

## CANCER

# Pancreatic carcinomas metastasize at a late stage in their development

The metastatic spread of pancreatic cancer to distant organs occurs at least a decade after the time of tumor initiation, report Christine Iacobuzio-Donahue and colleagues in *Nature*.

Pancreatic cancer has a poor prognosis because, in most cases, this treatment-resistant cancer has already metastasized by the time a diagnosis is made. “It was

commonly believed that pancreatic carcinomas are so aggressive because they metastasize rapidly after the carcinoma forms,” says Iacobuzio-Donahue.

The researchers sequenced the whole genome of purified metastatic pancreatic cancer cells obtained at the autopsy of seven patients who died from this disease. For each patient, Iacobuzio-Donahue and her group identified and classified the types of somatic mutations present in the autopsy sample. They then determined whether each of these mutations was present in the patient’s primary tumor and in all other metastases from that particular patient. Most aberrations were ‘founder’ mutations, present in all the samples from a particular patient. However, additional ‘progressor’ mutations were only present in metastases.

Mathematical modeling of tumor evolution led the investigators to estimate that an average of 11.7 years passed between the initiation of the pancreatic

tumor and the generation of the parental tumor clone that would eventually give rise to metastatic cancer cells.

Acquisition of metastatic capacity took another 6.8 years and the patient’s death occurred an average of 2.7 years after that.

“The major implication is that pancreatic cancers develop slowly, similar to other cancer types,” says Iacobuzio-Donahue. “Therefore, there is actually a long window of opportunity for early detection that has not been utilized or recognized before this work.”

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**Original article** Yachida, S. *et al.* Distant metastasis occurs late during the genetic evolution of pancreatic cancer. *Nature* **467**, 1114–1117 (2010)

**Further reading** Jones, S. *et al.* Core signaling pathways in human pancreatic cancers revealed by global genomic analyses. *Science* **321**, 1801–1806 (2008) | Campbell, P.J. *et al.* The patterns and dynamics of genomic instability in metastatic pancreatic cancer. *Nature* **467**, 1109–1113 (2010)

