rates, corrected for apoptosis in 3 types of childhood sarcoma for evidence of switch-like control effects.

Methods: Diagnostic tissue samples of 29 rhabdomyosarcomas (RMS), 14 Ewings sarcoma (ES) and 18 Osteosarcomas (OS), were studied using routine immunocytochemistry for S-phase related nuclear antigens (Moab against cDNA defined subsegment of the Ki67 antigen, MM1, Novocastra, UK) and in-situ labelling for apoptosis derived DNA fragments (CalBiochem, USA). Quantitation was based on established image analysis (Quantimet 570 C). Apoptosis corrected proliferation fraction was calculated as: Ki67 labelling % divided by (100 – Apoptosis %).

Results: In the groups studied results were distributed as follows:

Group	N	Low prolif fr.	N	High prolif. fr.	N	
RMS	29	<30%	9	>51%	19	(1 case 41%)
ES	14	<21%	8	>45%	6	
OS	18	<30%	12	>75%	6	

Conclusions: Clear binominal/non-Gaussian distribution was consistently observed in all 3 groups of childhood sarcoma. This suggest the presence/abscence of a cell cycling controlling effect, indicative of controller gene switching mechanism activation/suppression of which may be limited to a subgroup of lesions.

48 PUBLICATION

Expression of p53 protein in endometrial carcinomas: Relationship with ER and PR status

P. Athanassiades, P. Athanassiadou, E. Petrakakou, A. Karkabasi, N. Kavatzas, M. Demopoulos. *Department of Clinical Therapeutics, "Alexandra" Hospital; Department of Pathology, Cytology Laboratory, Medical School, University of Athens, Greece*

Purpose: To study the expression of p53 protein in endometrial carcinomas and the correlation of this finding with the hormonal status [oestrogen (ER) and progesterone (PR) receptors] and the histological type of the tumours.

Material and Method: Imprint smears from 50 surgically resected endometrial carcinomas were studied by immunoperoxidase method with the use of monoclonal antibody against p53. Twenty normal endometrial smears, were the control group.

Results: Expression of p53 was found in none of the 20 normal endometrial smears but was identified in 14/50 (22.2%) endometrial carcinoma smears. Nine of 14 p53 positive tumours were serous and clear cell carcinomas. No relationship was found between ER and PR status and the presence of p53 negative tumours ($p < 0.01$).

Conclusions: p53 immunoreactivity may have a prognostic role in patients with endometrial carcinoma.

49 PUBLICATION

Expression of novel growth suppresing gene, TOB, in patients with esophageal cancer

Y. Nonaka[1], T. Ikegami[2], S. Matuda[2], I. Hirose[1], S. Hanada[1], Y. Nomura[1], H. Yanagie[1], M. Eriguchi[1], T. Yamamoto[2], T. Muto[1]. [1]*Department of Surgery Institute of Medical Science, University of Tokyo;* [2]*Department of Oncology, Institute of Medical Science, University of Tokyo, Japan*

Purpose: Recently, a novel gene, termed TOB has been found to encode a 38-KDa protein homologue to the growth suppressing protein Btg-1. The gene product interacts with erb B2, which plays an important role in the progression of esophgeal cancer. Elevated expression of the TOB protein suppressed growth of NIH 3T3 cells. For the purpose of analysis of TOB's function in the progression of esophageal cancer, we examined TOB mRNA and protein expression in the tissue by immunostainig and RT in situ PCR.

Method: Tissue specimens of esophageal cancer and of noncancerous esophagus were obtained from patients who had undergone subtotal resection of esophagus at Department of Surgery, IMSUT. Paraffin-embbeded specimens were sliced into 4-μm-thick sections, then to which immunostaining and RT in situ PCR were performed.

Results: we found that TOB mRNA transcripts and proteins decreased in the tissue of esophageal cancer as compared with non cancerous tissues.

Conclusion: This study suggested that TOB may play a part in progression of esophageal cancer.

