
MCF10DCIS.com Xenograft Model of Human Comedo Ductal Carcinoma *In Situ*

Ductal carcinoma *in situ* (DCIS) is becoming increasingly common, accounting for 25%–30% of newly diagnosed cases of breast cancer (1). The comedo type represents about 40% of the cases and carries the worst prognosis (2). The subsequent incidence of recurrence in patients presenting previously with comedo DCIS was 20% compared with 5% for noncomedo DCIS in one study (3). National Surgical Adjuvant Breast and Bowel Project Protocol B-17 reported a 40% incidence of ipsilateral breast cancer after lumpectomy of comedo DCIS and found that comedo necrosis is the only important predictor for recurrence after lumpectomy (4).

A recurring theme in the National Institutes of Health Breast Cancer Progress Review Group report (<http://osp.nci.nih.gov/PRGReports/BPRGReport/bprgtableofcontents.htm>) is the need for xenograft models of early human breast disease such as DCIS. The MCF10 model includes normal immortalized breast epithelial cells (MCF10A), premalignant variants (MCF10AT lines) that form simple ducts in xenografts, and malignant variants (MCF10CA lines) (5–7).

The clonal cell line MCF10DCIS.com was cloned from a cell culture initiated from a xenograft lesion obtained after two successive trocar passages of a lesion formed by premalignant MCF10AT cells. Injection of MCF10DCIS.com within 22 passages resulted in rapidly growing lesions that are predominantly comedo DCIS. The tumor mass is composed of tightly packed tubular structures, many with central necrosis (Fig. 1). Silver staining reveals distinct intact basement membranes surrounding each ductular structure and emphasizes the necrotic centers

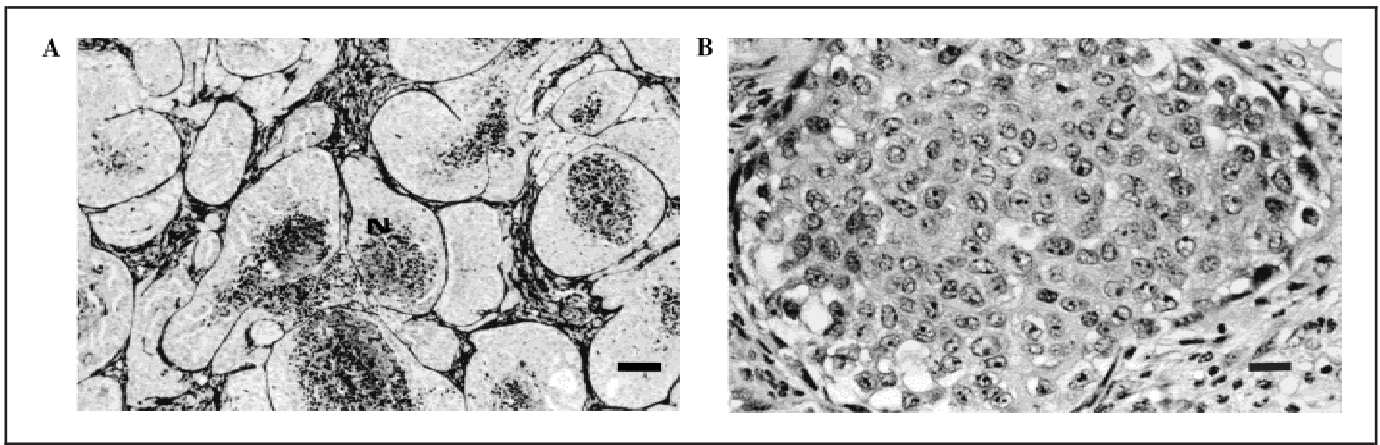


Fig. 1. Histologic appearance of MCF10DCIS.com xenografts in severe combined immunodeficient mice. **A)** Silver stain demonstrating basement membrane surrounding duct and comedo necrosis (N) within ducts in a day 36 xenograft of passage 17 MCF10DCIS.com (scale bar = 80 μ m). **B)** Day 22 xenograft of passage 22 MCF10DCIS.com (hematoxylin-eosin; scale bar = 20 μ m).

(Fig. 1, A). The central necrosis is coagulative and often infiltrated with neutrophils. Mitotic figures are frequent and epithelial cells have moderate amounts of foamy cytoplasm (Fig. 1, B). The nuclei are large and vesicular with large nucleoli. In some areas, the cytoplasm is clear and the cell boundaries are well defined. A distinct myoepithelial layer exists along the basement membrane. A desmoplastic response is evident around some ducts. Although early (3-week) lesions are predominantly DCIS, invasive areas develop and may account for half of the older (9-week) lesions. Further evidence of the progressive potential of the line is that late-passage cells (passage 37) have a more extensive invasive component.

These results are reproducible with both the early-passage MCF10DCIS.com and the late-passage progeny. Lesions that are composed predominantly of DCIS have been obtained in all lesions formed in mice in four independent trials (two/two lesions from passage 12; six/six from passage 17; six/six from passage 18; and two/two from passage 22). Similarly, late-passage cells formed mixed lesions with major invasive components in three independent experiments.

In summary, we have obtained a hu-

man cell line that forms DCIS when xenografted into immunodeficient mice. This property should render it very useful for the testing of chemopreventive agents, for the screening of cancer-causing agents, and for genetic analyses. The fact that this cell line is a member of the MCF10 panel of cell lines, derived from a single patient, representing sequential stages of progression as shown by xenograft lesion formed, makes it all the more valuable for the analysis of genetic progression in human breast disease.

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