Abstract 4575: Three-gene diagnostic classifier for ALK negative ALCL

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Abstract

Anaplastic Large Cell Lymphomas (ALCL) comprise approximately 12% of all T-cell Non-Hodgkin's lymphomas (T-NHL), representing a heterogeneous group whose definition, origin and relationship with other T-NHL remains controversial. The notion that ALCL strongly express CD30, and display recurrent chromosomal translocations involving the Anaplastic Lymphoma Kinase (ALK) gene, led to recognition of two subsets, according to ALK expression. Although ALK positive ALCL can be readily diagnosed, ALK negative ALCL still lack unique genetic features and their distinction from other CD30 positive Peripheral T-Cell Lymphomas (PTCL) is not trivial. To unravel the regulatory network underlying lymphomagenesis of ALCL, and to discover new genomic classifiers for the recognition of ALK-positive and ALK-negative ALCL patients, we undertook a systematic approach of pathway discovery through a gene expression profiling meta-analysis of 309 cases, using data generated by five sets of experiments. In agreement with previous studies, unsupervised analyses were not able to distinguish ALCL from the other T-NHL categories. However, pathway discovery and prediction analyses defined a minimum set of genes useful for the stratification of ALK negative ALCL and strengthened the hypothesis that ALCL correspond to a distinctive pathological subgroup within T-NHL. Application of RT-qPCR in independent data sets of cryo-preserved and formalin-fixed paraffin embedded samples confirmed the gene expression profiling predictions and validated a simple model based on the measurement of three genes. These data suggest the possibility to translate RT-qPCR protocols to routine clinical settings as a new approach to precisely define T-NHL and to select more appropriate therapeutic protocols.

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