SL-01 Ca^{2+} SENSITIZATION IN MYOMETRIAL SMOOTH MUSCLE CONTRACTION

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We used a timed-pregnant rat model to track changes in myometrial contractility during pregnancy and labor and to correlate these changes with upstream signaling events. Although contraction amplitudes increased at 16 and 20 days of pregnancy, contraction incidence and area under the force curve were inhibited, consistent with the myometrial quiescence of pregnancy. The Ca(2+) sensitivity of contraction was decreased at 20 days of pregnancy and this was partially reversed in labor. The protein content of h-caldesmon (h-CaD) was increased in pregnancy. A 40-fold increase in the signal from a phospho-CaD antibody specific for phosphorylation at an ERK1/2 site occurred during labor. ERK1/2 activation increased significantly at the onset of labor. Myosin light chain phosphorylation (LC20-P) increased significantly in labor compared with the nonpregnant state. Thus we conclude that the increase in CaD protein content during pregnancy may contribute to a suppression of the contractility of pregnant myometrium. Conversely, CaD phosphorylation, through an ERK1/2-mediated signaling pathway, as well as an increase in basal LC20-P, is suggested to contribute to the reversal of inhibition and promote contraction of the uterus during labor. The next study tested the hypothesis that ERK activation is an essential step in the onset of labor in a rat model of preterm labor. Rats treated with RU-486 displayed an increased in vitro uterine contractility. During RU-486-induced preterm labor ERK phosphorylation levels increased. Chronic treatment with U-0126 inhibited the RU-486-induced contraction and ERK phosphorylation.

Key Words: Caldesmon, Preterm labor, Myosin light chain phosphorylation, RU-486, ERK