Scientists Discover Cellular Masterminds Driving Skin Cancer Growth

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Researchers focusing on a common skin cancer called squamous cell carcinoma, which affects more than 1 million people each year in the United States, have discovered specialized cells that coordinate the growth of these tumors. Damon Runyon Physician-Scientist Andrew L. Ji, MD, and colleagues at Stanford University School of Medicine have identified a population of cancer cells living at the edges of a tumor that potentially guide the metastasis of skin cancer and help it evade the body's immune system.

These specialized cells communicate with many surrounding cells in the tumor microenvironment, recruiting them to help blunt the immune response and promote cancer invasion. "Prior to our study, we did not know the identity of the cells contributing to skin cancer being invasive and dangerous," says Ji.

"Identifying these cells is important because this opens the door to designing specific therapeutic strategies to target or disable them, possibly preventing tumors from progressing or becoming metastatic," he adds. The presence of these cells may also identify more aggressive tumors that need to be monitored closely or patients needing additional treatment after surgical removal of the primary tumor.

Studying a tumor one cell at a time

The researchers analyzed squamous cell carcinomas from 10 people including cell types and gene expression profiles at the single-cell level, precisely locating each cell and its neighbors within the three-dimensional space of the growing tumor. They then compared their findings with corresponding normal skin samples taken from the same patients. The researchers found that only the carcinomas had a subpopulation of cells called tumor-specific keratinocytes, or TSKs, which expressed genes that recruit specific cell types to the cancer site to promote tumor growth.

When the researchers knocked out the ability of the TSKs to communicate, the human squamous cell carcinomas that had been transplanted into mice stopped growing. They are now investigating whether their findings extend to other cancers and whether the specific mediators of crosstalk among these cells can be used to design drugs that block this communication.

These findings have led the researchers to believe that successful cancer therapies will have to do more than just attack tumor cells. “Our research suggests that the presence of TSK cells is likely preventing an immune attack on the tumors, and they might not be limited to skin cancers. We want to be able to specifically target the most harmful aspects of skin cancers (i.e., invasion and metastasis) and we may find that the key will be to go after a different cell type other than the tumor itself,” says Ji.

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