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P 55 IL 2 RECEPTOR EXPRESSION ON PERIPHERAL BLOOD LYMPHOCYTES FROM PATIENTS WITH HODGKIN'S LYMPHOMA AND WITH SOLID MALIGNANCIES.

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The aim of the study was to assess the possible existence and the extent of an impaired p 55 IL2 receptor (IL2R) expression in Hodgkin's Lymphoma (HL) and in some widespread solid malignancies (SM) in which a secondary immune deficiency arises in the course of disease. In HL and in most SM a defective IL2 production has been already found. 7 HL,6 head and neck,3 breast,3 lung (NSCLC),3 colorectal,cancer patients,as well as 6 normal subjects,were studied. Both a cytofluorimetric and a cultural assays were carried out,the last culturing the PBL in presence of PHA,IL2 and PHA+IL2 either with or without the non FITC-conjugated anti p 55 MoAb and assessing the $^{3}H$ TdR uptake,the former evaluating the percentage of fluorescent cells in cultures undergoing the same stimulation,after addition of FITC-conjugated anti p 55 MoAb. The results showed a full competition between IL 2 and MoAb for the p 55 IL2R,being the MoAb more avid for the ligand in such a way to prevent almost completely the binding of IL2. The flow cytometry assay indicated a p 55 expression significantly lower in HL PBL,at later times (72 h),compared to normal and SM PBL: this may suggest that also the p 55-75 heterodimer could be expressed at significantly lower levels in HL PBL,so providing new insights for the severe T cell immune impairment of HL. The almost normal pattern of p 55 expression in PBL of SM may support the perspective of the usefulness of IL2 administration in these patients.

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CHANGES IN ALPHA 1 AND BETA 2 ADRENOCEPTOR DENSITY IN HUMAN HEPATOCELLULAR CARCINOMA.

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To disclose the role of catecholamines in the mechanisms of liver cell proliferation in hepatocellular carcinoma (HCC), we examined $\alpha$1 and ß 2 adrenoceptors (AR) by radioligand binding and their coupling to adenylate cyclase in liver tissue from HCC patients (n=24) and on healthy livers from patients undergoing surgery for non-hepatic diseases (n=24). Twenty-two HCC had a 72% decrease of $\alpha$1-AR in tumorous compared to nonadjacent/nontumorous tissue and a 40% decrease compared to controls. Nonadjacent/nontumorous tissue had a 125% increase in $\alpha$1-AR compared to healthy livers. Twenty-three HCC had a 180% increase of ß-AR compared to nonadjacent/nontumorous tissue and to controls. ß-AR were coupled to adenylate cyclase as shown by isoproterenol-stimulated cAMP production. HCC yielded a larger increase in cAMP than nonadjacent/nontumorous and healthy tissue. A higher $\alpha$1-AR density characterizes nonadjacent/nontumorous tissue from HCC; an increase in ß and a decrease in $\alpha$1-AR characterize human HCC.

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ANGIOTENSINOGEN GENE PRODUCTS: PUTATIVE LIVER AUTOCRINE STIMULANTS

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Angiotensinogen protein is produced in the liver and converted to angiotensin (angio 1) by renin. The effects of angiotensinogen and angiotensins 1 and 2 on DNA-S in primary rat hepatocyte cultures were measured. All 3 proteins induced DNA-S, especially angio 2, which also amplified the actions of EGF 10-fold. Hepatocytes from regenerating liver and hepatoma lines were also stimulated. Hepatocytes had specific receptors for both angio 1 and 2 and hepatomas bound 2-10 fold more than normal hepatocytes. Regenerating rat liver had elevated levels of angiotensinogen mRNA, which was confined to hepatocytes. These autocrine hepatocyte growth stimulants are thus potential targets for pharmacological antagonism.

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INHIBITION OF GROWTH BY RU486 IN DIFFERENT HEPATOMA CELLS LINES

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The synthetic steroid RU486 is the first antiprogestin and antiglucocorticoid avaible for therapy. In a former investigation, we observed an antiproliferative effect of RU486 on HTC hepatoma cells. This action appeared to be dependent on the presence of glucocorticoid receptors (GR) and on the absence of cytochrome P450 isozymes. These 2 points served as a guide to further study the question in other rat hepatomas. Cells were chosen which contain (GR+) or which do not contain any GR (GR-). We mostly used H56 (GR+) and H56-125 (GR-) cell lines to study (i) the influence of RU486 on the growth rate, (ii) the capacity of the cells to metabolize the steroid.

In H56 cells, RU486 does not undergoe any degradation and exerts a high antiproliferative effect, like in HTC cells.

In H56-125 cells (GR-), RU486 also exerts a blockade of the cellular growth, but to a lower extent.These cells are able to metabolize efficiently RU486.

These results suggest that several mechanisms must be put forwards in order to explain the antiproliferative effect: one involves the GR whereas the other one may involve different cellular stuctures. Indeed binding studies in GR+ and GR- cells indicate that RU486 binds specifically to those cells. This observation strongly suggest the existence of another not yet characterized type of high affinty binding sites which may be involved in the growth inhibitory effect of RU486. Finally metabolization of RU486 can be also taken into account in the antiproliferative efficiency of this antihormone. Taken together, our results favour the idea that RU486 might represent a possible drug for the treatment of hepato-carcinomas.