# ABL1

ABL1 (Abelson proto-oncogene 1) is a human gene that encodes a protein known as ABL kinase. ABL1 is involved in various cellular processes, including cell growth, division, and signaling. The ABL kinase is a non-receptor tyrosine kinase, which means it can add phosphate groups to tyrosine residues on other proteins, thereby regulating their function.

One of the most well-known roles of ABL1 is its involvement in certain types of cancer, particularly chronic myeloid leukemia (CML). In CML, a genetic mutation leads to the formation of a fusion gene called BCR-ABL1, where part of the BCR gene on chromosome 22 fuses with part of the ABL1 gene on chromosome 9. This fusion gene produces an abnormal protein called BCR-ABL1 kinase, which is constitutively active and drives uncontrolled cell growth, leading to CML.

Targeted therapies known as tyrosine kinase inhibitors (TKIs), such as imatinib (Gleevec), dasatinib (Sprycel), and nilotinib (Tasigna), have been developed to specifically inhibit the activity of the BCR-ABL1 kinase. These drugs have revolutionized the treatment of CML, often leading to significant remission and improved survival rates for patients with this disease.

In addition to its role in CML, ABL1 may also play a role in other forms of cancer and in normal cellular processes such as DNA repair and cytoskeletal regulation. Research into the functions and regulation of ABL1 continues to provide insights into its significance in both health and disease.

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The Abelson (ABL) tyrosine kinase family members, ABL1 and ABL2, have been implicated in cancer cell migration, invasion, adhesion, metastasis, and chemotherapy resistance, and are upstream mediators of the oncogene c-MYC in fibroblasts and lung cancer cells. However, their role in medulloblastoma has not yet been explored. The purpose of this work was to elucidate the role of ABL1/2 in medulloblastoma LMD.

Methods: ABL1 and ABL2 mRNA expression of patient specimens was analyzed. shRNA knockdowns of ABL1/2 and pharmacologic inhibition of ABL1/2 were used for in vitro and in vivo analyses of medulloblastoma LMD. RNA sequencing of ABL1/2 genetic knockdown versus scrambled control medulloblastoma was completed.

Results: ABL1/2 mRNA is highly expressed in human medulloblastoma and pharmacologic inhibition of ABL kinases resulted in cytotoxicity. Knockdown of ABL1/2 resulted in decreased adhesion of medulloblastoma cells to the extracellular matrix protein, vitronectin (P = .0013), and significantly decreased tumor burden in a mouse model of medulloblastoma LMD with improved overall survival (P = .0044). Furthermore, both pharmacologic inhibition of ABL1/2 and ABL1/2 knockdown resulted in decreased expression of c-MYC, identifying a putative signaling pathway, and genes/pathways related to oncogenesis and neurodevelopment were differentially expressed between ABL1/2 knockdown and control medulloblastoma cells.

Conclusions: ABL1 and ABL2 have potential roles in medulloblastoma LMD upstream of c-MYC expression [1)].

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Jones JK, Zhang H, Lyne AM, Cavalli FMG, Hassen WE, Stevenson K, Kornahrens R, Yang Y, Li S, Dell S, Reitman ZJ, Herndon JE 2nd, Hoj J, Pendergast AM, Thompson EM. ABL1 and ABL2 promote

medulloblastoma leptomeningeal dissemination. Neurooncol Adv. 2023 Aug 7;5(1):vdad095. doi: 10.1093/noajnl/vdad095. PMID: 37781087; PMCID: PMC10540884.