



CANCER DISCOVERY

Research Watch

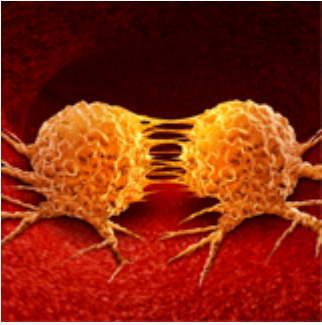
Seeds of Metastatic Colorectal Cancer Are Planted Early in Disease Progression

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Article

Info & Metrics

- **Major Finding:** Metastatic colorectal cancer may be seeded by clinically undetectable tumors.
- **Approach:** Exome sequencing and a spatial computational model were used to model tumor growth and metastasis.
- **Impact:** Mutations associated with early metastasis might help find patients who need aggressive treatment.



Although the dominant model of cancer progression is based on the assumption that the ability of cancer cells to metastasize arises in well-established primary tumors, there is some evidence that the evolution of metastatic capability may actually be an early event. Using exome-sequencing data from 118 biopsies gathered from 23 patients with metastatic colorectal cancer combined with a spatial computational model of tumor growth and a Bayesian statistical inference framework to time to metastasis, Hu and colleagues found further evidence supporting this notion, showing that metastases may be seeded by cells disseminated from primary tumors that are too small to be clinically detected—potentially years prior to diagnosis. By analyzing tumor-sequencing data (obtained in the MSK-Impact and Project GENIE studies) from 938 patients with metastatic colorectal cancer and 1,813 patients with early-stage colorectal cancer, the authors also demonstrated that combinations of mutations in specific genes (including classic colorectal cancer drivers) were far more prevalent in metastatic cases. For example, mutations in the *PTPRT* gene in combination with *APC*, *KRAS*, or *TP53* mutations were almost exclusively found in metastatic cases, suggesting their potential roles as prognostic biomarkers. Of note, *PTPRT*-mutated tumors have been reported to upregulate the STAT3 pathway and hence may be responsive to STAT3 inhibitors. Overall, these results highlight the need to develop noninvasive screening methods to assist in early cancer detection and illustrate the importance of identifying biomarkers to stratify early-stage patients at high risk of relapse for more aggressive therapy. Ultimately, it may also be possible to use such markers to guide molecularly targeted therapies directed at these specific genomic aberrations.

Hu Z, Ding J, Ma Z, Sun R, Seoane JA, Shaffer JS, et al. Quantitative evidence for early metastatic seeding in colorectal cancer. Nat Genet 2019 Jun 17 [Epub ahead of print].

Notes

Note: *Research Watch* is written by *Cancer Discovery* editorial staff. Readers are encouraged to consult the original articles for full details. For more *Research Watch*, visit *Cancer Discovery* online at <http://cancerdiscovery.aacrjournals.org/CDNews>.