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Indian Hedgehog as a Progesterone-Responsive Factor Mediating Epithelial–Mesenchymal Interactions in the Mouse Uterus

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Abstract

Genes encoding components of the hedgehog signaling pathway are dynamically expressed in the mouse uterus preparing for implantation. *Indian hedgehog* (*Ihh*), *patched* (*Ptc*), and *Gli3* are expressed at low levels in the endometrial epithelium on day 1 of pregnancy. Transcription of *Ihh* increases dramatically in the luminal epithelium and glands from day 3, reaching very high levels on day 4. Over the same period, *Ptc*, *Gli1*, *Gli2*, and *noggin* are strongly upregulated in the underlying mesenchymal stroma. Transcription of *Ihh* in ovariectomized mice is induced by progesterone but not by estrogen. Lower induction of *Ihh*, *Ptc*, and *Hoxa10* is seen in response to progesterone in the uteri of *Pgr*^{−/−} mutant mice lacking progesterone nuclear steroid receptor. This finding suggests that the hormone may regulate *Ihh* through both nuclear receptor-dependent and -independent pathways. We describe a method for culturing uterine explants in the absence of epithelium. Under these conditions, recombinant N-SHH protein promotes the proliferation of mesenchyme cells and the expression of *noggin*. We propose that IHH made by the epithelium normally functions as a paracrine growth factor for stromal cells during the early stages of pregnancy.


Keywords

Indian hedgehog; patched; gli; noggin; uterus; progesterone; pregnancy



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