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SEROTONIN REGULATION OF MAMMARY GLAND INVOLUTION AND ITS ROLE IN BREAST CANCER PROGRESSION EBOOKS 2019



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Waves of milk production, as seen during lactation, transition into milk stasis and involution of the mammary gland, upon weaning. This transition is under homeostatic control by systemic and local regulators. Significant knowledge has been gathered regarding involvement of systemic hormones in regulating involution. However, the local factors remain largely unstudied. Previously our lab discovered serotonin as a local regulator of mammary gland milk synthesis and involution. Here we explore the influence of serotonin in regulating involution associated events, especially tight junction disruption. We show that human mammary epithelial cells have an elaborate serotonin system including serotonin reuptake transporter and multiple serotonin receptors. Through this system, serotonin employs a complex signaling mechanism to mediate fine biphasic regulation of mammary epithelial tight junctions. This is important to meet the dynamic demands associated with milk stasis and involution. Further breast cancer cells show a profound change in this serotonin system (biosynthesis and receptor expression pattern). This results in a homeostatic imbalance between the suppressive vs pro-oncogenic activities of serotonin. The breast cancer cells become resistant to involution-associated suppressive actions of serotonin and enhance the pro-oncogenic effects of serotonin (through increased serotonin synthesis). Such action of serotonin support the finding that involution is associated with increased risk of breast cancer and promotes formation of aggressive tumors.

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