TGFbR2 Aberrant Methylation is Associated with Poor Outcome in Multiple Myeloma

Carvalho, F.[1]; Karia, B. T. R.[3]; Colleoni, G. W. B. [1]; Almeida, M. S. S.[1]; Carvalho A. L. [2]; Vettore, A. L. [3]

[1]Discipline of Hematology and Hemotherapy, Universidade Federal de São Paulo, UNIFESP/EPM, São Paulo, Brazil; [2]Barretos Cancer Hospital, Barretos, Brazil; [3]Biology Department, Federal University of São Paulo, UNIFESP, São Paulo, Brazil.

Multiple myeloma (MM) is an incurable hematological malignancy. Different studies demonstrated the occurrence of genetic and epigenetic alterations in MM. The DNA aberrant methylation is one of the most frequently epigenetic alterations in human genome. This study evaluated the DNA aberrant methylation status of 20 genes in 51 MM samples by quantitative methylation specific PCR (QMSP) and compared the methylation profile with clinicopathological characteristics of the patients. The QMSP analyses showed that *PTGS2* (100.0%), *SFN* (100.0%), *CDKN2B* (90.2%), *CDH1* (88.2%), *ESR1* (72.5%), *HIC1* (70.5%), *CCND2* (62.7%), *DCC* (45.1%), and *TGFbR2* (39.2%) are frequently hypermethylated in MM while aberrant methylation of *RARß* (16.6%), *MGMT* (12.5%), *AIM1* (12.5%), *CDKN2A* (8.3%), *SOCS1* (8.3%), *CCNA1* (8.3%), and *THBS1* (4.1%) are rare events. There was no methylation of *GSTP1, MINT31, p14ARF* and *RB1* in the samples tested. Hypermethylation of *ESR1* was correlated positively with isotype IgA, while aberrant methylation of *THBS1* correlated negatively with isotype IgG. Furthermore, hypermethylation of *DCC* and *TGFbR2* were correlated with poor survival. The multivariate analysis showed ISS and *TGFbR2* hypermethylation strongly correlated with poor outcome. This study represents the first quantitative evaluation of MM methylation profile and our data provide evidence that *TGFbR2* hypermethylation may be useful as prognostic indicator in MM.

Supported by FAPESP # 2006/61572-8