SESSION 9

Prevention of Breast Cancer

S29. A New Paradigm in Breast Cancer Prevention

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Early pregnancy imprints in the breast permanent genomic changes or a "signature" that reduces the susceptibility of this organ to cancer (Russo, J. et al. Endocrine Related Cancer 4:7, 1997; Russo, J. et al., Clin. Ca. Res. 11:931s, 2005). The breast attains its maximum development during pregnancy and lactation. After menopause the breast regresses in both nulliparous and parous women containing lobular structures designated Lob.1. The Lob. 1 found in the breast of nulliparous women and of parous women with breast cancer never went through the process of differentiation, retaining a high concentration of epithelial cells that are targets for carcinogens and therefore susceptible to undergo neoplastic transformation, these cell are called Stem cells 1, whereas Lob. 1 structures found in the breast of early parous postmenopausal women free of mammary pathology, on the other hand, are composed of an epithelial cell population that is refractory to transformation called Stem cells 2. The degree of differentiation acquired through early pregnancy has changed the "genomic signature" that differentiates the Lob. 1 from the early parous women from that of the nulliparous women by shifting the Stem cell 1 to a Stem cell 2, making this the postulated mechanism of protection conferred by early full term pregnancy. The identification of a putative breast stem cell (Stem cell 1) has reached in the last decade a significant impulse and several markers also reported for other tissues have been found in the mammary epithelial cells of both rodents and humans. Although still more work needs to be done in order to better understand the role of the Stem cell 2 and its interaction with the genes that confer it a specific signature, collectively, the data obtained thus far is supporting that the lifetime protective effect of an early pregnancy against breast cancer is due to the complete differentiation of the mammary gland, which results in the replacement of the Stem cell 1 that is a component of the nulliparous breast epithelium with a new stem cell, called Stem cell 2, which is characterized by a specific genomic signature. The pattern of gene expression of the stem cell 2 could potentially be used as useful intermediate end points for evaluating the degree of mammary gland differentiation and for evaluating preventive agents like human chorionic gonadotropin.

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