ASH: CALR mutations ID'd in myeloproliferative neoplasms

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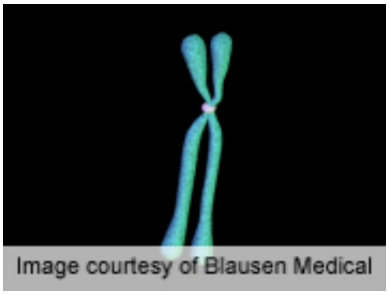

(HealthDay)—Many patients with myeloproliferative neoplasms without mutations in the Janus kinase 2 gene (*JAK2*) or in the thrombopoietin receptor gene (*MPL*) have mutations in the *CALR* gene encoding calreticulin, according to two studies published online Dec. 10 in the *New England Journal of Medicine*. The research was published to coincide with presentation at the annual meeting of the American Society of Hematology, held from Dec. 7 to 10 in New Orleans.

Thorsten Klampfl, Ph.D., from the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences in Vienna, and colleagues performed whole-exome sequencing to identify somatic mutations in six patients with primary myelofibrosis without mutations in *JAK2* or *MPL*. The researchers identified somatic insertions or deletions in exon 9 of *CALR* in all patients. Among patients with

essential thrombocythemia and primary myelofibrosis, *CALR* mutations were mutually exclusive with *JAK2* and *MPL* mutations. *CALR* mutations were seen in 67 and 88 percent, respectively, of those with essential thrombocythemia and primary myelofibrosis, with non-mutated *JAK2* or *MPL*.

Jyoti Nangalia, M.B.Chir., from the Cambridge Institute for Medical Research in the United Kingdom, and colleagues performed exome-sequencing of samples from 151 patients with myeloproliferative neoplasms. The researchers identified 1,498 mutations, with somatic *CALR* mutations in 70 to 84 percent of myeloproliferative neoplasms with non-mutated *JAK2*. The mutations were located in exon 9 and generated a +1 base-pair frameshift.

"Somatic mutations in the endoplasmic reticulum chaperone *CALR* were found in a majority of patients with myeloproliferative neoplasms with non-mutated *JAK2*," Nangalia and colleagues write.

Several authors from the Klampfl study reported holding pending patent applications regarding the use of calreticulin gene mutations for the diagnosis of diseases and targeting for therapy for myeloproliferative neoplasms.

More information: Abstract - Klampfl
Full Text
Abstract - Nangalia
Full Text
Editorial
More Information