

Leukaemia Section

Short Communication

t(9;14)(p24;q12) STRN3/JAK2

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Abstract

Review on t(9;14)(p24;q12), with data on clinics, and the genes involved.

Keywords

Chromosome 9; Chromosome 14; STRN3; JAK2

Clinics and pathology

Disease

Acute lymphoblastic leukemia (ALL).

Epidemiology

Only 1 case to date, a 12 year-old female patient with high-risk B-lineage ALL (Roberts et al., 2012).

Genes involved and proteins

Note

There was a IKZF1 deletion and p.Leu117fs (Frame shift) mutation.

JAK2 (janus kinase 2)

Location 9p24.1

Protein

1132 amino acids (aa); 130,7 kDa; JAK2 contains an Interaction with cytokine/interferon/growth hormone receptors region (aa 1-239), a FERM domain: (aa 37-380), a central Src homology 2 (SH2) domain (aa 401-482), and two C-terminal domains: a tyrosine kinase domain JH1 (also termed PTK or TyrKc domain (aa 545-809)), and a tyrosine kinase-like domain JH2 (also termed STYKc (aa

849-1124)). JAK Homology domains are the following: JH7 aa 25-137; JH6: aa 144-284; JH5: aa 288-309; JH4: aa 322-440; JH3: aa 451-538; JH2: aa 543-824; JH1: aa 836-1123.

JAK2 is a member of the Janus kinase (JAKs) family of non-receptor protein tyrosine kinases (JAK1, JAK2, JAK3, TYK2) .Janus kinases are protein tyrosine kinases of the non-receptor type that associates with the intracellular domains of cytokine receptors including the receptors for interleukins, interferons, growth hormone, erythropoietin, and leptin. Mediates signaling transduction. Janus kinases are constitutively bound to the cytoplasmic region of cytokine receptors. Binding of cytokines induces cytokine receptor dimerization, facilitating trans-phosphorylation of the associated JAKs and JAK/STAT signaling. Erythropoietin receptor (EPOR) and growth hormone receptor (GHR) bind JAK2 exclusively.

JAK2 is frequently mutated in myeloproliferative disorders. JAK2-V617F mutation occurs at the stem cell level and is present in hematopoietic stem cell progenitors (Strehl et al., 2006; Gangat and Tefferi, 2008; Hubbard, 2017).

STRN3 (striatin 3)

Location 14q12

Protein

797 amino acids (aa), contains caveolin-binding and calmodulin-binding regions in the N-term (aa 71-79 and 166-183 respectively), a coiled-coil domain (aa 77-136, which allow homo- and hetero-oligomerization), and 6 WD repeats (from aa 478 to aa 796; WD-repeat domain enables proteins to establish multiple protein-protein interactions).

STRN3 is a member of striatin family (STRN, STRN3, STRN4) which function as scaffold in different signal transduction pathways. STRN and STRN3 are the constituents of a multiprotein assembly called striatin-interacting phosphatase and kinase (STRIPAK). STRIPAK are regulators of cell cycle, differentiation, metabolism, immune regulation, Golgi assembly, cell polarity, cell migration, etc. STRN3 protects cells from oxidative stress. SG2NA is involved in maintaining ER homeostasis. Downregulation of SG2NA reduces the level of CCND1 (cyclin D1) and retains a population of cells in the G1 phase, and its overexpression extends G2 (Jain et al., 2017; Pandey et al., 2018).

Result of the chromosomal anomaly

Hybrid gene

Description

STRN3 exon 9 was fused to JAK2 exon 17.

Fusion protein

Description

835 amino acids. The N-term striatin domain was fused to the pseudo kinase domain and C-term Tyr kinase domain). Sequence junction: .ARAEEV_LQER....

References

Berry EM. Problem-oriented article summary. *Lancet*. 1985 Aug 24;2(8452):452

Hubbard SR. Mechanistic Insights into Regulation of JAK2 Tyrosine Kinase. *Front Endocrinol (Lausanne)*. 2017;8:361

Hubbard SR. Mechanistic Insights into Regulation of JAK2 Tyrosine Kinase. *Front Endocrinol (Lausanne)*. 2017;8:361

JAK2 (janus kinase 2). Strehl, S *Atlas Genet Cytogenet Oncol Haematol*. 2006;10(1):3-6.

JAK2 mutations in myeloproliferative neoplasms. Gangat N, Tefferi A *Atlas Genet Cytogenet Oncol Haematol*. 2009;13(8):612-617.

Pandey S, Talukdar I, Jain BP, Tanti GK, Goswami SK. GSK3beta and ERK regulate the expression of 78kDa SG2NA and ectopic modulation of its level affects phases of cell cycle *Sci Rep* 2017 Aug 8;7(1):7555

Roberts KG, Morin RD, Zhang J, Hirst M, Zhao Y, Su X, Chen SC, Payne-Turner D, Churchman ML, Harvey RC, Chen X, Kasap C, Yan C, Becksfort J, Finney RP, Teachey DT, Maude SL, Tse K, Moore R, Jones S, Mungall K, Birol I, Edmonson MN, Hu Y, Buetow KE, Chen IM, Carroll WL, Wei L, Ma J, Kleppe M, Levine RL, Garcia-Manero G, Larsen E, Shah NP, Devidas M, Reaman G, Smith M, Paugh SW, Evans WE, Grupp SA, Jeha S, Pui CH, Gerhard DS, Downing JR, Willman CL, Loh M, Hunger SP, Marra MA, Mullighan CG. Genetic alterations activating kinase and cytokine receptor signaling in high-risk acute lymphoblastic leukemia *Cancer Cell* 2012 Aug 14;22(2):153-66

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