P53 gene deletion in multiple myeloma Deleção da gene P53 no mieloma múltiplo

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The role of P53 gene abnormalities in the pathogenesis of multiple myeloma (MM) and their potential use as prognostic indicator remains uncertain. To further define this question, we studied genomic DNA from 50 MM and one plasma cell

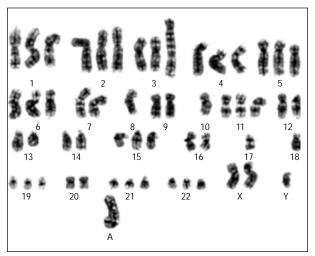
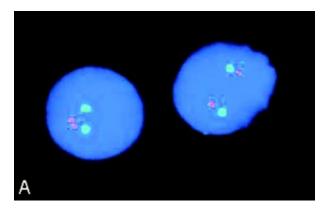


Fig. 1 – G-banded multiple myeloma patient karyotype: 55, XY, +X, +1, +2, +3, +4, +5, +6, del(6)q21, add(7)q36, -8, -10, +11, del(13)q14, +15, -17, -18, +19, +21, +22, +mar (A)

leukaemia patients by polymerise chain reaction single strand conformation polymorphism and sequencing, and fluorescence in situ hybridisation in order to detect P53 mutations and deletions, respectively. Kaplan-Meier survival curves and the log-rank test were used to analyse the survival data.



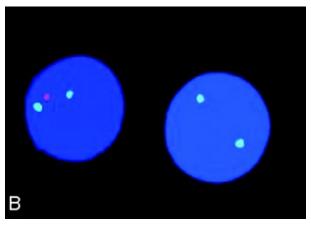


Fig. 2 – Interphase fluorescence in situ hybridisation analysis in multiple myeloma patient, using specific probes for chromosome 17 centromere (•) and P53 locus (•) (Vysis, Downers Grove, IL, USA). (A): two hybridisation signals for each probe in normal interphase nuclei and, (B) abnormal nuclei exhibiting a monoallelic (left) and biallelic (right) deletions of P53 locus

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No P53 mutation was detected in our patients. In contrast, P53 deletion, predominantly monoallelic, was detected in 8 out of 51 (15.7%) patients. Patients with P53 deletions had significantly shorter median overall survival compared with those without a deletion (7.4 vs. 139.0 months, P<0.0001). In univariate regression analysis, P53 deletion was a parameter for predicting shortened survival (P=0.02).

We concluded that P53 mutation might be seen as a prognostic indicator of limited value in MM. In contrast, P53 deletion might be seen as a prognostic indicator of poor outcome. These results have already been accepted for publication in Annals of Hematology and has been submitted to Rev. Bras. Hematol. Hemoter., with the purpose of presenting the images obtained by conventional and molecular cytogenetics analyses performed in study (Figures 1 and 2).

Referências Bibliográficas

- Avet-Loiseau H, Li JY, Godon C et al. P53 deletions is not a frequent event in multiple myeloma. Br J Haematol 1999;106:717-9.
- 2. Corradini P, Inghirami G, Astolfi M, et al. Inactivation of tumor suppressor genes, P53 and Rb1 in plasma cell dyscrasias. Leukemia 1994;8:758-67.
- 3. Drach J, Ackerman J, Fritz E et al. Presence of a P53 gene deletion in patients with multiple myeloma predicts for short survival after conventional-dose chemotherapy. Blood 1998;92:802-9.
- 4. Owen RG, Davis SAA, Randerson J et al. P53 gene mutations in multiple myeloma. J Clin Pathol Mol Pathol 1997;50:18-20.

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