was fully inhibited by the 5-HT3 receptor antagonists ondansetron but not by granisetron. Serotonin and the 5-HT3 receptor antagonists recovered the reduction of Na+, K+, ATPase activity by EMP when Na+, K+, Cl− cotransport activity was blocked by bumetanide. The data show that ondansetron possesses a distinct ability to regain Na+, K+, Cl− cotransport activity of cells exposed to EMP and that this property differs from that of granisetron. Thus, highly 5-HT3 receptor-specific antiemetic agents may have different effects on ion transport of tumour cells during treatment with cytotoxic drugs.

771 PUBLICATION

Immune implications of cytostatics loaded in drug carriers of second generation. nanoparticles

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Purpose: Nanoparticles represents the second generation of solid coloid transports carrier which are used in the systemic administration for chemotherapy. Our study followed to establish the effects of free epirubicin and loaded in nanoparticules on the mouse peritoneal macrophages (enzymatic activity).

Methods: The experiment was carried out on three groups of Swiss female mice: control free nanoparticles (FN) and epirubicin loaded in nanoparticles (EN). The tests were performed on peritoneal macrophages at 24, 48 and 72 h after the treatment. The peroxidase, acid phosphatase and alpha-naphtilacetate esterase of peritoneal cells were assayed using histochemical methods. The number of cells with intensive and moderate enzymatic activity was determined.

Results: The *peroxidase activity* is constantly low to control. For FN activity grow to 48 h and touch the maximum level at 72 h. For EN the activity decrease dramatically at 72 h after a high value at 24 h. The *esterase activity* is significant for free and EN at 24 h. The *acid phosphatase activity* has a high level in control group. FN induce high activity at 48 h and decrease at 72 h. EN induce high activity at 24 h and 48 h and a low level at 72 h.

Conclusion: The enzymatic reactions represents macrophages activation markers. The results almost heterogenous reveal 2 types of reactions of peritoneal macrophages under nanoparticles influence: the differentiated reactivity of lizozomal enzymes with low expression of esterase and epirubicin loaded in nanoparticles have a cytotoxic effect on peritoneal cells; the resting cells maintain a constant phosphatase level.

772 PUBLICATION

Energy status and mitochondria oxidative phosphorylation in doxorubicin-sensitive and doxorubicin-resistant solid Guerin's carcinoma

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Purpose: The cell energy status of any tissues influences their viability. The indices of energy status and mitochondria oxidative phosphorylation of solid Guerin's carcinoma with different sensitivity to doxorubicin were studied.

Methods: The ATP, ADP, AMP content and energy charge served as the indices of energy status. The ATP, ADP and AMP content was estimated by means of thin-layer chromatography. The mitochondria oxidative phosphorylation indices were studied by the polarographic method with using of the covered combined platinum electrode of the Clark type.

Results: The mitochondria oxygen consumption rate (in presence of succinate or glutamate) during phosphorylation of ADP in doxorubicin-sensitive tumours was higher than in drug-resistant tumours. The ATP/O ratio in mitochondria of both substrains of Guerin's carcinoma was practically equal. The ATP level and the energy charge were higher in doxorubicin-sensitive tumours as compared with drug-resistant variant. On the other hand the AMP level was higher in drug-resistant carcinoma than in sensitive substrain.

Conclusion: Thus, the mitochondria oxygen consumption rate during phosphorylation of exogenous ADP as well as the ATP level and energy charge are reliably higher in doxorubicin-sensitive Guerin's carcinoma than in drug-resistant tumours.

Breast cancer genetics & biology

773 POSTER DISCUSSION

Frequent loss of heterozygosity (LOH) & monoallelic expression of the *p73* gene, a *p53*-homologue, in inflammatory breast carcinomas

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Inflammatory breast cancer (IBC), which accounts for 3–5% of BC, is a very aggressive form of the disease of a very poor prognosis which had been thoroughly defined in our institution by clinical criteria (Rouéssé *et al., JCO*, 1986). The *p73* gene, a *p53* homologue gene recently discovered, locates at 1p36-33 a chromosomal locus which is putatively imprinted in SK-N-SH cells (Kaghad et al Cell 1997) and submitted to LOH in breast carcinomas (BC). To study whether invalidation of this locus is associated with BC agressiveness, *p73* genomic and allelic status were determined in 61 invasive BC, including 41 NBC (non IBC) & 20 IBC.

Results: 1) Genomic DNA polymorphism analysis revealed a frequency of informativity of 39% (24/61). Among heterozygous tumors, 8 IBC and 16 NBC, *p73* LOH was found to be significantly higher in IBC than in NBC, respectively 5/8 (62%) versus 2/16 (12.5%) (Fisher' exact test, $P = 0.02$). 2) cDNA polymorphism study on 16 cases showed monoallelic expression in 4/5 (80%) IBC versus 2/11 (18%) NBC (Fishers' exact test, $p = 0.05$). 3) Semi-quantitive RT-PCR revealed that gene expression was lower in IBC than NBC and normal breast epithelium.

Conclusion: A p73 expression decrease (LOH or/and monoallelism) is associated with IBC aggressiveness: it could be a genetic marker of agressiveness of the disease. *Supported by CRC 98-20, IGR/Sanofi Recherche/Ligue, Comité des Hauts de Seines France.*

774 POSTER DISCUSSION

Defective iodination within the breast: A feature of breast carcinoma?

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The thyroid and breast possess a common ability to actively transport and organify dietary iodide, a process recently demonstrated to be under the control of a specific transmembrane protein, the sodium iodide symporter (NIS). However little data exists on the involvement of iodination in the natural history of breast cancer. To study extrathyroidal control of iodide transport we investigated iodine content and NIS expression in human breast tissues and the ability of serum from patients with breast disease to modulate NIS activity. Mean tissue iodine levels measured by dry ashing (80.9 ± 9.5 ngI/mg protein in 22 benign tumours; fibroadenomata) were significantly higher than those in both breast cancer (18.2 ± 4.6 ng/mg) or in morphologically normal tissue (31.8 ± 4.9 ng/mg) taken from within the tumour bearing breast ($N = 17$; $p < 0.001$ in each case). The iodine content of normal breast was also significantly > that in breast cancer ($p < 0.01$). Breast tissue iodine was orders of magnitude < that in 2 thyroid tissues (704 and 850 ng/mg). RT-PCR showed NIS expression not only in thyroid but in breast tissues including fibroadenomata and breast carcinoma tissue isolates. In contrast, NIS was not expressed in control tissues. Significant inhibition (i.e. >mean + 3 S.D. of control sera) of 125 I uptake into NIS transfected CHO cells was observed in serum from 29/104 (27.9%) of Graves' patients. Such inhibition was only detected in 1/33 control sera but was present in sera from 20/105 (19.0%) breast carcinoma and 8/49 (16.3%) benign breast disease ($p < 0.05$). The coincidence of low tissue iodine with NIS blocking activity in breast carcinoma cohorts suggests a defect in iodine handling within the breast and supports the thesis for an as yet undetermined role for iodine in the natural history of breast carcinoma.