very little about how microenvironmental signals and cross-talk can rapidly change the phenotypes of cancer and normal cells within the tumor microenvironment and how various signaling pathways, from the cell membrane to various cellular organelles, and *vice versa*, control these complex interactions. Uncoding the plasticity of this process may be essential in explaining metastatic behavior (89).

We are just beginning to understand the cell surface and surrounding properties of malignant cells (and normal cells) that are important in explaining metastasis to secondary sites as well as the properties of target organs for metastatic colonization. This information will not be easily forthcoming, but it will be essential in the eventual development of new therapeutic approaches to limit or destroy metastases. It will also be important in reducing the symptoms of cancer and eliminating the adverse effects of cancer therapy (90).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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