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Mechanisms of Early Pregnancy-Mediated Breast Cancer Protection

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Pregnancy at early, but not late age, has a substantial and life-long protective effect againstbreast cancer. The expected overall increase in breast cancer incidence in the coming yearsdemands the development of strategies to mimic early-age pregnancy-mediated protection.Recently, converging results on molecular and cellular mechanisms underlying the protectiveeffect of early-age pregnancy were reported in rodent models and women. In particular, earlyparity induces differentiation and downregulates the Wnt/Notch signaling ratio and the in vitro and in vivo proliferation potential of basal stem/progenitor cells in mice. These early parityinducedchanges of gene expression and dynamics of mammary stem/progenitor cells werecaused primarily by a decrease in the proportion of hormone-sensitive and Wnt4-secretingluminal epithelial cells. Furthermore, they were of life-long duration and absent upon latepregnancy. Similar findings were made in humans confirming that decreased hormone- andWnt4-mediated Wnt signaling in mammary stem/progenitor cells plays a key role in theprotective effect of early-age pregnancy against breast cancer. However, in addition to decreased Wnt signaling, increased cellular quiescence induced by TGFβ signaling might also be involved in the breast cancer-protective effect of early pregnancy in humans. These congruent andcomplementary findings in mouse and human mammary epithelial stem/progenitor cells provide promising initial targets for translational studies directed toward the development ofpharmacological breast cancer prevention strategies.

Biography

Fabienne Meier-Abt completed her MD at Yale University School of Medicine, New Haven, USA, and her PhD in experimental oncology at the Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland. She is now working clinically in the Department of Internal Medicine at the University Hospital of Basel, Switzerland. Her scientific interests continue to be focused on translational cancer and stem cell research.

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