



Methods and Models in Mammary Gland Biology and Breast Cancer Research

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Abstract

The collection on Methods and Models in Mammary Gland Biology and Breast Cancer Research showcases recent advances in tools and models that enhance our understanding of mammary gland development and breast cancer. This collection includes sixteen articles, collectively addressing approaches to investigate key aspects of mammary gland biology and tumorigenesis, including hormonal signaling, tissue architecture, tumor microenvironment, and species-specific mammary development. The issue highlights innovations such as optimized progesterone receptor reporters, improved menopause models, and 3D-printed mammary epithelial structures. It also features advancements in organoid-based studies, in situ labeling of epithelial proliferation in large animals, preclinical models for breast cancer prevention, and high-resolution imaging techniques. Methodologies for studying macrophage-cancer cell interactions and lysosomal function are provided as step-by-step protocols. Additionally, review articles provide insights into diverse mammalian organoid systems, rat mammary tumor models, and strategies for modeling breast cancer metastasis. Together, these contributions advance mammary gland research by refining experimental approaches, expanding model diversity, and fostering translational applications in breast cancer.

Main Text

The articles in the Methods and models in mammary gland biology and breast cancer special issue collectively explore the diverse aspects of mammary gland biology, emphasizing the use of advanced tools and models to investigate e.g. hormonal signaling, tumor dynamics, and mammary tissue development across species. The collection comprises of nine original research articles, three reviews, two protocol articles, and two meeting reports.

In particular, this special issue highlights the advances in tools for studying normal mammary gland development and breast cancer. In their original research article, Aarts and colleagues describe luciferase and fluorescent reporters

based on optimized Progesterone Responsive Element (PRE) for studying progesterone receptor (PR) signaling in human breast epithelial cells [1]. PR signaling is essential for mammary physiology and breast cancer [3, 15], however tools for sensitive measuring and imaging of PR activity have been lacking. Hence, the authors have generated constructs enabling quantitative analysis of PR activity in cell populations or at the level of single cells and which further enhance the understanding of PR signaling and target gene induction.

Fluctuating hormone levels in perimenopause and near complete loss of circulating estrogen and progesterone in menopause lead to complex reorganization and regression of the mammary gland, while rendering it vulnerable to endocrine-disrupting chemicals. To study these critical windows of susceptibility for breast cancer, mouse ovariectomy model has been traditionally used though it comes short in recapitulating the gradual transition typical for human natural menopause. Therefore, Sacki and colleagues employed a chemically-induced menopause model using 4-vinylcyclohexene dioxide (VCD) [10] and characterized the VCD-induced morphological changes to mammary epithelium as well as sensitivity to hormones [19]. Upon demonstrating that VCD treatment provides mammary gland

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