Conclusion: AFP–endostatin shows comparable in vitro effectivity to rh-endostatin. Efficacy in tumour therapy is significantly higher compared to rh-endostatin (100 mg/kg/24h rh-endostatin versus 1.2 mg/kg/72h AFP-endostatin for an inhibition rate of 80%) published in the literature. The application frequency could be reduced with AFP-endostatin, which leads to better patients compliance and reduced therapy costs.

3512 POSTER

Non-resectable esophageal cancer treated with chemotherapy and radiotherapy of multiple 3D beams

A. Boladeras[1], A. Navarro Martin[1], R. Galiana[1], I. Modolell[2], R. Gracia[2], M. Macià[1], M. Cambray[1], M. Galan[3], V. Navarro[4]. *[1]Catalan Oncology Institute – L'Hospitalet, Radiation Oncology, L'Hospitalet del Llobregat, Spain; [2]Catalan Oncology Institute – L'Hospitalet, Physics Department, L'Hospitalet del Llobregat, Spain; [3]Catalan Oncology Institute – L'Hospitalet, Medical Oncology Department, L'Hospitalet del Llobregat, Spain; [4]Catalan Oncology Institute – L'Hospitalet, Clinical Research Department, L'Hospitalet del Llobregat, Spain*

Purpose: The objective of this study is to evaluate the feasibility of treatment in non-resectable esophageal cancer with high dose radiotherapy by multiple 3D beams.
Methods: From July 2005 to February 2007, 18 patients with non-resectable esophageal cancer were treated in our institution with radical intention. Stage distribution was 3p. (17%) T4 N1 M0, 2p. (11%) T4 N0 M0, 4p (22%) T3 N1 M0, 3p (17%) T3N1M1a, 3p (17%) T3 N0 M0 and 3p (17%) T1-T2 N0 (non operable by comorbility). Esophagous sublocation were: 3p (17%) Cervical, 8 p (44%) Upper-esophageal, and 7 p. (39%) were distal. We administered four cycles of chemotherapy (CDDP 80 mg/m^2/day iv $\times$ 1 day + 5 FU 800 mg/m^2/day iv $\times$ 5 days the first and the fourth week radiotherapy) in 11p. (61%). Gross tumour volume (GTV) was defined according to CT Scan-PET images. Clinical tumour volume (CTV) was defined by GTV with a 3 cm cranial-caudal and 1 cm radial expansion. PTV was defined by CTV with a 1 cm around. Boost dose tumour was defined by GTV with a 1 cm around. A "combined" plan was created to treat the PTV receiving 44 Gy in 22 fractions using 3D planning, followed by a boost until final dose at 66 Gy in 11 fractions. Treatment planning goals were spinal cord max dose <46 Gy, lung dose restricted to a combined V20 < 35% and heart dose restricted to V60 < 30%.
Results: Our doses in critical organs were: the mean of maximum dose received in spinal cord was 40.9 with standard deviation (sd) of 5.9 and 17 p. (94.4%) received doses lower than 46.2 Gy. In heart V60 mean was 4.02% (sd, 7.43, range 0.02−24) and irradiated heart volume was less than 24% in all cases. Finally V20 mean for lung was 23.96 (sd 9.09, range 11−37) and 17 p. (94.4%), V20 was less than 36%. No high grade acute complications were observed during the treatment course.
Conclusions: The irradiation with multiple 3D beams in non-resectable esophageal cancer is a good option for radical treatment, achieving high doses in PTV. However, though we didn't have acute complications, the maxim dose in critical organs is not negligible. Late complications should be analyzed during the follow up of this cohort.

3513 POSTER

Interleukin-13 exerts autocrine growth promoting effects in human pancreatic cancer and its expression correlates with a propensity for lymph node metastases

A. Formentini[1], O. Prokopchuk[1], G. Leder[1], J. Straeter[2], J. Kleeff[3], M. Korc[4], D. Henne-Bruns[1], M. Kornmann[1]. *[1]University of Ulm, Department of General Visceral and Transplantation Surgery, Ulm, Germany; [2]University of Ulm, Department of Pathology, Ulm, Germany; [3]University of Heidelberg, Department of General and Visceral Surgery, Heidelberg, Germany; [4]Dartmouth Medical School, Department of Medicine Pharmacology and Toxicology, Hanover, USA*

