

Unlocking the Mystery of Cancer Metastasis

Metastatic cancer, which accounts for more than 90% of cancer deaths, tends to be less responsive to treatment than primary tumors.

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Metastatic tumors, which arise when a cancer spreads from the original tissue throughout the body, tend to be less responsive to therapy than primary tumors. Metastasis is often lethal for this reason, accounting for over 90% of cancer deaths. But given that primary and metastatic tumors within the same patient have the same genetic mutations, it is not clear why metastatic tumors are more aggressive.

This is the scientific mystery that former Damon Runyon Clinical Investigator Karuna Ganesh, MD, PhD, and her colleagues have been investigating for years in her lab at Memorial Sloan Kettering Cancer Center. Recently, they had a breakthrough.

To better understand what distinguishes metastatic tumors from their primary counterparts, the team collected and analyzed three tissue samples from thirty-one patients undergoing colorectal cancer surgery: healthy colon tissue, primary tumor tissue, and metastatic tumor tissue. They found that, as colorectal cancer spreads, the cancer cells lose their identities as colon cells, regressing into a “fetal state” before differentiating into cells that resemble squamous cells, which line the internal surfaces of the body, or neuroendocrine cells, which make and release hormones. Metastatic cancer cells are like method actors, getting lost in a role.

As mentioned above, however, their genetic makeup does not change. Rather, their epigenetic plasticity increases—they can turn genes “on” and “off” more readily, depending on the demands of their environment. Excitingly, Dr. Ganesh and her team identified the specific transcription factor that becomes dysregulated in this process, allowing these abnormal patterns of gene expression. Targeting this protein, known as PROX1, may represent a means of slowing metastasis.

These findings, Dr. Ganesh writes, “suggest powerful opportunities to anticipate, intercept and target [cell] differentiation in the clinic... we are working on this!”

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