The recent evidence that tumors already possess the potential to metastasize or have already done so when the primary tumor is removed has been interpreted as being incompatible with the current multistep carcinogenesis model (1). However, the model could still be true even if the molecular signatures for metastasis, independently proposed by van de Vijver et al. (2), Pomeroy et al. (3), and Singh et al. (4), are confirmed by larger studies. The multistep carcinogenesis model proposes that tumors start with benign growth and then develop the invasive and metastatic phenotype through the accumulation of somatic mutations. These mutations could occur at very early stages, long before the tumor is actually diagnosed with early detection methods such as mammography. Atypical crypt foci, the very first sign of carcinogenesis in the colon, are estimated to have already undergone thousands of mutations (5). Detecting tumors early does not necessarily mean that they are detected before they have completed most of the steps on the way to metastasis.

It is now well established that a critical step in tumor development is the acquisition of the ability to stimulate angiogenesis in the tumor to provide oxygen and nutrients (6). Blood vessels also provide the major route for tumor cell dissemination. The process of angiogenesis relies on many of the same mechanisms used for cell migration. The switch to the angiogenic phenotype occurs long before the tumor becomes clinically overt. Most of the multistep carcinogenesis process, thus, could already have occurred when the tumor is detected, consistent with the recent microarray data.

In addition to the need for a molecular signature for treatment-related decisions, the emerging microarray data support the need for prevention strategies that target the angiogenic switch in specific high-risk populations (7).

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REFERENCES


NOTES

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