

3D tissue models for the study of the effects of low-dose irradiation

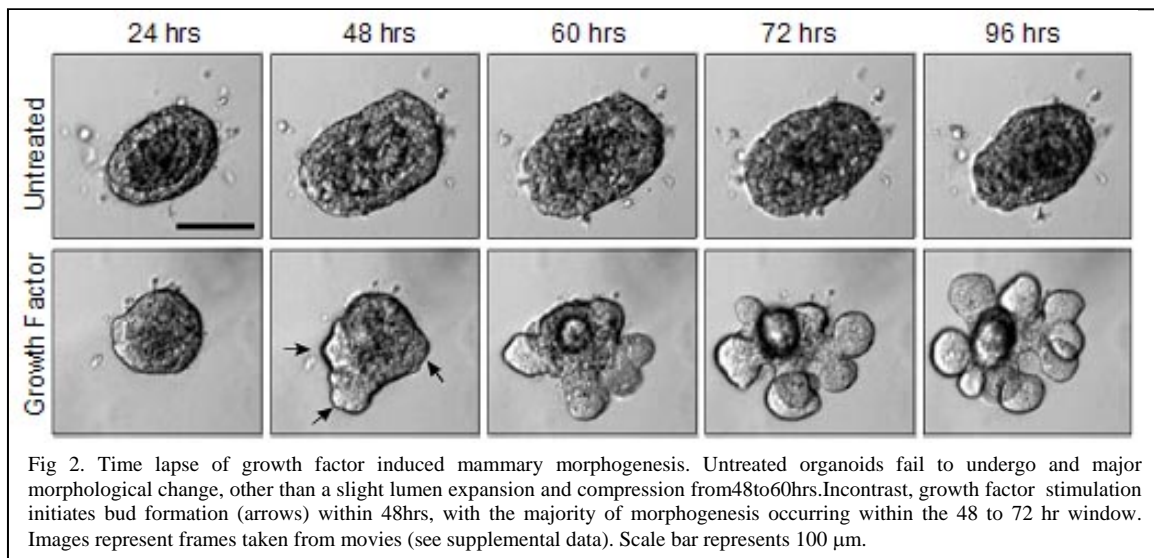
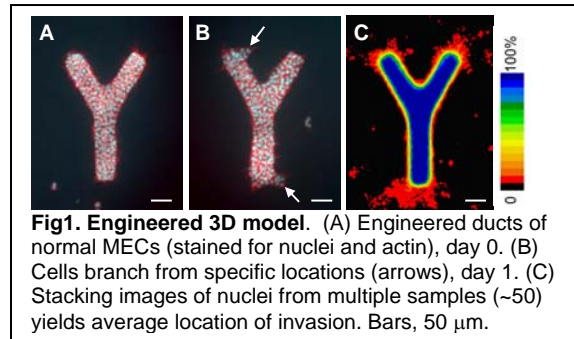
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We have previously developed three-dimensional tissue models to study the effects of irradiation of the ability of mammary epithelial cells to form polarized acinar structures and demonstrated that irradiation induced heritable epigenetic perturbations in cell polarity and multicellular organization (1). More recently we have developed a number of more quantitative models of important developmental processes in the mammary gland which can be applied to the study of the interactions between low-dose irradiation, the tissue microenvironment and tissue structure and function.

We have used a micropatterning technique to control the initial three dimensional structure of mammary epithelial tubules (Fig 1A) which can then be stimulated and monitored for changes in the patterns of invasion and branching morphogenesis caused by the stimulus (Fig 1B). The ability to analyze large numbers of similarly sized structures in parallel (by generating stacks of images from multiple samples, Fig 1C) has allowed us to perform robust statistical analyses.

A second model allows us to follow the pattern of branching morphogenesis which takes place in explanted mouse mammary gland organoids cultured on top of matrigel. These structures, composed of all mammary gland cell types, can be induced to reorganize and branch upon stimulation with appropriate growth factors (Fig 2). Many organoids can be analyzed in parallel using time-lapse microscopy. This will facilitate our analysis of the effects of low-dose irradiation heterotypic cell-cell interactions and tissue morphogenesis.

We believe that these models will be exquisitely sensitive to detect the potentially subtle effects of low dose irradiation.



1. Park, C.C., Henshall-Powell, R.L., Erickson, A.C., Talhouk, R., Parvin, B., Bissell, M.J., and Barcellos-Hoff, M.H. 2003. Ionizing radiation induces heritable disruption of epithelial cell interactions. *Proc Natl Acad Sci U S A* 100:10728-10733.