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INTRODUCTION TO INVITED REVIEW ARTICLES

Novel therapeutic strategy based on genetic and epigenetic abnormalities for myeloid neoplasms

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Acute myeloid leukemia (AML) and myelodysplastic syndromes (MDSs) are representative diseases of myeloid neoplasms [1]. There are some similarities of the molecular pathogenesis between AML and MDS, but it is not entirely identical [1–3]. Genetic and epigenetic abnormalities are crucial to the understanding their pathogenesis, and are also the bases of the development of new therapeutic agents.

AML is a heterogeneous hematologic malignancy. AML blasts expand not only in bone marrow, but also to peripheral blood and other organs including central nervous system [1]. Clinical importance to more reveal and understand what happens in AML blasts at genetic and epigenetic levels is emphasized to establish more precise risk classification and more appropriate molecularly targeted therapies [4–7]. Examination of cytogenetics is widely performed in diagnosing leukemia in clinic. Chromosomal abnormalities of t(8;21), inv (16), and t(16;16) are specific to AML, while t(15;17) is a hallmark of acute promyelocytic leukemia [1]. Chromosomes 5 and 7 are frequently found both in MDS and AML in elderly [8]. Next generation sequence could describe genetic abnormalities in AML blasts [5–7]. They include signaling pathway mutations (*FLT3, KRAS, NRAS, PTPN11, NF1, KIT*), transcription factor mutations (*RUNX1, CEBPA*), epigenetic regulator mutations (*IDH1/2, DNMT3A, TET2, ASXL1, EZH2*), RNA splicing factors mutations (*SF3B1, SRSF2, U2AF1, ZRSR2*), and tumor suppressor gene *TP53* mutation.

MDS is characterized by peripheral pancytopenia due to ineffective hematopoiesis and dysplastic changes of myeloid, erythroid, and megakaryocytic lineages in bone marrow [1]. The disease also holds the potential to develop to leukemia. Abnormalities at genetic and epigenetic levels have extensively been investigated recently in association with the development of MDS [9–11]. Chromosomal abnormalities detected in MDS are +8, −7, del (7q), −5, del (5q), del (20q), −Y, i(17q), t(17q), −13, del (13q), del(11q), del (12q), and t(12q) [1]. Frequently mutated genes found in MDS include *SF3B1, TET2, ASXL1, RUNX1, TP53, U2AF1, EZH2, NRAS, JAK2, ETV6, CBL, IDH2, NPM1,* and *IDH1* [9–11].

The following articles comprehensively summarize the recent progress of the studies of genetic mutations and the development of novel therapeutic strategies in AMS and MDS. Miyamoto and Minami summarized the significance of gene mutations for AML. *FLT3, NPM1, EVI1, RUNX1, TP53,* and *CEBPA* were discussed for their impact on the outcome of allogeneic hematopoietic stem cell transplantation. They also described clinical efficacies of molecularly targeting agents, *FLT3* inhibitors and *IDH* inhibitors. They outlined the ongoing HM (hematologic malignancies)-SCREEN-Japan, a genetic screening project for AML, conducted by National Cancer Center Hospital East and collaborative institutions. Hosono gave an overview of the recent progresses in molecular pathogenesis of MDS. Representative cytogenetic abnormalities and gene mutations were described. Among them, *CUX1* located on 7q22 and LUC7L2 located in the most commonly deleted region of −7/del7q; 7q34 were detailed. The author concluded that the diagnostic classification of MDS will be revised, and targeted therapies will be individualized to appropriate patients by the genome-wide profiling that is connected to clinical information.

Compliance with ethical standards

Conflict of interest No author has any conflict of interest.

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