#3721 Mutational spectrum of the p53 gene, tumor p53 protein overexpression and serum p53 autoantibody generation in patients with breast cancer. Angelopoulou, K., Yu, H., and Diamandis, E.P. *Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, Toronto, Ontario M5G IX5, Diagnostic Systems Laboratories, Webster, Texas.*

Autoantibodies against the p53 tumor suppressor protein have been detected in serum of a proportion of cancer patients. The generation of such antibodies has been proposed to be due to one or both of the following: (a) tumor p53 protein accumulation or (b) p53 gene mutation. These hypotheses are examined in the present study. Using immunofluorometric assays, 195 patients with primary breast cancer were analyzed for the presence of p53 antibodies in serum and p53 accumulation in the corresponding tumor. Seventeen patients (9%) were p53 antibody-positive and 77 (39.5%) overexpressed p53. Ten of the 17 p53 antibody-positive patients had tumor p53 accumulation and 7 were negative for p53. Statistical analysis revealed an association between the presence of p53 antibodies and p53 accumulation ($p = 0.05$). Direct DNA sequencing of exons 1–11 of the p53 gene was performed for 16 p53 antibody-positive and 16 p53 antibody-negative patients. Five of the seropositive patients had a p53 gene mutation; 1 in exon 4, 1 in exon 5, 2 in exon 6 and 1 in exon 7. Eight of the negative patients had a mutation in the gene; 1 in exon 5, 4 in exon 7 and 3 in exon 8. Four of the 5 mutations in the p53 antibody-positive patients affected a Tyr residue, whereas none of the abnormalities in the negative patients had such an effect. In conclusion, p53 antibodies tend to be developed by patients with tumor p53 accumulation, without p53 accumulation being a sufficient prerequisite for the

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