

 GASTROINTESTINAL CANCER

# Establishing a family tree

A key question in the study of cancer metastasis is whether distant lesions always originate from lymph-node foci. The results of a study conducted by Kamila Naxerova and colleagues now indicate that this is not always the case for patients with colorectal cancer.

Naxerova describes their approach as “a reconstruction of tumour ‘family trees’ through the analysis of repetitive DNA regions in tumour samples collected routinely during surgery. We deployed this method to interrogate the lineage relationships between lymphatic and distant metastases.” The investigators analyzed primary tumours, and

“**Lymph-node ... and distant metastases originated from the same subclone in only 35% of the patients**”

lymph-node and distant metastases (239 samples in total) from 19 patients with colorectal cancer and liver, ovary, or omentum metastases.

Finding DNA regions that contain genetic variation is the major challenge in the study of tumour phylogenetics. Polyguanine repeats accumulate mutations at a greater rate (by several orders of magnitude) than other DNA regions. Naxerova explains: “the analysis of only a few dozen polyguanine repeats typically provides enough data for a high-confidence phylogenetic reconstruction”.

The variation pattern of these repeats indicated that, in 73% of

lymph-node metastases, the genetic divergence with distant metastases was higher than with the primary tumour and, similarly, 69% of distant metastases had greater divergence with any lymph-node metastasis than with the primary tumour — indicating a different origin. Lymph-node metastases and distant metastases originated from the same subclone in only 35% of the patients.

The investigators mainly examined metastases in the liver, which is anatomically related to the gastrointestinal tract. Thus, Naxerova and colleagues “are examining whether metastases are seeded through lymph nodes at a higher frequency in organs other than the liver.” The question now is whether these metastatic seeding patterns — common versus distinct origin — would result in different clinical outcomes.

*Diana Romero*

**ORIGINAL ARTICLE** Naxerova, K. *et al.* Origins of lymphatic and distant metastases in human colorectal cancer. *Science* **357**, 55–60 (2017)

**FURTHER READING** Naxerova, K. & Jain, R. K. Using tumour phylogenetics to identify the roots of metastasis in humans. *Nat. Rev. Clin. Oncol.* **12**, 258–272 (2015)



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