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Disruption of Testis Cords by Cyclopamine or Forskolin Reveals Independent Cellular Pathways in Testis Organogenesis

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Abstract

Most studies to date indicate that the formation of testis cords is critical for proper Sertoli cell differentiation, inhibition of germ cell meiosis, and regulation of Leydig cell differentiation. However, the connections between these events are poorly understood. The objective of this study was to dissect the molecular and cellular relationships between these events in testis formation. We took advantage of the different effects of two hedgehog signaling inhibitors, cyclopamine and forskolin, on gonad explant cultures. Both hedgehog inhibitors phenocopied the disruptive effect of *Dhh*$^{-/-}$ on formation of testis cords without influencing Sertoli cell differentiation. However, they exhibited different effects on other cellular events during testis development. Treatment with cyclopamine did not affect inhibition of germ cell meiosis and mesonephric cell migration but caused defects in Leydig cell differentiation. In contrast, forskolin treatment induced germ cell meiosis, inhibited mesonephric cell migration, and had no effect on Leydig cell differentiation. By carefully contrasting the different effects of these two hedgehog inhibitors, we demonstrate that, although formation of testis cords and development of other cell types normally take place in a tightly regulated sequence, each of these events can occur independent of the others.

Keywords

desert hedgehog; *Patched1*; Sertoli; Leydig; germ cells; meiosis; PKA

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