



Multiple Myeloma

Multiple myeloma (MM) is the most common type of primary bone tumor, and the second most prevalent blood cancer (10%) after non-Hodgkin's lymphoma, affecting approximately 50,000 patients only in the United States. It represents more than 1% of all cancers. Although it is currently not curable, recent advancements in treatment are bringing myeloma closer to becoming a chronic disease instead of a terminal illness. To achieve these goals, treatments are becoming more and more individually tailored for each patient based on the patient's age, overall health status, symptoms, and laboratory test results. Diagnostic technology, especially cytogenetic testing, are used to tailor treatment for each individual to work toward achieving better response rates, longer periods of remission, and improved quality of life.

The cytogenetic abnormalities seen in MM are typically complex, involving at least 3 chromosomes in 80% of patients. Because of the many DNA breaks necessary for immature B cells to become mature plasma cells, B cells already have inherent genetic instability. DNA breaks are necessary for VDJ recombinations, somatic mutations and isotype switching and it is therefore not surprising that genetic alterations frequently occur at the Ig heavy chain site at 14q32, which is abnormal in three quarters of myeloma patients. The main chromosomal abnormalities seen in MM recommended in routine diagnostic testing as they define patients at high genetic risk for early progression after conventional therapies are:

- Translocations involving Ig heavy chain site at 14q32, and in particular the rearrangements t(4;14), t(11;16), t(14;16) (60% of the patients);
- Deletion of chromosome 13q (30-40% of the patients)
- Deletion of 17p13 (10% of the patients)
- Presence of hypodiploid or hypotetraploid karyotype, frequently associated to deletion of chromosome 13 or gain of 15q22 and 9q34

Moreover:

- Amplification of 6q21 and 15q22
- Deletion of 19q13 (novel prognostic marker associated to short survival)
- Deletion of p53

Kreatech Diagnostic offers the complete range of FISH probes for Multiple Myeloma, tailored to investigate all cytogenetic aberrations specific for Multiple Myeloma for early detection and patient identification with different prognosis.

As Ig heavy chain site at 14q32 is highly instable, it is possible that high level IgH chromosomal deletions can lead to difficulties in detecting FISH probe signal.

Kreatech Diagnostic FISH probes that recognize the IgH region (KBI-10601; KBI-10602 KBI-10603; KBI-10604 and KBI-10605) yield highly stable signal patterns compared with other FISH probes currently present in the market. In fact, they can detect more than 1.5 MB genetic region, thereby covering the complete gene locus.

TECHNICAL TIPS OF THE MONTH

November 2008



Do you know that Kreatech Diagnostic offers two different probes for the cytogenetic analysis of t(11;14)? They are:

✓BCL1/IGH t(11;14) Dual-Fusion (KBI-10604): recognize the translocation breakpoints scattered within the 120 kb BCL1 region. The bcl-1 locus on chromosome band 11q13 can juxtapose next to the IgH locus on chromosome band 14q32, leading to deregulation of the cell cycle regulatory protein cyclin D1 (CCND1).

✓MYEOV/IGH t(11;14) Dual Fusion (KBI-10605): this probe recognize the breakpoint region frequently scattered within a 360-kb region between the CCND1 (BCL1) and MYEOV gene. This common translocation of MM is also observed in mantle cell lymphoma and other leukemias, resulting in up-regulation of CCND1 and/or MYEOV. The MYEOV gene (myeloma overexpressed gene in a subset of t[11;14]-positive multiple myelomas) is a novel putative oncogene activated in the amplification core proximal to CCND1.

Please remember that MM investigations are done on plasma cells, therefore enrichment using CD-138 is highly recommended.

The CD-138 is a transmembrane heparan sulfate proteoglycan macromolecule also known as syndecan-1, specifically expressed from plasma cells (normal and malignant human plasma cells), and also from endothelial cells. It is not expressed by virgin/naive B cells, memory B cells, T cells, or monocytes.

If you would like to receive suggestions on how to sort plasma cells by using CD-138 antibody, you are welcome to contact us at customerservice@kreatech.com.

And remember our new FISH probe ON MAF/IGH t(14;16) Fusion Probe (cat.no. 10610)!

For more information, please consult our Kreatech Newsletter November 2008!!!

Multiple Myeloma		
ON MM 19q13 / P53 (17p13)	red/green	KBI-10501
ON MM 11q23 / DLEU (13q14)	red/green	KBI-10502
ON MM 1q21 / 8p21	red/green	KBI-10503
ON MM 15q22 / 6q21	red/green	KBI-10504
ON MM 1q21 / SRD (1p36)	red/green	KBI-10507
ON MM 15q22 / 9q34	red/green	KBI-10508
ON IGH (14q32) Break	red/green	KBI-10601
ON FGFR3 / IGH t(4;14) Fusion	red/green	KBI-10602
ON BCL1 / IGH t(11;14) Fusion	red/green	KBI-10604
ON MYEOV / IGH t(11;14) Fusion	red/green	KBI-10605
ON MAF / IGH t(14;16) Fusion	red/green	KBI-10610

NEW!!