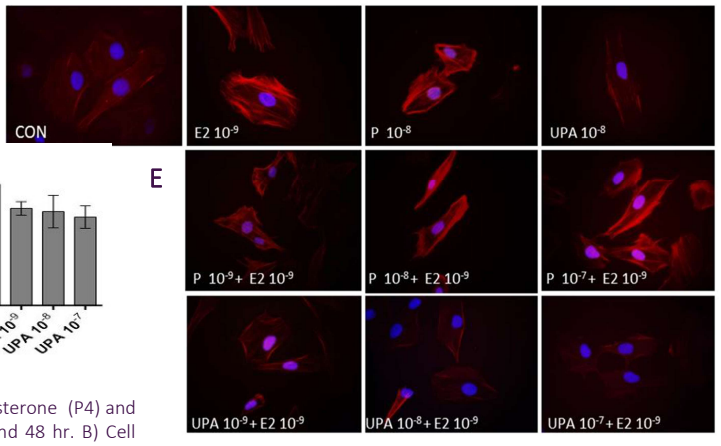

Fig. 3 Immunofluorescence of ESCs. E) Cells were treated with E2, P4, UPA and P4 or UPA + E2. then ESCs were stained with texas red phalloidin for actin cytoskeleton and DAPI for nuclei. F) Pixel intensity were quantified in 10 cells per condition using the NIH Image j software and the membrane/cytoplasmic ratio was plotted as Media±SD.

Results: UPA did not stimulate ESC migration and did not induce phosphorylation of MOESIN, FAK. MOESIN (Membrane-organizing Extesion Spike protein) functions as a cross-linker between plasma membrane and the actin cytoskeleton. FAK (Focal Adhesion Kinase) is a non-receptor tyrosine kinase that regulates the formation of focal adhesion complexes, which provide anchoring sites for cell attachment to the extracellular matrix. Accordingly, we show that UPA does not induce the rearrangement of actin filaments at the leading edge. On the other hand, UPA in presence of E2 or P4 decrease the stimulatory effect observed by the hormones separately, driving to the reduction of actin cytoskeleton rearrangement and cell migration.

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