

Detection of genomic aberrations in molecularly defined Burkitt's lymphoma by array-based, high resolution, single nucleotide polymorphism analysis.

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Source

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Abstract

BACKGROUND: Knowledge about the genetic lesions that occur in Burkitt's lymphoma, besides the pathognomonic IG-MYC translocations, is limited.

DESIGN AND METHODS: Thirty-nine molecularly-defined Burkitt's lymphomas were analyzed with high-resolution single-nucleotide polymorphism chips for genomic imbalances and uniparental disomy. Imbalances were correlated to expression profiles and selected micro-RNA analysis. Translocations affecting the MYC locus were studied by fluorescence in situ hybridization.

RESULTS: We detected 528 copy number changes, defining 29 recurrently imbalanced regions. Five hundred and eighteen regions of uniparental disomy were found, but these were rarely recurrent. Combined imbalance mapping and expression profiling revealed a strong correlation between copy number and expression. Several recurrent imbalances affected the MYC pathway: the micro-RNA-supercluster 17-92 was frequently gained and the transcription factor E2F2 was recurrently deleted. Molecular Burkitt's lymphoma lacking MYC translocations showed MYC gains. Amplifications of the polymerase iota gene were associated with increased frequency of positions scored as aberrant.

CONCLUSIONS: The present findings suggest that uniparental disomies do not play a major role in the pathogenesis of Burkitt's lymphoma, whereas some genes may contribute to the development of this lymphoma through gene dosage effects. Amplifications of the polymerase iota gene may be functionally linked with increased genomic alterations in Burkitt's lymphoma. The pattern and rarity of chromosomal changes detectable, even at the high resolution employed here, together with aberrations of genes regulating MYC activity, support the hypothesis that deregulation of the MYC pathway is the major force driving the pathogenesis of Burkitt's lymphoma, but show that this deregulation is more complex than previously known.

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