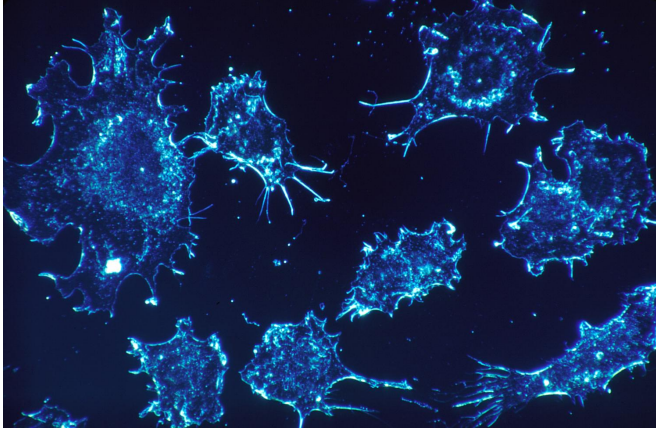


New tool predicts deadly form of rare cancer

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Two patients with mycosis fungoides (MF) can appear to have identical diseases upon first diagnosis but can have radically different outcomes. MF is an unusual cancer of the T lymphocyte that begins in the skin rather than in the lymph nodes, with the first sign often being a rash. Most patients with MF, the most common type of cutaneous T cell lymphoma (CTCL), have a very slow-growing disease and often have normal life expectancies. But a subset of patients will develop an aggressive, deadly form of the disease that can spread throughout the skin and beyond, becoming untreatable. If identified early, patients with this aggressive form of MF may be eligible for a stem cell transplant to cure the disease, but once MF progresses and becomes treatment resistant, it is nearly impossible to achieve the complete remission required for a successful stem cell transplant.

A tool to accurately determine which early-stage patients are at risk of dying from MF and which patients are likely to only require conventional therapy is desperately needed. Investigators from Brigham and Women's Hospital have found that next-generation, high-throughput sequencing of a specific gene (T-cell receptor beta or TCRB) is a

stronger predictor of which early-stage patients will develop aggressive, progressive MF than any other established factor. The team's results are published this week in *Science Translational Medicine*.

"We are excited to bring precision medicine to the management of MF patients," said senior author Thomas Kupper, MD, chair of the BWH Department of Dermatology. "While more work needs to be done, we think this approach has the potential to prospectively identify a subgroup of patients who are destined to develop aggressive, life-threatening disease, and treat them in a more aggressive fashion with the intent to better manage, and ideally cure, their cancer."

More than 80 percent of early-stage patients with MF will have a lifelong course free of disease progression. But patients with advanced forms of MF have a dismal prognosis, with [life expectancies](#) ranging from one-and-a-half to four years, even with current therapies. Kupper and colleagues founded the Cutaneous Lymphoma Clinic at Dana-Farber Cancer Institute in 1999, with one of the goals being to develop better diagnostic and prognostic tools for MF as well as other forms of CTCL. Since 2002, almost 900 patients have participated in a longitudinal study to follow their disease progression through biopsies and blood samples. In the current study, researchers sequenced T cell receptor genes from biopsied skin tissue at the site of lesions from more than 300 early-stage patients with CTCL, most of whom had MF. The team used high-throughput DNA sequencing, a technique that allowed them to sequence massive amounts of DNA at once, producing a snapshot of the TCRB genes from a large number of [cells](#) at the site of the lesion. The team could use this to measure "tumor clone frequency (TCF)" - the percentage of T cells that are clones of the mutated MF lymphoma T cells. An elevated TCF predicted the likelihood of progression and overall survival of patients with MF with high sensitivity and specificity.

"Under the microscope, benign T cell and MF T

cells are hard to distinguish," said Kupper.
"However, every T cell has a unique DNA sequence of its T cell receptor, which we can detect by high-throughput DNA sequencing. High throughput DNA sequencing and calculations of TCF allow us to make predictions that would never before have been possible. As a physician who has treated patients with this [disease](#) for decades, I am excited to be involved with work that so directly and profoundly affects the care and management of these [patients](#)."

More information: A. de Masson et al., "High-throughput sequencing of the T cell receptor ? gene identifies aggressive early-stage mycosis fungoides," *Science Translational Medicine* (2018).
[stm.sciencemag.org/lookup/doi/ ... scitranslmed.aar5894](https://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aar5894)

Provided by Brigham and Women's Hospital

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