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Mayo Clinic completes first genome-wide analysis of peripheral T-cell lymphomas

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Researchers at Mayo Clinic have completed the world's first genome-wide sequencing analysis of peripheral T-cell lymphomas, unlocking the genetic secrets of this poorly understood and highly aggressive cancer of the immune system.

Andrew Feldman, M.D., a Mayo Clinic pathologist and Damon Runyon Clinical Investigator, and a team of researchers affiliated with Mayo's Center for Individualized Medicine and Mayo Clinic Cancer Center, found 13 genomic abnormalities that were seen in multiple peripheral T-cell lymphomas. Of particular interest, five of these abnormalities relate to production and behavior of the p53 protein -- often called the "guardian of the genome" because of the central role it plays in regulating cell life cycles and, therefore, suppressing cancers.

The study, entitled "Genome-wide Analysis Reveals Recurrent Structural Abnormalities of TP63 and other p53-related Genes in Peripheral T-cell Lymphomas," is scheduled for early release in the online edition of the journal *Blood* on Wednesday, Aug. 1, 2012.

"Every time I diagnose a peripheral T-cell lymphoma, I know that two out of three patients will succumb to that lymphoma," says Dr. Feldman. "That's a very unsatisfying feeling, and I hope that our research can help change those statistics."

Peripheral T-cell lymphomas account for about 12 percent of non-Hodgkin's lymphomas and carry remarkably high mortality rates. Fewer

than 35 percent of patients live five years beyond diagnosis.

New diagnostic biomarkers (chemical or genetic clues in the body's system) and treatments aimed at specific subgroups of peripheral T-cell lymphomas could lead to improved outcomes, says Dr. Feldman. Developing these, however, has been a challenge for several reasons. Lymphomas that look remarkably similar under a microscope may differ substantially in their overall prognoses and responses to treatment. Additionally, scientists and doctors have a relatively poor understanding of how peripheral T-cell lymphomas develop and proliferate.

"The most common type of T-cell lymphoma is called 'not otherwise specified.' It's basically a wastebasket diagnosis because we don't understand enough about the specific genetic abnormalities to be able to pinpoint subtypes of T-cell lymphomas that might trigger different treatments by the treating oncologist," says Dr. Feldman.

Dr. Feldman's study will be used to improve diagnostic tests and develop targeted treatments for peripheral T-cell lymphoma.

Among the key findings in the genomic abnormalities of peripheral T-cell lymphoma are:

- Thirteen recurrent chromosomal rearrangements
- Five of the 13 rearrangements involve p53-related genes, important for tumor-suppressor function
- Novel rearrangements involving the TP53 homologue and TP63, which were associated with shortened survival times
- Four interchromosomal abnormalities, including the previously known ALK and DUSP22-IRF4 translocations