p53 gene mutations in multiple myeloma

We were interested in the article by Owen et al on the same subject. They had studied the p53 exons 5–9 by PCR-SSCP and they found only one p53 mutation among 36 DNA samples from 31 patients with multiple myeloma. They concluded that p53 mutations are rare and confined to end stage leukemias. We have studied p53 protein expression in myeloma cases determined by immunohistochemistry, and our results and conclusions were different from Owen and colleagues’.

Our study group comprised 31 patients with multiple myeloma and four with isolated plasmacytoma. Twenty of the myeloma cases were newly diagnosed and the other 11 had relapsed or had resistant disease. All of the multiple myeloma patients were in stage III and 13 cases had also renal involvement. Fresh bone marrow aspiration samples from myeloma patients and paraffin wax embedded tissue sections from plasmacytoma cases were stained by the ABC method. To determine p53 protein expression, a monoclonal antibody against the p53 suppressor gene product (DO-7 Novacasta K-32; Novacasta, Newcastle upon Tyne, UK) recognizing both normal and mutant forms of protein was used. Eight of the 35 cases showed p53 protein expression, none of the plasmacytomas showed p53 protein expression; therefore, p53 protein expression was found in 26% of cases of multiple myeloma. Four of the eight p53 positive cases were newly diagnosed and four of them were resistant or/and relapsed cases. Four of the 24 newly diagnosed, four of 11 relapsed cases, four of the 18 stage IIIA, and four of the 13 stage IIIB cases had p53 expression. There was no significant difference for p53 expression between newly diagnosed or relapsed cases or between IIIA and IIIB cases (p < 0.25). None of our patients had features of leukemic phase disease.

p53 gene alterations in plasma cell dyscrasias have not been as well studied as we have studied. We have studied p53 protein expression in myeloma cases determined by immunohistochemistry, and our results and conclusions were different from Owen and colleagues’.

It is well known that p53 gene has a complex structure and that functional inactivation can result from the loss of p53 gene function. Therefore, there is no ideal method for the detection of p53 gene alterations; however, by using more than one technique such as immunohistochemistry and PCR-SSCP, the results may be more informative. We believe that if immunohistochemistry could be used concurrently with PCR-SSCP analysis, Owen et al’s results and comments might be more useful.

We conclude that p53 mutations are not particularly rare in multiple myeloma. We agree that p53 mutation is not an initial step in myelomagenesis. We need larger studies with more patients and methods to determine the pathogenetic role of p53 mutations in multiple myeloma.

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Dr Owen and colleagues comment: Using PCR-SSCP we found only one patient with multiple myeloma from 31 cases who had a mutation of p53. We agree that the incidence of detectable p53 protein expression is higher. In a small group of cases (not the same as those described in the paper) we found four of 17 (23.5%) in which p53 was present in proportion of the polyclonal antibody 1801. In three of the cases, p53 was present in a small minority of the plasma cells. The presence of p53 in a minor proportion of tumour cells is seen commonly in other types of B lymphoproliferative disorders, and there is no evidence that this is due to stabilisation of the protein by mutation. In general, the association between p53 expression and mutation in lymphoproliferative disorders is much less firmly established than for epithelial tumours. The incidence of p53 immunoreactivity, therefore, cannot be assumed to be directly relevant to establishing the incidence of p53 mutations in myeloma. Equally, the occurrence of mutated p53 in myeloma does not of itself need to be considered an indication of the incidence of p53 mutation in clinical samples.

We have not correlated the presence of renal impairment with the presence of p53 mutation or overexpression of the protein. In addition, the investigation of myeloma involves multiple factors including calcium, Bence-Jones protein, and the development of amyloid. It is difficult to postulate a role for p53 expression or mutation in renal impairment not be considered as any indication of the incidence of p53 mutation in clinical samples.

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Thus, the first two chapters are devoted to the gene, any gene, and how the structure of DNA and genes are currently investigated. The next two chapters constitute a lead into the more specialist topic of endocrinology, dealing with the mechanism of action of the two major classes of hormones. These are followed by chapters devoted to specific topics. All the chapters are authoritative, and despite the continuing rapid advances in the various fields, are reasonably up to date. Although the chapters are written by different authors, the editors have achieved a unified style of language and presentation. All the figures are black and white; however, they are well drawn, clear, and informative. The referencing is adequate but very extensive.

The subject matter adheres strictly to classical endocrinology, and it seems a pity that the discussion of nuclear receptors does not include helix-turn-helix receptors to any extent. Although the aryl hydrocarbon receptor probably does not come withing the strict compass of endocrinology, it seems a pity that a chapter was not given to this. Nevertheless, even with these minor criticisms, this book is a useful investment for anyone in this field of research, and an excellent source book for teachers to dip into time and time again when preparing undergraduate lectures.

D B RAMSDEN


This second edition of Leucocyte Antigen Facts Book provides an update on the ever increasing number of leucocyte antigens, both with and without a CD number. It includes all the changes from the International Workshop in 1996. An introduction is followed by two sections, the first three chapters giving details of how these molecules have been discovered and analysed, an overview of the various protein superfamilies, and how they interact with the various ligands. In the last chapter there is an update of the interaction between B and T lymphocytes and the ligands involved. I feel this could have been slightly expanded to include other cell-cell interactions such as neutrophil and endothelial cells, and antigen presenting cells. The second section lists all the relevant CD antigens along with many of them that are yet to be designated a CD number. The molecular weight, carbohydrate content, gene location, tissue distribution, structure, and function of each antigen is

Book reviews


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