The year 2011 marks the golden anniversary of the first formal description of the classic myeloproliferative neoplasms (MPN) by William Dameshek (1900–1969) [1]. Dr. Dameshek underscored the histologic similarities between polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF), and chronic myelogenous leukemia (CML), and coined the term “myeloproliferative disorders (MPD),” in 1951 [2], to describe them. In 1960, Peter Nowell (1928) and David Hungerford (1927–1993) discovered the Philadelphia chromosome (Ph+) and its invariable association with CML [3]. In 1967, 1976, 1978, and 1981, Philip Fialkow (1934–1996) and colleagues used polymorphisms in the X-linked glucose-6-phosphate dehydrogenase (G-6-PD) locus to establish the stem cell-derived clonal nature of CML, PV, PMF, and ET, respectively [1]. The disease-causing mutation has since been determined for CML (BCR-ABL1) but not for PV, ET, or PMF [4].

Beginning in 2005, novel mutations involving JAK2, MPL, TET2, ASXL1, IDH1, IDH2, CBL, IKZF1, or LNK have been described in a subset of patients with BCR-ABL1-negative MPN [5]. With the exception of JAK2V617F, which occurs in approximately 95% of patients with PV and 60% of those with ET or PMF, these mutations are relatively infrequent and occur in a minority of patients with PV, ET, or PMF. Furthermore, none of these mutations, including JAK2V617F, has been shown to be a cardinal event in disease initiation or progression [5]. It is, therefore, not surprising that current efforts with anti-JAK2-targeted therapy have not produced the results that are usually seen with anti-BCR-ABL1 (i.e., imatinib) therapy in CML. Nevertheless, JAK-STAT hyperactivation directly or indirectly contributes to the pathogenesis of certain MPN-associated disease aspects, and several anti-JAK ATP mimetics have accordingly been developed and currently undergoing clinical trials (http://ClinicalTrials.gov).

The above-mentioned development in the pathogenesis of PV, ET, and PMF has also played an essential part in the 2008 revision of the WHO classification system for MPN, which now includes eight separate entities: CML, PV, ET, PMF, systemic mastocytosis (SM), chronic eosinophilic leukemia-not otherwise specified (CEL-NOS), chronic neutrophilic leukemia (CNL), and “MPN unclassifiable (MPN-U).” The 2008 WHO revision also includes improved diagnostic criteria for PV, ET, and PMF, whereas PDGFR- or FGFR1-rearranged
myeloid/lymphoid malignancies associated with eosinophilia were formally separated from CEL-NOS and excluded from the MPN category. As is the case with the classic $BCR-ABL1$-negative MPN, the genetic underpinnings of non-classic MPN remain unresolved, although certain mutations, such as $KIT$ D816V in SM, are believed to contribute to disease pathogenesis and are reasonable targets to consider during new drug development.

The above-mentioned exciting developments in both classic (PV, ET, PMF) and non-classic (CEL-NOS, SM, CNL, MPN-U) $BCR-ABL1$-negative MPN are the focus of the current book, which provides a timely and comprehensive review of disease pathology, molecular pathogenesis, diagnosis, prognosis, and treatment. The experts in their respective fields have done an outstanding job in preparing a scientifically robust educational document that we regard as an essential reading for both practicing physicians and students of hematology.

Houston, TX  
Srdan Verstovsek, MD, PhD  
Rochester, MN  
Ayalew Tefferi, MD

References

Myeloproliferative Neoplasms
Biology and Therapy
Verstovsek, S.; Tefferi, A. (Eds.)
2011, X, 230 p., Hardcover
ISBN: 978-1-60761-265-0
A product of Humana Press