

First study of clonal evolution in Maxillary Sinus Carcinoma

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Knowing how tumors evolve can lead to new treatments that could help prevent cancer from recurring, according to a study published today by the Translational Genomics Research Institute (TGen) and Scottsdale Healthcare.

TGen researchers tracked several years of tumor evolution in a 47-year-old male patient with maxillary sinus [carcinoma](#) (MSC), a rare cancer of the sinus cavities beneath the cheeks that often requires surgical removal that is disfiguring. Fewer than half of MSC patients live more than 5 years after diagnosis.

"The ability to characterize clonal evolution of this [rare cancer](#) and identify its Achilles' heel can significantly impact treatment, leading to more personalized medicine," according to the study published today in the journal [PLOS ONE](#).

Clonal evolution refers to the often-rapid genetic changes that occur in [cancer cells](#), which continually mutate and, thus, frequently resist anti-cancer drug compounds intended to destroy them.

"If we can understand the genomic basis of how this cancer evolves, perhaps we can find new treatments that could help improve the longevity and quality of life for patients," said Dr. Glen Weiss, Clinical Associate Professor at TGen, and Director of Thoracic Oncology at Virginia G. Piper [Cancer Center](#) Clinical Trials at Scottsdale Healthcare, a partnership with TGen. Dr. Weiss is one of the study's senior co-

authors.

MSC represents nearly four of every five cases of paranasal sinus cancers, which grow rapidly and invade nearby tissues but also are usually slow to spread to distant sites. Patients usually die from a local [recurrence](#) of the tumor, even after [aggressive treatment](#).

"This is the first report to study the clonal population of MSC arising in longitudinal samples from the same patient," the study said. "One of the aims of this study was to closely follow [disease progression](#) and the clonally evolving [metastases](#) for molecular profiling and accumulation of data for future use in development of personalized treatment."

The patient in the study received conventional treatment, which included surgical removal of his tumors, radiation therapy and chemotherapy, and participation in a clinical trial.

Over time, however, the cancer spread to his upper right lung, lower left lung, left kidney, brain and part of his intestine. He eventually was hospitalized, received hospice care and prior to passing away gave permission to have his cancer studied after death in a rapid autopsy research program.

"Because his cancer resumed growth despite several courses of systemic chemotherapy and radiation therapy, we speculated that acquired secondary genetic changes evolved with the evolution of resistance to these therapies," said Dr. Michael Barrett, Associate Professor in TGen's Clinical Translational Research Division, and the study's other senior co-author.

Analysis of his tumors following surgeries, biopsies and autopsy revealed several genetic aberrations, including multiple copies of a region on chromosome 4q, which includes the KIT gene. KIT is an oncogene, a

gene with the potential to cause cancer, and is a potential treatment target.

The authors suggest the results provide a unique description of how the drug resistant cancer cells replicate and progress to metastatic MSC. Additional findings included the loss of the gene PKP4, which is associated with increased tumor size.

"These results show that molecular analyses of patient samples can add to the information about the tumor and help us in tracking back the progression of the disease," the authors concluded. "Identification of selected [genetic changes](#), and the biological processes they regulate arising in primary MSC tumors, will advance individualizing therapy and improve the outcome of patients with rare cancers."

"These kinds of cutting-edge studies are made possible through the collaboration of major research and clinical practices, such as the partnership between [TGen](#) and Scottsdale Healthcare," said Dr. Mark Slater, Vice President of Research at Scottsdale Healthcare.

The authors remain particularly grateful to the patient and his family for their contribution to understanding more about this type of cancer and hope this dissemination of knowledge may help others.

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More information: [dx.plos.org/10.1371/journal.pone.0045614](https://doi.org/10.1371/journal.pone.0045614)

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