



Introduction to a review series on myelodysplastic syndromes

The group of disorders collectively named myelodysplastic syndromes (MDS) is characterized by ineffective hematopoiesis and cytopenias, and particular characteristic cytomorphological features of blood and marrow. MDS are seen at any age although more frequently in older individuals. These conditions have always presented a challenge to hematologists, with regard to both establishing the diagnosis and offering an effective treatment. The specificity of the diagnosis is a challenge because there is substantial diversity of conditions across the entire spectrum of MDS. Furthermore, the boundaries between MDS and various other related myeloid disorders can be vague. In recent years, an explosion of new scientific information has emerged that has shed light on the pathogenesis and pathobiology of MDS. The emerging knowledge appears clinically useful to both support the diagnostic process and to generate entirely novel concepts of treatment beyond the traditional approaches of care.

The review series in this issue of *Blood* presents a comprehensive compendium that examines the intriguing landscape of MDS from different angles. These reviews highlight the scale of advances in the biological and clinical science of MDS and include the following articles:

- Eline Pronk and Marc H. G. P. Raaijmakers, "The mesenchymal niche in MDS"
- David A. Sallman and Alan List, "The central role of inflammatory signaling in the pathogenesis of myelodysplastic syndromes"
- Seishi Ogawa, "Genetics of MDS"
- Charlotte M. Niemeyer and Christian Flotho, "Juvenile myelomonocytic leukemia: who's the driver at the wheel?"
- Alyssa L. Kennedy and Akiko Shimamura, "Genetic predisposition to MDS: clinical features and clonal evolution"

- Tiffany N. Tanaka and Rafael Bejar, "MDS overlap disorders and diagnostic boundaries"

- Uwe Platzbecker, "Treatment of MDS"

The first article explores the marrow niche, which, as we know today, may exert effects on initiating or supporting the development of MDS. The second examines the inflammatory signals and innate immune signals that may act as strong pathogenetic drivers of the disease. Thus, these 2 reviews offer updates on critical extrinsic mechanisms of disease initiation and progression. The subsequent 4 articles of this series focus on various aspects of genomics in relation to disease variation and molecular diagnostics. One examines the discovery of a rich variety of molecular drivers and molecular patterns of disease evolution and describes their correlations with clinical disease phenotypes. The following review discusses juvenile chronic myelomonocytic leukemia (JMML), which represents a distinct subset of MDS that is mainly seen in childhood. Recently, significant genomic and epigenomic insights into the origin of JMML have been gained. The advance of genetic technologies has also paved the way toward the recognition of inherited susceptibility as a basis for MDS development. The rapidly expanding area of clinically relevant knowledge about hereditary MDS is the subject of the fifth review. The sixth review deals with "precision diagnostics" and describes the diagnostic issues of defining MDS relative to other so-called "boundary" conditions. For instance, aplastic anemia, myeloproliferative neoplasms, and acute myeloid leukemia may present as MDS "look-alikes" or vice versa. The final paper in this review series comprehensively summarizes state-of-the-art approaches to treatment and examines upcoming therapeutic directions.

We hope that you will enjoy reading these papers from leaders in the field about the truly kaleidoscopic world of MDS.

Bob Löwenberg
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