Genome-wide analysis of cytogenetic aberrations in ETV6/RUNX1-positive childhood acute lymphoblastic leukaemia

The chromosomal translocation t(12;21) resulting in the ETV6/RUNX1 fusion gene is the most frequent structural cytogenetic abnormality among patients with childhood acute lymphoblastic leukaemia (ALL). We investigated 62 ETV6/RUNX1-positive childhood ALL patients by single nucleotide polymorphism array to explore acquired copy number alterations (CNAs) at diagnosis. The mean number of CNAs was 2·82 (range 0–14). Concordance with available G-band karyotyping and comparative genomic hybridization was 93%. Based on three major protein-protein complexes disrupted by these CNAs, patients could be categorized into four distinct subgroups, defined by different underlying biological mechanisms relevant to the aetiology of childhood ALL. When recurrent CNAs were evaluated by an oncogenetic tree analysis classifying their sequential order, the most common genetic aberrations (deletions of 6q, 9p, 13q and X, and gains of 10 and 21) seemed independent of each other. Finally, we identified the most common regions with recurrent gains and losses, which comprise microRNA clusters with known oncogenic or tumour-suppressive roles. The present study sheds further light on the genetic diversity of ETV6/RUNX1-positive childhood ALL, which may be important for understanding poor responses among this otherwise highly curable subset of ALL and lead to novel targeted treatment strategies.