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Heightened uterine mTOR signaling induces preterm delivery in mice

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Abstract

High incidence of preterm birth caused by maternal ageing is currently one of the major clinical problems in reproductive medicine. The relationship between chronic uterine inflammation and preterm labor has been suggested, but its pathophysiology remains to be elucidated. We examined here the mechanism of senescence-induced prematurity by using uterine specific p53 deleted mice as a novel model of preterm delivery which is accompanied by uterine senescence. Using mutant mice, mimicking aspects of human preterm birth, we showed that uterine decidual senescence early in pregnancy via heightened mammalian target of rapamycin complex 1 (mTORC1) signaling is a significant contributor of preterm birth and fetal death, and that these adverse phenotypes are rescued by a low dose of rapamycin, an inhibitor of mTORC1 signaling. This role of mTORC1 signaling in determining the timing of birth in mice may help us better understand the mechanism of the timing of birth in humans and develop new and improved strategies to combat the global problem of preterm birth.