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Investigation of prognostic markers in endemic Burkitt lymphoma

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Background
Unlike many other childhood cancers, genomic abnormalities are not used in the clinical management of paediatric Burkitt lymphoma (BL) and few prognostic biomarkers have been identified. In sporadic BL gain of chromosome 7 and deletion of 13q are the only abnormalities that have been associated with an adverse prognosis in the context of a clinical trial. Gains of 13q have also been reported, including gain of the miR17HG locus, but the prognostic value in endemic BL is unknown.

Objectives
To test the prognostic value of chromosome 7 and 13q abnormalities in a clinically annotated cohort of endemic Burkitt lymphomas.

Methods
Fine-needle aspirates from 80 endemic BL patients were screened for chromosome 7 and 13 copy number abnormalities. The genomic breakpoints of the detected abnormalities were mapped using Affymetrix Oncoscan arrays and the genomic landscape investigated.

Results
Gain of chromosome 7 and deletion of 13q were identified in 2/59 (3%) and 1/58 (2%) samples, respectively. All 3 patients had an adverse outcome. Gains of 13q were detected in 5/64 (8%) samples, and 9/57 (16%) of patients had gain of the miR17HG locus. miR17HG gain is associated with a significant decrease in 12 month event-free survival (p <0.05 log rank). 7/9 patients either relapsed or died of disease. There is an increased risk of an adverse event occurring in patients with miR17HG gain during the first 6 months after diagnosis (hazard ratio 2.851; 95% confidence interval, 1.138-7.14; p=0.025). Genomic analysis of patients with chr7 and 13 abnormalities revealed a complex genome and identified recurrent abnormalities.

Conclusion
We have identified the first molecular marker of adverse outcome in endemic Burkitt lymphoma and shown that gain of the miR17HG locus infers an increased risk of an adverse event within 6 months of diagnosis.