Developmental Stage and Time Dictate the Fate of Wnt/beta-Catenin-Responsive Stem Cells in the Mammary Gland.

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Public Summary:
During pregnancy, the mammary gland undergoes extensive growth and remodeling, suggesting the presence of stem cells, yet their origin, identity, and behavior in the intact tissue remain unknown. Using an Axin2CreERT2 allele, we labeled and traced Wnt/β-catenin-responsive cells throughout mammary gland development. This reveals a switch in Wnt/β-catenin signaling around birth and shows that, depending on the age of mice, Axin2+ cells contribute differently to the different epithelial cell lineages of the mammary gland. Moreover, an important difference exists between the developmental potential tested in transplantation assays and that displayed by the same cell population in situ. Finally, Axin2+ cells in the adult build milk-producing structures over multiple pregnancies, demonstrating the existence of a Wnt/β-catenin-responsive adult stem cell. Our study uncovers dynamic changes in Wnt/β-catenin signaling in the mammary epithelium and offers insights into the developmental fate of mammary gland stem and progenitor cells.

Scientific Abstract:
The mammary epithelium undergoes extensive growth and remodeling during pregnancy, suggesting a role for stem cells. Yet their origin, identity, and behavior in the intact tissue remain unknown. Using an Axin2(CreERT2) allele, we labeled and traced Wnt/beta-catenin-responsive cells throughout mammary gland development. This reveals a switch in Wnt/beta-catenin signaling around birth and shows that, depending on the developmental stage, Axin2(+) cells contribute differently to basal and luminal epithelial cell lineages of the mammary epithelium. Moreover, an important difference exists between the developmental potential tested in transplantation assays and that displayed by the same cell population in situ. Finally, Axin2(+) cells in the adult build alveolar structures during multiple pregnancies, demonstrating the existence of a Wnt/beta-catenin-responsive adult stem cell. Our study uncovers dynamic changes in Wnt/beta-catenin signaling in the mammary epithelium and offers insights into the developmental fate of mammary gland stem and progenitor cells.