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JAK2 mutations other than V617F: A novel mutation and mini review

To the Editor,

We identified a novel *JAK2* mutation, c.1849-1852GTCT → TTTC predicting a p.V617F; p.C618R alteration of JAK2, in a blood specimen from a 67-year-old patient with polycythemia vera (PV). Mutation analysis of DNA from peripheral blood and buccal cells was performed by denaturating high-performance liquid chromatography (DHPLC) of purified PCR products. Specimens showing abnormal DHPLC profiles were reamplified and sequenced (Fig. 1).

Several mutants of JAK2 other than $JAK2^{V617F}$ have been reported. Like $JAK2^{V617F}$, many of these mutants affect amino acids located within the pseudokinase domain JH2 suggesting a similar mode of action [1–5]. While $JAK2^{C616Y}$ has been identified in a patient with PV [3], some of these novel mutations have been identified in cases of acute lymphoblastic [1,5] or acute myelogenous leukemia [2] (ALL, AML) or unclassified MPS [4] suggesting a genotype–phenotype relationship. Mutant $JAK2^{L611S}$ has been observed in a case of childhood ALL [1]. A five amino-acid deletion, $JAK2^{\Delta IREED}$, was identified in ALL blasts from a patient with Down syndrome [5]. Expression of this mutant in Ba/F3 cells conferred constitutive activation of the JAK-STAT pathway and growth factor independent cell proliferation [5]. A $JAK2^{K607N}$ mutant was detected in a case of AML [2]. Mutant $JAK2^{D620E}$ was identified in a patient with unclassifiable myeloproliferative syndrome [4]. A novel activating $JAK2^{T875N}$ mutation affecting the JH1 kinase domain of JAK2 has been discov-

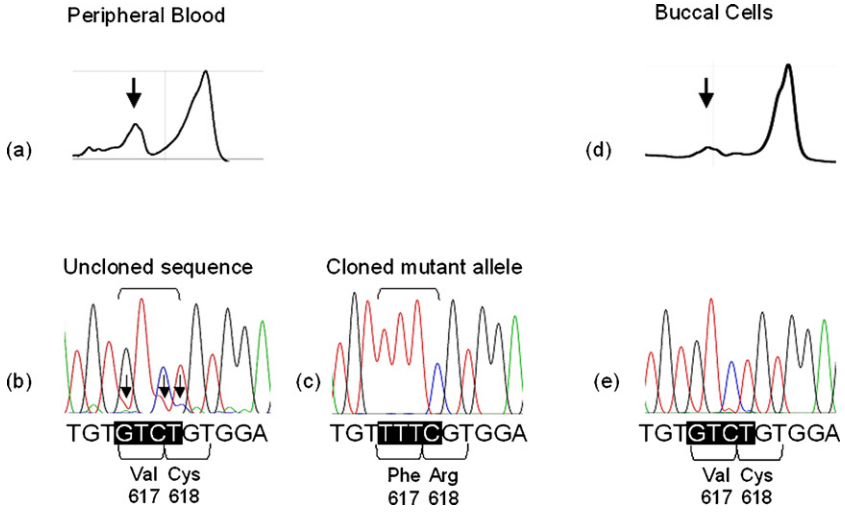

Fig. 1. A novel *JAK2* mutation, c.1849-1852GTCT > TTTC (p.V617F; p.C618R) in a patient with polycythemia vera. DHPLC chromatogram suggests the presence of a mutation in DNA extracted from peripheral blood (panel a, arrow). Sequence analysis of uncloned DNA was consistent with the presence of a small clone harboring several sequence changes (arrows, panel b). Mutation c.1849-1852GTCT > TTTC (p.V617F; p.C618R) was detected by resequencing cloned PCR products harboring the mutant allele only (panel c). Analysis of DNA extracted from buccal cells suggests minimal contamination of buccal cells with blood cells carrying a mutant allele (panels d and e).

ered in an acute megakaryoblastic leukemia cell line [6]. Recently, Scott and coworkers described four novel mutations, $JAK2^{F537\text{-}K539delinsL}$, $JAK2^{H538QK539L}$, $JAK2^{K539L}$, and $JAK2^{N542\text{-}E543del}$, in ten individuals with a $JAK2^{V617F}$-negative and distinctive myeloproliferative syndrome who received a diagnosis of PV or idiopathic erythrocytosis [7]. In conclusion, we describe a novel mutation, $JAK2^{V617FC618R}$, associated with PV. Notably, this mutation would have been missed by allele specific methods searching for a c.1849G → T mutation of *JAK2*.

Conflict of interest

The authors declare no competing financial interests.

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