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Complexity and Dynamic Heterogeneity of the Process of Cancer Metastasis[1]

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Cancer metastasis – the spread of cancer from a primary tumor to distant parts of the body – is responsible for most cancer deaths. If cancer is detected early, before it has spread, it can often be treated with local therapies like surgery and radiation. If cancer is detected after it has already spread, it is much harder to treat successfully. Cancer cells may be distributed to many organs, may be present as tiny micrometastases that are hard to detect, and cancer cells can be in a dormant state that may be resistant to treatment that is directed against actively dividing cells. A better understanding of the process of metastasis thus is needed in order to improve survival from cancer. Cancer is not a static disease, but one that can undergo stepwise evolution and progression from early, treatable cancer to aggressive cancer that is harder to treat. Furthermore, cancers are made up of many cells, and there is considerable heterogeneity among the cells in a tumor. Thus, cancer is "plastic," with heterogeneity among cancer cells and changes over time. Understanding this "dynamic heterogeneity" has proven to be difficult. Input from physical sciences disciplines may help to shed light on this complex aspect of cancer biology. Here the process of cancer metastasis will be discussed, and experimental models for imaging the process described. The concept of "dynamic heterogeneity" of the metastatic process will be discussed, and some of the questions that need to be addressed for better understanding of metastasis will be outlined. An evolving dialogue between cancer biologists and physical scientists may lead to new ways of studying and understanding this lethal aspect of cancer.

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