

# 多発性骨髄腫の ゲノム異常多様性と 臨床応用

## KEY WORDS

- IGH転座
- 高2倍体
- 次世代シーケンサー
- PVT1キメラ
- ゲノム異常多様性

Genomic heterogeneity of multiple myeloma for the identification of new therapeutic targets.  
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## Abstract

Multiple myeloma (MM) is a clinically, phenotypically, and molecularly heterogeneous plasma cell malignancy. The primary cytogenetic abnormalities associated with disease development are either nonrandom chromosomal gains known as hyperdiploid, which is characterized by trisomies of chromosomes 3, 5, 7, 9, 11, 15, 19, and 21, or structural rearrangements involving the immunoglobulin heavy chain gene (IGH) located at 14q32.33 (IGH translocation). The subsequent, multistep acquisition of various types of additional chromosomal abnormalities, genetic hits, and/or epigenetic abnormalities promotes disease progression from monoclonal gammopathy of undetermined significance (MGUS) to MM, and the variety of molecular abnormalities ultimately exhibits significant inter-patient diversity and intra-clonal heterogeneity even in a single patient. Secondary cytogenetic abnormalities implicated in disease progression include 8q24 rearrangements, gain of the long arm of chromosome 1 (1q+), and loss of the short arm of chromosome 17 (17p-). We have analyzed the 8q24 rearrangements in patients with multiple myeloma and cell lines by FISH and SKY combined with oligonucleotide arrays showing frequent *PVT1* rearrangements with several partners and novel *PVT1-NBEA* and *PVT1-WWOX* chimeric genes. These findings suggest that the rearrangements of *PVT1*, a long intergenic noncoding RNA (lincRNA), may represent a novel molecular paradigm underlying the pathology of multiple myeloma with 8q24 rearrangements.