The phenotypic spectrum of basal-like breast cancers: a critical appraisal.

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There are 2 well-recognized cell populations lining the mammary duct system: the epithelial cells lining the lumen and the myoepithelial cells surrounding them. The mammary stem cell, a putative third cell type, has not yet been well characterized. It is not established whether the putative stem cell expresses the full complement, a subset, or none of the markers of normal epithelial and/or myoepithelial cells. However, it is likely that they would have distinctive markers of their own; whether these are retained or lost in their neoplastic progeny is unknown. All 3 cell types may theoretically undergo malignant transformation. Until recently, however, nearly all attention has been focused on carcinomas of epithelial derivation/differentiation. The advent of oligonucleotide and cDNA microarrays has facilitated gene expression profiling of breast cancers, revealing molecular subclasses that may be prognostically relevant. One such subclass, the basal-like breast carcinomas, has been found in numerous independent datasets to be associated with a comparatively worse overall and disease-free survival. These cancers show expression of molecules characteristic of the normal myoepithelial cell, such as basal cytokeratins, and reduced expression of estrogen receptor-related and Erb-B2-related genes and proteins. The classifier genes that formed the basis for the delineation of basal-like carcinomas were derived from datasets that were composed predominantly of ductal type cancers. Therefore, the clinical significance of a basal-like gene expression or immunohistochemical profile in the other breast cancer subtypes is presently unknown. Herein, we evaluate in detail the current state of knowledge on the pathologic features of breast carcinomas classified as basal-like by immunohistochemical and/or gene expression profiling criteria, with an emphasis on their full phenotypic spectrum and also previously underemphasized areas of heterogeneity and ambiguity where present. There seems to be a phenotypic and biologic spectrum of basal-like or myoepithelial-type carcinomas, just as there is a wide range among tumors of luminal epithelial derivation/differentiation. It is critical to promote lucid morphologic definitions of the molecular subtypes, if this information is intended for use in targeted therapies and patient management.