Medical Xpress

Follicular lymphoma: A tale of two cancers

December 13 2016

Follicular lymphoma (FL), the second most common form of non-Hodgkin lymphoma, is a largely incurable disease of B cells, yet in many cases, because of its indolent nature, survival can extend to well beyond 10 years following diagnosis. Yet in a small number of cases, histological transformation - where fast-growing cells outnumber the smaller, slow-growing cells - or early progression to aggressive lymphoma occurs. The events leading to this increased and early mortality are poorly understood. In a study published in *PLOS Medicine*, Sohrab Shah and colleagues from the BC Cancer Agency in Vancouver, Canada, investigate the molecular events underlying transformation and progression and show that disparate evolutionary trajectories and mutational profiles drive these two distinct clinical endpoints.

Using whole genome sequencing, the authors analyse the genome sequence of tumours and matched normal specimens from 41 patients and classify them according to their clinical endpoints: 1) patients who presented with transformation, 2) patients who experienced tumor progression within 2.5 years after starting treatment, without evidence of transformation, 3) and those who had neither transformation nor progression up to 5 years post-diagnosis. In addition, the authors use targeted capture sequencing of known follicular lymphoma associated genes in a larger cohort of 277 patients to investigate discrete genetic events that drive transformation and early progression.

The authors show that tumors that progress early evolve in different ways than those that transform. Assessing mutations at two time points and following treatment they show that for tumours that transform, the cells or clones which constitute the majority of the aggressive tumour were extremely rare at diagnosis, if at all present. In contrast, for early progressive disease the clonal architecture remains similar from the time of diagnosis to relapse, indicating that the diagnostic tumour may already contain the properties that confer resistance to treatment. Analysis of the larger cohort pinpointed key genes and biological processes that were associated with transformation and progression.

These findings provide a basis for future research on prognostic assay development and potential strategies for monitoring and treatment of patients with FL.

More information: Robert Kridel et al, Histological Transformation and Progression in Follicular Lymphoma: A Clonal Evolution Study, *PLOS Medicine* (2016). DOI: 10.1371/journal.pmed.1002197

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