Acute Lymphoblastic Leukemia Research

JAK3 Pathway Highlighted as Leukemia Target

*Expert Review of Anticancer Therapy* published a study revealing that the signaling protein JAK3 represents a viable target in the treatment of a broad range of B-lineage cancers, including acute lymphoblastic leukemia (ALL). The analysis was carried out by Dr Fatih Uckun, who is a Professor at the Keck School of Medicine at the University of Southern California and the Leader of the Developmental Therapeutics Program of the Children's Center for Cancer and Blood Diseases at the Childrens Hospital Los Angeles and his colleagues Jason Pitt of the US NIH (Bethesda, MD, USA) and Sanjive Qazi of Gustavus Adolphus College (MN, USA).

Leukemia and lymphoma are malignant diseases of blood cells. They can affect both T cells, which are immune cells that directly attack foreign substances in the body (cell-mediated immune response; T-lineage malignancy), and B cells, which are immune cells that produce antibodies against foreign antigens (humoral immune response; B-lineage malignancy). JAK3 plays an important role in several signaling pathways involved in blood cell proliferation and survival. Mutations that directly cause JAK3 activation are extremely rare in B-lineage leukemias but over-activation of JAK3 has been reported in a proportion of ALL patients, as well as in various other B-lineage malignancies.

In this article, Uckun and his colleagues demonstrate for the first time that leukemic cells taken from ALL patients overexpress a number of proteins involved in the JAK3 signaling pathway and their receptors, leading to increased JAK3 activation. Analysis of eight previous studies revealed that this amplified expression of JAK3-stimulatory proteins, along with a deficiency of JAK3-inhibitory signaling proteins, occurs in vivo in a number of B-lineage malignancies. Therefore, despite the rarity of JAK3-activating mutations it appears that JAK3 is permanently active in many B-lineage lymphoid malignancies, including ALL, and is an exciting target for novel therapeutic approaches.

The authors conclude that clinical studies are warranted to evaluate the activity of JAK3 inhibitors in B-lineage leukemia, in order to elucidate their activity and side-effect profiles.

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