Abstract

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Evaluation of Current and Emerging Pre-Clinical Models in Breast Cancer

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ABSTRACT

Introduction: Breast cancer represents a significant global disease burden, with an urgent need for more effective therapies. Despite advances in research, high attrition rates in drug development highlight limitations in current pre-clinical models. Many widely used models fail to accurately replicate in situ tumours, particularly in terms of cellular heterogeneity and tumour microenvironment (TME) interactions. This literature review evaluates current and emerging pre-clinical models in breast cancer research.

Methods: A narrative literature review was conducted, examining key studies, reviews, and landmark papers on in vitro and in vivo breast cancer models. Focus was placed on model design, biological relevance, and translational limitations, including comparisons between traditional and emerging technologies.

Results: Two-dimensional (2D) cell lines remain widely used due to their accessibility and cost-efficiency but are limited by their inability to model tumour heterogeneity. Three-dimensional (3D) models, including spheroids and organoids, improve representation of cell–cell and cell–TME interactions, though they present challenges related to clonal selection and technical complexity. Tumour-on-a-chip (ToC) systems offer enhanced physiological relevance through microfluidic integration of multiple human cell types but are resource-intensive. In vivo models, such as xenografts, genetically engineered mouse models (GEMMs), and humanised mice, enable whole-organism study but are limited by immune system discrepancies, cost, and ethical considerations. The choice between cell lines and primary tissues further influences model validity.

Conclusions: No single pre-clinical model fully captures the complexity of breast cancer. Careful model selection and continued efforts toward standardisation are essential to improve translational relevance and reduce drug development attrition.

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