Predictors of cancer disease progression improve patient selection for metastasis-directed therapy

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Tumor metastasis, the ability of cancer cells to migrate from their tissue of origin and colonize elsewhere in the body, accounts for over 90% of cancer deaths. When patients die from cancer, it is usually caused by distant metastases established by malignant cells that split off from the primary cancer and began growing in new settings.

Scientists from the Ludwig Center at the University of Chicago hypothesized over 15 years ago that an intermediate state of tumor spread or metastasis exists between patients with extensive metastasis and patients whose disease stays confined to one local tumor with no spread. The scientists termed this intermediate state oligometastasis or metastasis limited in number and location. They then demonstrated that some patients with oligometastasis can be cured with therapies – including surgery and radiotherapy – that are directed locally at the metastasis.

In a paper published December 10 in PLOS ONE, the Ludwig investigators led by Dr. Ralph Weichselbaum in collaboration with Dr. Yves Lussier at the University of Illinois, took their research a step further. They analyzed patients with lung metastasis who underwent surgical resection with curative intent.

What they found was that some patients were cured, some developed rapid metastasis, and some developed metastasis at a very slow rate of

progression. They then asked themselves what accounted for these radical differences in patient outcomes.

The answer: microRNAs or small molecules that suppress gene expression or protein synthesis. The investigators had pinpointed the culprit. They identified the microRNAs associated with oligometastatic progression and then found that these microRNAs differ from those associated with patients who developed widespread metastatic disease.

The microRNAs associated with oligometastasis have tumor suppressor characteristics that differ from microRNAs associated with patients who developed widespread metastatic disease. The results demonstrate a biological basis for oligometastasis and a potential for using microRNA expression to identify patients most likely to remain oligometastatic after metastasis-directed treatment.

"With these findings, we are now able to use microRNA expression to characterize oligometastasis and ultimately better select patients with tumor metastasis for curative interventions," said study author Ralph Weichselbaum, MD, director of the Ludwig Center for Metastasis Research at the University of Chicago. "Also understanding the molecular basis of tumor metastasis will allow for the targeting of specific biological processes to treat patients with more advanced tumor spread."

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