Blood. 2011 Jul 7;118(1):139-47. Epub 2011 Apr 12.

Translocations activating IRF4 identify a subtype of germinal center-derived B-cell lymphoma affecting predominantly children and young adults.

Salaverria I, Philipp C, Oschlies I, Kohler CW, Kreuz M, Szczepanowski M, Burkhardt B, Trautmann H, Gesk S, Andrusiewicz M, Berger H, Fey M, Harder L, Hasenclever D, Hummel M, Loeffler M, Mahn F, Martin-Guerrero I, Pellissery S, Pott C, Pfreundschuh M, Reiter A, Richter J, Rosolowski M, Schwaenen C, Stein H, Trümper L, Wessendorf S, Spang R, Küppers R, Klapper W, Siebert R;
Molecular Mechanisms in Malignant Lymphomas Network Project of the Deutsche Krebshilfe; German High-Grade Lymphoma Study Group; Berlin-Frankfurt-Münster-NHL trial group.

Source

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Abstract

The prognosis of germinal center-derived B-cell (GCB) lymphomas, including follicular lymphoma and diffuse large-B-cell lymphoma (DLBCL), strongly depends on age. Children have a more favorable outcome than adults. It is not known whether this is because of differences in host characteristics, treatment protocols, or tumor biology, including the presence of chromosomal alterations. By screening for novel IGH translocation partners in pediatric and adult lymphomas, we identified chromosomal translocations juxtaposing the IRF4 oncogene next to one of the immunoglobulin (IG) loci as a novel recurrent aberration in mature B-cell lymphoma. FISH revealed 20 of 427 lymphomas to carry an IG/IRF4-fusion. Those were predominantly GCB-type DLBCL or follicular lymphoma grade 3, shared strong expression of IRF4/MUM1 and BCL6, and lacked PRDM1/BLIMP1 expression and t(14;18)/BCL2 breaks. BCL6 aberrations were common. The gene expression profile of IG/IRF4-positive lymphomas differed from other subtypes of DLBCL. A classifier for IG/IRF4 positivity containing 27 genes allowed accurate prediction. IG/IRF4 positivity was associated with young age and a favorable outcome. Our results suggest IRF4 translocations to be primary alterations in a molecularly defined subset of GCB-derived lymphomas. The probability for this subtype of lymphoma significantly decreases with age, suggesting that diversity in tumor biology might contribute to the age-dependent differences in prognosis of lymphoma.

PMID: 21487109 [PubMed - indexed for MEDLINE]