

hematopoietic and lymphoid systems (251). Mutations in *p53* frequently occur at six discrete hotspot codons within the DNA-binding domain of the molecule, namely, at codons 175, 245, 248, 249, 273, and 282 (252). Where mutations occur, the strongest correlations between poor prognosis have been found mainly for breast cancer and CLL (253). But convincing correlations have not been found, for example, in the case of colorectal cancer.

g. Cytogenetics for Diagnosis and Prediction—MDS

Chromosomal abnormalities are detected in about 50% of patients with de novo MDS and in up to 80% of patients with MDS secondary to chemotherapy (254). Deletions of the long arm of chromosome 5 (del(5q)) are the most frequent chromosomal abnormality in de novo MDS.

The IPSS applies only to de novo MDS. This scoring system assigns a “risk category” for risk of death or transformation to AML. These risk categories reflect the percentage of bone marrow blasts, number of cytopenias, and presence or absence and type of chromosomal abnormalities. The chromosomal abnormalities, which are used to assign risk, are defined by the IPSS as good, poor, and intermediate. The chromosomal abnormalities associated

with good, poor, and intermediate prognosis are as follows (255):

- Good prognosis. Normal, isolated -Y, del(5q), and del(20q).
- Poor prognosis. Complex (≥ 3 abnormalities) and/or any chromosome 7 anomalies.
- Intermediate prognosis. All other abnormalities.

Because it is simple, the IPSS score is suitable for use as a gentle introduction to the cytogenetics of MDS. That said, the following serves as an introduction to the tremendous variability of MDS cytogenetics.

In a large study of MDS, Haase et al. (256) acquired cytogenetic data on 2072 MDS patients. Of these, 988 did not show chromosomal abnormalities, and 1084 had chromosomal abnormalities. Thus, about 50% showed abnormal cytogenetics. The variety of abnormalities was remarkable, as the abnormalities fell into 684 different categories. Many of the patients contained only one chromosomal abnormality (333 patients had only one abnormality). Some of the patients (83 patients) contained two abnormalities. A significant number of patients had three abnormalities (32 patients), four to six abnormalities (59 patients), or greater than six abnormalities (41 patients).

²⁵¹Robles AI, Harris CC. Clinical outcomes and correlates of TP53 mutations and cancer. Cold Spring Harbor Perspect. Biol. 2010;2(15 pp.).

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²⁵⁴Haase D, Germing U, Schanz J, et al. New insights into the prognostic impact of the karyotype in MDS and correlation with subtypes: evidence from a core dataset of 2124 patients. Blood 2007;110:4385–95.

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