EGR1 knock-out uterus displays abnormal hyperproliferation and suppressed immune response after estrogen treatment

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Early Growth Response protein 1 (EGR1) is a transiently and rapidly activated transcription factor involved in various cellular processes such as differentiation, mitogenesis and neuronal activity. It has been reported that EGR1 knock-out mice exhibit an implantation failure, and an impaired hormone signaling in uterine epithelium. Because EGR1 is an immediate early response transcription factor, and estrogen is a major hormone at the very beginning of the period between ovulation and implantation, we scrutinized how the absence of EGR1 alters the early transcriptional response of the uterine tissue upon estrogen exposure. When comparing EGR1 knock-out mice and wild type mice at each elapsed time, we could only identify a small number of differentially expressed genes. In contrast, estrogen-responsive gene sets of each group were significantly different, and the difference was increased more over time. EGR1 knock-out mice exhibited an enhanced proliferation and suppressed immune response compared with EGR1 wild type mice, and these phenotypes have a significant overlap with the estrogen response of the pre-puberty uterus. We also found that the enrichment of poly-ADP ribosylation target genes among estrogen-induced genes, which was transient in wild-type mice, was prolonged and increased in the EGR1 knock-out mice.