

## Screening for the JAK2 V617F Mutation in Patients with Hemoglobinopathies

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### ABSTRACT

Some clinical and hematological features of patients with hemoglobinopathies can mimic those of a myeloproliferative neoplasm (MPN). Given the shifting epidemiology of hemoglobinopathies, the occurrence of the MPN-associated *JAK2* V617F mutation and reasons for testing were audited in hemoglobinopathy patients from Ireland. The *JAK2* V617F mutation was not detected in any hemoglobinopathy patients. Given the possible coexistence of an MPN and hemoglobinopathy in the same patient, clinical, hematological and morphological features should be carefully considered prior to molecular investigation.

**Key words:** *JAK2* V617F; Myeloproliferative neoplasms; Hemoglobinopathies; Molecular diagnostics

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### LETTER TO THE EDITOR

The Philadelphia chromosome-negative myeloproliferative neoplasms are molecularly characterised by the acquisition of driver mutations of *JAK2*, *CALR* and *MPL* genes. The specific *JAK2* V617F mutation is present in 95% of patients with polycythemia vera and in 50-65% of patients with essential thrombocythemia and primary myelofibrosis with identification of a first-line objective in MPN molecular diagnostic algorithms<sup>[1]</sup>. As some hematological and clinical features of patients with hemoglobinopathies can mimic those of myeloproliferative neoplasms (MPN) such as splenomegaly, increased thrombotic events, an apparent erythrocytosis and occasionally thrombocytosis<sup>[2]</sup>, several studies have screened for the presence of *JAK2* V617F in large patient cohorts in areas where hemoglobinopathies are endemic to determine the incidence of a latent MPN<sup>[3-6]</sup>. Given that the prevalence of hemoglobinopathies such as sickle cell disease and  $\beta$ -thalassemia are increasing in Western Europe<sup>[7,8]</sup>, the value of *JAK2* V617F mutation screening was assessed in Irish patients with hemoglobinopathies.

From January 2007 to December 2020 inclusive, a total of 20,139 requests for *JAK2* V617F mutation analysis were received at a center for hematological malignancy molecular diagnostics. The *JAK2* V617F mutation detection methodology was unchanged throughout the audit period and of these requests, 3,523 (17.5%) were positive. A total of 32 individual patient referrals were identified from hemoglobinopathy patients (sickle cell disease n = 22; beta-thalassemia n = 6; alpha-thalassemia n = 2; unspecified hemoglobinopathy n = 2). Referral clinical details included thrombosis (n = 17), thrombocytosis (n = 5), splenomegaly (n = 2) and not provided (n = 8). The *JAK2* V617F was not detected in any of the 32 patient samples.

Acknowledging the small size of the patient population examined it appears that screening for the *JAK2* V617F in current Irish

hemoglobinopathy patients with clinical and hematological features that mimic an MPN is unwarranted. Given the rare but documented coexistence of a hemoglobinopathy and MPN in the same patient<sup>[9-11]</sup>, assessment of the clinical, hematological and morphological aspects of MPN diagnosis should be considered prior to molecular investigations.

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