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Identification of a MYCN and Wnt-related VANGL2-ITLN1 fusion gene in neuroblastoma.

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Key words: Neuroblastoma; MYCN; Wnt/β-catenin signalling pathway; Wnt/planar cell polarity (PCP) pathway; Precision Medicine; Genome Medicine; Genomic Rearrangements; Chromothripsis; RNA-seq; Genomics; fusion gene; ITLN; VANGL.

Abstract

The genomic fusion of two genes can lead to the expression of a fusion protein that can have oncogenic potential. The important contribution of such fusion genes to oncogenesis and tumour progression is being increasingly recognised. Here we report the presence of a novel VANGL2-ITLN1 fusion gene in the IMR32 neuroblastoma cell line. The fusion gene was identified by applying FusionHunter analysis to neuroblastoma cell line RNA sequencing data. This fusion results in the dramatic overexpression of a fusion transcript incorporating the full length ITLN1 coding sequence. Furthermore, the tumour expression levels of both components of the fusion gene (ITLN1 and VANGL2) are predictive of neuroblastoma patient outcome. High ITLN1 expression levels correlate with worse outcome across all neuroblastoma tumour stages and across MYCN amplification statuses. Survival probability was markedly worse for patients with both elevated MYCN and ITLN1 expression. We show that the VANGL2-ITLN1 fusion transcript can be transcriptionally upregulated upon lithium

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