Background: Pancreatic cancer cells express receptors for interleukin-13 (IL-13). It is not known, however, whether IL-13 modulates pancreatic cancer cell growth and spread.
Materials and Methods: Cell growth and signaling were analyzed by cell counting, MTT assays, FACS, and kinase activity assays. IL-13 expression and secretion were determined by Northern blot analysis and ELISA, respectively. Localization of IL-13 and IL-13 receptors (IL-4R and IL-13R) in primary pancreatic ductal adenocarcinoma (PDAC) was characterized by immunohistochemistry.
Results: IL-13 significantly enhanced the growth of ASPC-1, CAPAN-1, and COLO-357 pancreatic cancer cells. This was associated with enhanced p44/42 MAPK phoshorylation. In contrast to p44/42 MAPK, IL-13 also induced PI-3 kinase activity in IL-13 unresponsive MIA PaCa-2, PANC-1, and T3M4 cells. All tested cell lines expressed and secreted IL-13. Neutralizing IL-13 antibodies inhibited the growth of ASPC-1 and CAPAN-1 cells. High IL-13 (30/70) and IL-4R (28/70) immunoreactivity was present in PDAC tumor samples. Fifteen of 16 specimen (94%) exhibiting high levels of both IL-13 and IL-4R displayed lymph node metastases, while only 30 of the remaining 54 samples (56%) had positive lymph nodes ($p = 0.0134$).
Conclusions: IL-13 may is an autocrine growth factor in PDAC. Moreover, endogenous expression of IL-13 in conjunction with IL-4R in the cancer cells may facilitate lymph node metastasis by modulating the interactions between tumor cells and immune cells.

3514 POSTER

Altered expression of hepatocyte nuclear factors in pancreatic ductal adenocarcinoma cell lines, varying on the level of differentiation

N. Lazarevich, A. Kuznetsova. *Cancer Research Center, Institute of Carcinogenesis, Moscow, Russian Federation*

The work is devoted to the analysis of the impact of hepatocyte nuclear factors (HNFs) in the control of pancreatic cell lines proliferation and differentiation.
HNFs were identified as the main regulators of liver development and differentiation. We have previously identified the essential role of the dysfunction of HNFs network in the progression of hepatocellular carcinoma. The central player of HNFs network in the liver is HNF4a, which is downregulated in highly malignant tumors. Restoration of HNF4a expression in dedifferentiated hepatocellular carcinoma can promote the reversion of tumors toward a less invasive highly differentiated slow-growing phenotype.
While HNFs were first discovered in the liver, they are expressed in different combinations in the epithelium of other organs including pancreas and clearly participate in gene regulation and tissue differentiation together with other tissue-specific factors. Being derived from the common ontogenetic precursor, the liver and pancreas demonstrate very similar patterns of HNFs expression. The most significant difference in HNF set between the liver and pancreas is substitution of "adult" HNF4a1 isoform of by "embryonic" HNF4a7 one driven by the alternative promoter.
On the basis of these facts we decided to analyze the role of HNFs in differentiation and malignant transformations in the pancreas. For this study we used four cultures derived from pancreatic ductal adenocarcinomas: Capan-2, Panc1, AsPC-1 and MIA PaCa-2. These cultures were arranged by their level of differentiation: first consists of typical epithelial cells, able to form well-defined monolayer and three-dimensional structures resembling ducts and acini, and last – of poor differentiated fibroblastoid single cells, therefore presenting an interesting model for investigation of EMT in the process of malignisation.
Using semi-quantitative RT-PCR we have found that HNF4a7 and vHNF1 expression correlates with the level of differentiation. On the contrary the expression of OC2 and CEBPa in differentiated cell cultures is minimal and increases towards the less differentiated ones. Forced expression of HNF4a7 in dedifferentiated cell culture MIA PaCa-2 reduced the cell proliferation and altered the expression of differentiation markers in this pancreatic cell line.
The work was supported by grants from Russian Foundation for Basic Research and President of Russian Federation award for young Doctors of Science (MD-8329.2006.4).

3515 POSTER

Cisplatin is more cytotoxic than oxaliplatin in oesophageal adenocarcinoma cells demonstrated by Expression of ERCC1 and XPA

R. Mehmood, K. Sales, S. Dijk, M. Winslet. *Royal Free Hospital, Surgery, London, United Kingdom*

Background: Xeroderma Pigmentosum protein A (XPA), recognises DNA damage, its low levels with decreased expression of Excision Repair Cross Complementing 1(ERCC1), an endonuclease of Nucletide excision repair pathway, were found responsible for pronounced cisplatin sensitivity. While increased levels of XPA and ERCC1has demonstrated cisplatin resistance. We want to compare the levels of XPA and ERCC1 gene expression in oesophageal adenocarcinoma cells (OE33) after treating them with cisplatin and oxaliplatin.
Methods: Lethal doses 50 (LD50) of oxaliplatin and cisplatin in OE 33 cells for 24 hours were determined by the alamarBlue assay. Cells were treated with that LD50 at 2, 4, 6 and 24 hours. Using RT-PCR and specific primers, expression of ERCC1 and XPA gene levels with cisplatin and oxaliplatin treatments were compared at 2, 4, 6 and 24 hours interval, by Syngene Gene Tools programme.
Results: XPA was undetectable with cisplatin treatment, while it was overtly expressed with oxaliplatin treatment at all time intervals. Small amounts of ERCC1 were seen in 2, 6 and 24 hours with below detectable levels at