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Identification of epigenetic signatures associated with T-cell Prolymphocytic Leukemia

Tcell prolymphocytic leukemia (T-PLL) is a rare disease representing ~2% of the mature lymphocytic leukemias in adults. It shows a rapid clinical course and responds poorly to chemotherapy and immunotherapy. Whole-genome and whole-exome sequencing of T-PLL cases have identified the prevalence of structural variants including inversions, translocations and copy number variations, most notably inv(14)(q11q32), t(14;14)(q11;q32) and t(X;14)(q28;q11). Also, recurrent somatic mutations were identified in numerous epigenetic genes encoding chromatin regulators. How the extent of epigenetic changes has not been investigated yet. We hypothesize that genetic and epigenetic interaction may play a key role in T-PLL pathogenesis. To systematically test this hypothesis, we mapped gene regulatory regions in T-PLL patients and healthy individuals using chromatin immunoprecipitation and sequencing (ChIP-seq) for histone H3 lysine 4 monomethylation (H3K4me1) and trimethylation (H3K4me3), as well as for H3 lysine 27 acetylation (H3K27ac) and trimethylation (H3K27me3). We identified a major loss of active enhancers (enriched with H3K27ac) in T-PLL, of which about 40% were in a poised state enriched with H3K4me1 but depleted of H3K27ac. Most importantly, we revealed a gain of super-enhancers targeting oncogenes such as TCL1A, which is known to involve in structural variation in T-PLL. Together, our analysis highlighted the roles of epigenetic alterations in the T-PLL pathogenesis.

Biography

Huihuang Yan is an associate professor in the Division of Biomedical Statistics and Informatics, Department of Health Sciences Research at Mayo Clinic. He received his PhD from the Chinese Academy of Agricultural Sciences in Genetics. As part of the Mayo Clinic Center for Individualized Medicine, his term primarily focuses on cancer genomics and epigenetics in translational research. He has published 50 peer-reviewed articles.

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