You Don't Know JAK!

By Menaka Pai, MD, and Joseph
Mikhael MD, MEd, FRCPC

The ASH Education Session on Myeloproliferative Disorders is worth an early morning wake-up call! Dr. D. Gary Gilliland will be chairing this session, offered yesterday and again today from 7:30 to 9:00 a.m. The session will focus on recent advances in the pathophysiology and treatment of myeloproliferative disorders (MPD).

Dr. Ross Levine will begin by reviewing the activity of JAK2 V617F kinase – a constitutively active enzyme formed by a unique acquired clonal point mutation in the JAK2 pseudo-kinase autoinhibitory domain. Along with other mutations in patients with MPD, JAK2 V617F kinase ensures that the JAK-STAT signal transduction pathway is never switched off. The relentless signaling results in dysregulated cell apoptosis. Many members of ASH will remember how the link between CML and the Philadelphia chromosome was established in 1960. This link not only revolutionized the diagnosis and monitoring of the disease, it led to molecularly targeted therapy. As the relationship between JAK2 kinase and myeloproliferative disorders solidifies, Dr. Levine will help us answer the million- dollar question. If we can design a molecularly targeted therapy to switch off JAK-STAT signaling, can we short-circuit MPD?

Dr. Ayalew Tefferi will show us how JAK2 kinase has impacted our approach to MPD at the bedside. JAK2 kinase testing is entering the realm of routine clinical practice. With Dr. Tefferi's help, the hematologist will learn how JAK2 status can assist in accurate diagnosis, predict disease progression, and influence treatment in patients with MPD. JAK2 V617F is found in nearly all patients with polycythemia vera (PV) and in a variable proportion of patients with other myeloproliferative disorders. It has not yet been detected in patients with secondary myeloproliferation or lymphoid disorders. JAK status is rapidly becoming a promising tool, and Dr. Tefferi will guide us through its use in MPD, discussing both its strengths and its pitfalls.

Finally, Dr. Tiziano Barbui will strengthen our clinical understanding of MPD by discussing management issues. MPD patients are at risk of both bleeding and clotting. This presents a unique challenge, particularly during pregnancy and in the perioperative setting. There is very limited literature on optimal management during these high-risk periods. Dr. Barbui will present practical strategies, based on both published data and empiric principles. His session should help the clinician manage MPD patients as they navigate the often stormy course of their disease.

This education session will spark your interest in the exciting field of myeloproliferative disorders. Keep the JAK2 ball rolling by attending the Scientific Plenary Session on Sunday at 1:45 p.m. Dr. Alessandro Vannucchi will present abstract #5, "Influence of the JAK2 V617F Mutational Load at Diagnosis on Major Clinical Aspects in Patients with Polycythemia Vera." By the time you catch your flight home, you'll really know JAK!