f. Mechanism of action of 5-aza-deoxycytidine

5-Aza-deoxycytidine is a hypomethylating agent, that is, it reduces the amount of methyl groups that are naturally attached to deoxycytidine residues of the chromosomal DNA. As a consequence of this reduced methylation, genes are activated in the target cells, where the activation of genes that cause cell differentiation causes a cancerous cell to be non-cancerous. The mechanism of action of 5-aza-deoxycytidine likely includes the following scenario (163). The drug is an analogue of deoxycytidine, and is incorporated into the chromosome during DNA replication. Normally, specific residues of deoxycytidine in our chromosome are enzymatically methylated. Methylation is catalyzed by DNA methyltransferase. But when this enzyme attempts to catalyze the methylation of 5-aza-deoxycytidine, the enzyme gets covalently bound to the DNA and is trapped. The consequence is a reduction of the amount of this enzyme in the cell, failure to methylate DNA, and the generation of under-methylated chromosomes and conversion of the cell to a non-cancerous cell.

III. SUMMARY

Many of the topics relevant to solid tumors are also relevant to the hematological malignancies, for example the endpoint of survival, use of induction chemotherapy, prognostic regarding outcome for untreated patients, and predictive factors that predict the success of drugs. But the hematological malignancies are distinguished by the fact that the concept of metastasis is usually not applied, by the phenomenally high cure rate for some of the leukemias, for example hairy cell leukemia and acute promyelocytic leukemia, by the fact that these hematological neoplasms may be unusually difficult to distinguish from each other, and by the fact that the RECIST criteria are generally not used.

IV. CYTOGENETICS AND THE HEMATOLOGICAL CANCERS

The nomenclature used in identifying human chromosomes is as follows. The human chromosomes are numbered 1 to 22, with two additional chromosomes called X and Y. Chromosomes 1 to 22 occur as two copies in every somatic cell. The X chromosome occurs as two copies in every female somatic cell, but only once in every male somatic cell. The Y chromosome occurs only once in every male somatic cell. Thus, the sex chromosomes in males are XY, and the sex chromosomes in females are XX. Altogether, human somatic cells have 46 chromosomes (164). During mitosis, the genome condenses to form chromosomes that can be seen using a light microscope. The appearance of these chromosomes is called the *karyotype*.

[163] Patel K, Dickson J, Din S, Macleod K, Jodrell D, Ramsahoye B. Targeting of 5-aza-2′-deoxycytidine residues by chromatin-associated DNMT1 induces proteasomal degradation of the free enzyme. *Nucleic Acids Res*. 2010;38:4313–4324.

[164] Tijio JH, Levan A. The chromosome number in man. *Hereditas*. 1956;42:1–6.