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Environmental exposures that increase breast cancer risk typically occur decades prior to disease onset, reinforcing the concept that breast cancers evolve from long-lived premalignant clones. The biological description of these premalignant clones is incomplete, hindering efforts to improve breast cancer chemoprevention strategies. To create an experimental framework for isolating and targeting premalignant breast disease, Li and colleagues (in a study beginning on page 173) drew inspiration from classical mouse models of multistage skin carcinogenesis. By combining chemical carcinogenesis with an inducible transgenic mouse model of breast cancer, mammary carcinogenesis was resolved into discrete initiation and progression stages. Mechanistically, carcinogen-induced HRas<sup>Q61L</sup> mutations mark the clonal link between long-lived, subclinical mammary lesions and subsequent transgene-driven mammary cancers. The cover image shows a carmine-stained whole-mount of a mammary gland from a carcinogen-exposed mouse. The gland, harvested after two weeks of transgene-driven activation of the Wnt pathway, harbors a focal ductal lesion progressing toward overt mammary cancer amid a background of diffuse Wnt-driven hyperplasia. Variations on this multistage modeling strategy may help identify and validate novel cellular and molecular targets for breast cancer chemoprevention.