Impact of conditional deletion of fibulin-5 on development of pelvic organ prolapse in mice

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Compromise of elastic fiber integrity in connective tissues of the pelvic floor is most likely acquired through aging, childbirth-associated injury, and genetic susceptibility. Mouse models of pelvic organ prolapse have systemic deficiencies in proteins that affect elastogenesis. Prolapse, however, does not occur until several months after birth. To determine the impact of compromised levels of fibulin-5 (Fbln5) during adulthood on pelvic organ support after vaginal delivery, tissue-specific conditional knockout (cKO) mice were generated using the smooth muscle \textsuperscript{2}actin promoter-driven reverse tetracycline transactivator and tetracycline responsive element-Cre recombinase. Fbln5 was decreased significantly in the vagina of cKO mice compared with controls in which perineal body length (PBL) and bulge increased significantly after delivery but declined to baseline values within 6-8 weeks. Although overt prolapse did not occur in cKO animals, these transient increases in PBL (and bulge) did not recover to baseline. This lack of recovery from parturition was associated with increased MMP-9 and nondetectable levels of Fbn5 in the postpartum vagina. Taken together, conditional knock-down of Fbln5 in stromal cells of the pelvic floor results in animals that undergo normal elastogenesis during development but lose Fbn5 as adults. The results indicate that vaginal fibulin-5 during development is crucial for baseline pelvic organ support and is also important for protection and recovery from parturition-induced prolapse.