50 PUBLICATION

Genomic instability as assessed by micro satellite analysis in childhood rhabdomyosarcoma (RMS)

C. Riddell, L.M. Ball, L. Resch, K. Samson, J. Mu, K. Laybolt, D. van Velzen. *Department of Molecular Genetics, IWK/Grace Hospital, Halifax; Department of Quantitative Pathology, IWK/Grace Hospital, Halifax; Department of Image Analysis, IWK/Grace Hospital, Halifax; Department of Haemato-Oncology, IWK/Grace Hospital, Halifax, Canada*

Purpose: Microsatellite instability (MSI) as a reflection of inherent genomic instability, may be of relevance to sensitivity to genome directed therapy. We studied MSI in a representative series of childhood RMS, related to proliferation and apoptosis.

Methods: Diagnostic tissue samples of 30 consecutive, unselected RMS cases were studied. Patients, 18 M/12 F, age 3 m–17 y (mean 6 y4 m)/2 m–16 y (7 y5 m), were diagnosed as Embryonal (20, 8 with mets), Alveolar (6, 3 with mets) and variants (4). After routine extraction, amplifications were carried out at the loci D3S1304 and D3S1537 (both closely distal to the VHL tumour suppressor gene), ELN gene, D7S1870, IFNA, D1S243 (1p36) with isotopic labelling during amplification, non-denaturing gel electrophoresis and autoradiography. Apoptotic (Frag-EL) and proliferation fraction (Ki-67labelling) were determined in all cases.

Results: Limited abnormal amplification products were seen in 5 patients: 1. F, 13 y11 m, embryonal thumb lesion, metastatic disease at presentation, deceased; 2. F, 13 y9 m, alveolar, neck node primary, deceased; 3. M, 2 y4 m, embryonal, thigh lesion, alive; 4. M, 3 m, atypical, axillary mass, deceased; 5 M. 9 y2 m, embryonal, nasopharynx, deceased. Apoptotic corrected proliferation fraction of these lesions was high compared to other lesions.

Conclusion: Microsatellite abnormality was recorded in only 5/30 cases of RMS association with high proliferation rates warrants further studies.

Prevention of therapy-related side effects

51 ORAL

The modification of bleomycin-induced lung toxicity in a S.C. mice model and an I.T. rat model

L.Y. Dirix, J. Hendricks, P. Vermeulen, P. Lauwers, E. Van Marck, P. Van Schil, E. De Bruijn, A. Van Oosterom. *Department of Medical Oncology, University Antwerp, Belgium*

Purpose: Bleomycin (BLM) remains an important drug in the treatment of a variety of tumours, e.g. teratocarcinoma, Kaposi's sarcoma, lymphomas. The main toxicity of BLM is a dose-dependent pulmonary fibrosis. This study investigated the potential of the cytoprotective agent amifostine (A), WR-2721, for the prevention or attenuation of BLM induced lung damage.

Methods: Eight week old Swiss NIH mice were injected twice weekly with 5, 10, 20 and 40 mg/kg of BLM for two, four or six consecutive weeks. Routine and trichome stained analysis of lung changes were performed. Two groups six mice each were treated with BLM 20 mg/1 g 2x/week with or without A at 200 mg/kg also twice weekly s.c.

In a third set of experiments adult male Wistar rats were treated with unique intratracheal dose of BLM at 1.5 IU and 2.5 IU. A third group received prior to this I.T. administration a once daily s.c. dose of A.

Results: In the mice experiments BLM s.c. produced a dose-dependent increase in lung damage measured by alveolar wall thickness, intra-alveolar mononuclear cells and pulmonary consolidation. Treatment with amifostine resulted in a decrease in mortality and in an improvement in different pathological parameters. In the rat model with i.t. administration a clear protective effect was again observed with a complete pathological protection in 2/4 animals in the 1.5 IU group.

Conclusion: Both in the chronic s.c. model in mice as in the acute i.t. model in rats, amifostine treatments results in an impressive attenuation of BLM induced lung toxicity.