Paper highlight: 'Hi-JAK-ing' cancer by inhibiting Jak2

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Myeloproliferative neoplasms (MPN) comprise a family of blood cancers characterized by clonal expansion of a single blood cell type.

Untreated, these cancers can progress to bone marrow failure and acute myeloid leukemia.

Several groups have identified activating mutations in the JAK2 gene as associated with MPN; JAK2 inhibition has therefore emerged as approach to MPN therapy. Thus far, however, JAK2 inhibition strategies have had limited efficacy and have been accompanied by significant toxicity.

In this paper, Ross Levine and his group at the Memorial Sloane Kettering Cancer Center, New York, describe an indirect approach to reducing JAK2 activity by pharmacologically targeting HSP90, a protein that stabilizes JAK2.

Inhibiting HSP90 normalized blood counts and improved survival in two mouse models of MPN, and the treatment promoted JAK2 degradation in samples from MPN patients.

The authors believe that targeting HSP90, perhaps in combination with JAK2 inhibition, may be the way forward in the treatment of patients with MPN.

More information: HSP90 is a therapeutic target in JAK2-dependent myeloproliferative neoplasms in mice and humans: www.jci.org/articles/view/4244 … 7ef55d4a4ce9ffed3af0

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