

Multiple Myeloma's Molecular Cytogenetics.

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ABSTRACT

A plasma cell malignancy known as multiple myeloma (MM) is typified by several genetic abnormalities. It is possible to discriminate between two primary categories of abnormalities: hyperdiploid and hypodiploid, where the chromosome number is primarily composed of either by monosomies or trisomies, in turn. The development of Fluorescence In Situ Hybridization (FISH) has made it possible to detect genomic abnormalities that are included in prognostic scoring systems that also account for clinical factors. This straightforward analysis can inform the patient's initial assessment and help tailor his care.

Keywords : Myeloma; Cytogenetics; Fish

INTRODUCTION

Unlike acute leukemias, Multiple Myeloma (MM) is characterized by chromosomal abnormalities that can be investigated using conventional methods.

Low mitotic activity of tumor cells has impeded cytogenetics in this disease [1,2]. The use of molecular-based cytogenetic tools in analyzing MM and its predecessor, Monoclonal Gammopathy of Undetermined Significance (MGUS), has led to significant improvements in understanding plasma cell tumor biology. Fluorescence In Situ Hybridization (FISH) can reveal complex chromosomal abnormalities in almost all MM and MGUS patients, providing valuable prognostic information [3].

Conventional cytogenetics

Cytogenetic analysis is only useful for less than 30% of MM patients due to the high mitotic activity of tumor cells in MM, which is higher than in other haematological illnesses.

low. Nearly half of individuals have a complicated karyotype with over 10 anomalies [4].

Numerical changes

The numerical changes include monosomies on chromosomes 13, 14, 16, and 22, and trisomies on chromosomes 3, 5, 7, 9, 11, 15, 19, and 21 [5]. Regardless of the finding of specific Chromosome banding analysis can provide significant prognostic information by detecting aberrant metaphases and tumor cell ploidy in informative cases [6]. Patients with a normal karyotype have a much longer life rate than those with cytogenetically abnormalities [7]. Tumors with abnormal metaphases can be classified based on their chromosomal number, which might impact prognosis. Hypodiploidy has been linked to poorer outcomes across multiple studies. However, undesirable genetic characteristics, such as monosomy 13/13q deletion and t(4;14).

The numerical changes include monosomies on chromosomes 13, 14, 16, and 22, as well as trisomies on chromosomes 3, 5, 7, 9, 11, 15, 19, and 21 [5]. Regardless of the identification of specific Chromosome banding analysis can provide important prognostic information by detecting abnormal metaphases and tumor cell ploidy in relevant circumstances [6]. Patients with a normal karyotype live a significantly longer life than those with cytogenetically abnormalities [7]. Tumors with aberrant metaphases can be classified according to their chromosomal number, which may affect prognosis. Hypodiploidy has been associated to inferior outcomes in numerous studies. However, unfavorable genetic traits, such as monosomy 13/13q deletion and t(4;14), In MM, test for 13q14 and 17p deletions (13q-, 17p-), IGH locus translocations (t(4;14)(p16.3;q32), t(11;14)(q13;q32), t(14;16)(q32;q23), and abnormalities of the chromosomes 1p and 1q [2]. The majority of these probes are available.

Most laboratories use probes to detect 13q deletion in chromosomal band 13q14, although the essential area of 13q- remains unclear. Probes that contain the p53 gene are commonly used to detect 17p-. DNA probes can identify translocations in the immunoglobulin heavy-chain (IgH) locus by mapping to both the constant (CH) and variable regions [13]. Differentially labeled probes colocalize to detect reciprocal translocations.

Colocalization of differently labeled probes for IgH and its translocation partner (e.g. 11q13, 4p16, 16q23), ideally on both derived chromosomes (double fusion). The cut-off levels for positive results are based on bone marrow samples from healthy participants. For dual fusion or break-apart probes, a

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10% cut-off level is acceptable. For single fusion results with dual fusion probes, a 20% cut-off level is recommended. However, some laboratories use a 10% threshold. Proper cut-off levels should be chosen by each laboratory [2].

13q deletion

FISH investigations indicate that -13/13q- is present in approximately 50% of MM patients, making it the most common aberration [14]. Using standard cytogenetics, the incidence of chromosomal 13 deletions in patients with informative karyotypes have a comparable incidence of 10% to 20%, as established in major cytogenetic studies.

In patients with t(4;14)(p16.3;q32) or t(14;16)(q32;q23), roughly 90% have -13/13q-. In traditional cytogenetics, -13/13q- is linked to a poorer response rate.

MM is associated with higher rates, shorter event-free survival (EFS), and lower overall survival (OS). This applies to individuals who have undergone conventional chemotherapy, High-Dose Chemotherapy (HD-CTX), or Autologous Stem Cell Transplantation (ASCT) [15].

Karyotyping for -13/13q- results in a worse prognosis than FISH for the identical anomaly. This finding is likely owing to a combination of poor prognostic indicators, including a greater rate of proliferating cells [16]. FISH identifies considerably more 13q-deleted patients than conventional cytogenetics (40-50% versus 15-20%).

17p deletion

Mutations or deletions of the p53 tumor suppressor gene have been linked to disease development in many human cancers. In most FISH datasets, the occurrence of p53 Deletion rates among newly diagnosed individuals were between 5% and 10% [17,18]. Functional deletion of the gene is seen in up to 40% of advanced myeloma patients and over 60% of human myeloma cell lines, indicating tumor progression [19]. FISH-identified deletion of the p53 gene region predicts poorer survival rates regardless of treatment method (conventional or HD-CTX) [20].

Chromosome 1q

Cytogenetic studies have linked 1q aberrations to advanced illness, tumor development, and shorter event-free survival. The gene implicated appears amplified and is CKS1B, a cell cycle regulator located on chromosomal band 1q21, has been linked to a poor prognosis [21-23].

CONCLUSION

Using cytogenetics and molecular cytogenetics to analyze genomic rearrangements in MGUS and MM has helped us better comprehend clonal plasma cell diseases. Evaluation

of a complete panel of chromosomal imbalances and translocations is essential for clinical care.

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