

Germ Line Mutation Associated Acute Myeloid Leukemia: Different Genetic Landscape and Therapeutic Strategies

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It is estimated that acute myeloid leukemia from the germ line mutation associated cause is about 15% and it could be more.

To increase the recognition for myeloid leukemia/MDS associated with inherited or germ line mutations, The major changes made by adding of the germ line mutation in the classification of myeloid neoplasms and acute leukemia in the new version of classification of tumors of the hematopoietic and lymphoid tissues published by the World Health organization (WHO) in 2016 including: 1) myeloid neoplasms with germ line predisposition without a preexisting disorder or organ dysfunction, 2) myeloid neoplasms with germ line predisposition and preexisting platelet disorder and 3) myeloid neoplasms with germ line predisposition and other organ dysfunction. Myeloid neoplasms associated with inherited bone marrow failure syndromes (IBMFS) are listed, commonly including Fanconi anemia (FA), dyskeratosis congenital (DC), Shwachman-diamond syndrome (SDS), diamond blackfan anemia (DBA), congenital amegakaryocytic thrombocytopenia (CAMT), severe congenital neutropenia (SCN) and thrombocytopenia absent radii (TAR) which they are often diagnosed at a young age. They require different treatment strategies due to the underlying gene defects.

IBMFS are complex mixture of genetic disorders characterized by insufficient blood cells production usually associated with one or more somatic abnormality and an increased cancer risk.

Fanconi anemia (FA) is usually inherited as an autosomal recessive (AR) trait, but it can also be X-linked recessive (XLR). FA is the most common and representative type of IBMFS. So far, 22 genes responsible for FA were identified and also found that FA is susceptible to malignancies, commonly in acute myeloid leukemia. Patients with FA are characterised with progressive bone marrow failure, congenital abnormalities and susceptibility to malignancies, commonly in MDS, AML, and solid tumors. Very importantly, cells from patients with FA are more sensitive to chemotherapy than patients without FA which it can cause severe results from chemotherapies.

The cytogenetic and molecular technologies for leukemia testing provide huge improvements for diagnosis, prognostic stratification, disease monitoring and therapeutic guidelines.

To deal with germ line mutated leukemia, it not only requires to increase the awareness for germ line mutations, to taking family history from patients and to offer genetic counseling for the relevant to malignant diagnosis, it also requires to understand the developments of the genetic landscapes.

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