Metastasis is a grim diagnosis, but as scientists learn more about the genetic, cellular, and molecular mechanisms that promote it, there are reasons to be hopeful.
As a medical diagnosis, metastasis instills fear. As a biological process, metastasis instills awe. A cancer cell’s journey from a primary tumor to a metastatic site is a veritable obstacle course, and it is a miracle that any cell makes it to the end. After detaching from the primary tumor, a cancer cell must invade through local tissue, squeeze into blood or lymphatic vessels, survive the harsh conditions within those vessels, squeeze out of them, and begin growing in a new tissue, the microenvironment of which is often radically different from that of the primary tumor.

It was once thought that metastases are seeded by rare, rogue tumor cells endowed with specialized features that allow them to survive this perilous journey. As scientists apply new technologies to study metastasis, models of the process are evolving. Primary tumor cells do not always act alone but can invade as a group, circulate as a group, and seed growth at a distant site as a group. Upon arrival at that distant site, tumor cells may find that the microenvironment is already primed for their growth, thanks to signals sent in advance from the primary tumor via extracellular vesicles called exosomes. Comparative genomic analyses of primary tumors and metastases, although still works in progress, have already revealed considerable intertumor and interpatient variability in the origin, route, direction, and timing of metastasis. Somewhat disappointingly, there is no evidence to date of druggable “metastasis driver genes.”

Nonetheless, there are reasons to be hopeful. Immune checkpoint inhibitors have shown encouraging results in patients with metastatic melanoma. Other immune-based therapies, such as drugs targeting neutrophils, are showing promise in preclinical models. Perhaps one day the research inspired by the awe will stamp out the fear.
Metastasis: An evolving story
Paula A. Kiberstis

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