

## **Biology of Myelodysplastic Syndromes.**

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Myelodysplastic syndromes (MDS) are characterized by dysplastic features and various kinds of cytopenias in the peripheral blood. Although the exact molecular biological features common to MDS formation have not yet been revealed, some factors influencing or associated with hematologic features for MDS have been postulated. One factor is the clonal expansion of cytotoxic T-lymphocytes that directly or indirectly attack MDS stem cells, resulting in apoptosis of MDS cells and thereby being related to cytopenia. Another factor is interaction between MDS stem cells and stroma cells, though the exact mechanism of this relation is unclear. These two factors, cytotoxic T-lymphocytes and interaction between stroma cells and MDS cells, might be major factors for modification of hematologic features of low risk MDS. We do not know the exact common pathogenesis of MDS, however, these factors are essential for MDS, therefore, therapy targeting these factors are currently been applied.

Programed cell death, namely apoptosis, is a challenge in research on MDS. Cell replication without telomerase activity causes telomere loss. In MDS marrow cells, telomere shrinking is apparent, regardless of the type of MDS, thus indicating that it is an essential event in MDS. Moreover most MDS marrow cells show narrow-range telomere signals, irrespective of chromosome difference, when compared to normal marrow metaphases. This suggests that telomere shortening is a basic pathogenetic factor in MDS and that other factors, including proliferative advantage and/or regulation of transcription factors of more malignant MDS cells, might affect the disease progression of MDS and may be linked to genetic instability related to cytogenetic abnormalities.