Co-ordinating contraction in the pregnant uterus

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Uterine contractions require Ca^{2+} influx through voltage-gated Ca^{2+} channels, raising the critical question as to events mediating the depolarization necessary for opening these channels. In gut, Interstitial cells of Cajal (ICC) play a key role in pacemaking. We investigated the possibility that ICC-like cells underpin uterine contractions. ICC were stained with vimentin and smooth muscle (SM) cells localized with SM actin in uteri from 20 women undergoing caesarean delivery. Uteri from 23 pregnant mice were also studied. Contractions were recorded simultaneously with membrane potential, using intracellular microelectrodes. Ionic currents were recorded via conventional patch clamp, the characterized cells were then subjected to single cell PCR. In human tissue, ICC occupied 1.3±0.3% of SM bundles, but occupied 2.6±0.4% of the space between bundles (p=0.01). Ca^{2+}-sensitive K^+ channels were rare in ICC (maximum current 58±10pA) (facilitating excitability), but abundant in SM cells (904±163pA) (facilitating quiescence). This was confirmed using single-cell PCR. In mouse uterus, ICC staining was absent from longitudinal (LSM) layer, was present in circular (CSM) layer and abundant between the two layers. Vimentin-staining co-localized with c-Kit staining. LSM cells had membrane potentials of -68±1mV and were quiescent, while CSM had membrane potentials of -55±1mV (p=0.008) and had spontaneous contractions. The c-Kit antagonist imatinib did not abolish spontaneous activity in CSM but it blocked the spread of activity, generated in CSM, to LSM. We conclude that ICC are not responsible for generating contractions in uterus but may be involved in propagation of activity. Human uterus consists of an intricate network of thin bundles of SMC. Efficient communication between bundles is critical for coordinated organ contraction. Targeting uterine ICC could have therapeutic possibilities.