THE ROAD TO METASTASIS

In some cancers, such as breast cancer and melanoma, tumor cells can leave the primary tumor site early in the tumor’s formation and colonize new tissues, where they may receive molecular signals from surrounding cells, known as the niche, that keep them dormant for long periods. Mutations in the cancer cells themselves or changes to the niche may later awake these dormant cells, enabling them to proliferate and form metastatic tumors.

1. DISSEMINATION: In some cancers, including breast cancer, cancer cells can move away from the site of the primary tumor very early in the progression of the disease, before doctors can even detect a primary tumor.

2. DORMANCY: It’s thought that most of these cells die, but a few disseminated cancer cells survive the bloodstream. These cells may already have mutations needed to colonize a new niche, such as the lungs, or they may adapt once they arrive. The cells tend to stay close to blood vessels, where they receive signals from epithelial cells directing them to stay dormant.

3. PROLIFERATION: If something changes—either in the surrounding healthy tissue, where stress or other factors can alter the dormancy signals that cancer cells receive, or in the cells themselves, which sometimes stop responding to the signals, or both—the cancer cells can begin to proliferate, forming metastatic tumors.

4. BONE MARROW: A SENTINEL
The presence of disseminated tumor cells in the bone marrow—which can be sampled from patients relatively easily—can indicate that such cells are present elsewhere in the body as well, predicting future metastasis. The bone marrow can also play a direct role in metastases at other sites by producing dormancy cues, or, conversely, by awakening resident, dormant cancer cells, which then enter the bloodstream and travel to other tissues, where they proliferate.