administration. RGTA-OTR4120 did not have an effect on amylase or total protein secretion.
Conclusion: RGTA-OTR4120 administration has a positive effect on salivary flow rates in irradiated mice on the short term. The effect was absent 10 weeks after radiotherapy, while at that time point, mucin producing activity of acinar cells was elevated by RGTA-OTR4120 administration. Given these results and the advantages of RGTA use in irradiated patients, further investigation on the potential of this drug to treat radiation-induced xerostomia, alone or in combination with other drugs, such as amifostine, is suggested.

1084 POSTER

Claudin-1 Acts as a Tumour Suppressor in Hepatoma Cell Lines

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Background: Altered expression of tight junction proteins such as occludin and claudins is widely implicated in carcinogenesis. In our previous study, we detected an overexpression of claudin-1 in a subset of HCCs. Furthermore, in an immunohistochemical study by Higashi et al., correlation was found between decreased claudin-1 expression and dedifferentiation, as well as portal invasion of HCCs. Our aim was to investigate how claudin-1 influences cell proliferation in hepatoma cell lines and to determine whether it acts as a tumour suppressor.
Methods: To establish a cell line that stably overexpresses claudin-1, low-expressing HepG2 cells were transfected with pCI-neo vector containing full-length claudin 1 cDNA and selected with geneticin. The control line was transfected with empty pCI-neo vector. Downregulation of claudin-1 expression was carried out by siRNA targeted to claudin-1 in Hep3B cells that exhibit high basal claudin-1 levels. Down- and upregulation of claudin-1 expression was confirmed by quantitative RT-PCR and Western blotting. Cell proliferation was investigated with sulforhodamine-B test. HepG2 cells (20 million/animal) were injected subcutaneously into nude mice (5−5 for CLDN1-overexpressing and control cells) in order to investigate the tumour formation.
Results: Stably transfected HepG2 cells showed an overexpression of claudin-1 (10-fold at mRNA, and 2-fold at protein level) as compared with control cells. On the other hand, siRNAs decreased claudin-1 expression by 67%. According to the sulforhodamine-B test, downregulation of claudin-1 expression resulted in an accelerated cell proliferation of Hep3B cells (1.35-fold; $p < 0.01$), whereas increased claudin-1 production minimally decreased the proliferation index of HepG2 cells (0.97-fold; $p < 0.01$). Tumour formation of HepG2 controll cells was observed in 3/5 mice, whereas no subcutan nodules could be detected in animals with HepG2-CLDN1 cells ten weeks after the injection.
Conclusions: The minimally reduced cell proliferation together with the inhibited tumour formation of HepG2 cells due to claudin-1 overexpression, as well as the accelerated cell division by siRNA silencing in Hep3B cells indicate that claudin-1 acts as tumour suppressor in HepG2 an Hep3B hepatoma cell lines.
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1085 POSTER

The Longitudinal Trajectory of Post-Traumatic Growth: a Longitudinal Study

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Background: The aim of the study is to investigate longitudinally the trajectory of post-traumatic growth (PTG; Tedeschi & Calhoun, 2006) in cancer patients. Secondly the study aims to study the relationship between PTG and intrusion vs. avoidance symptoms. Recently, empirical evidence highlights the presence of PTG (i.e. changes in the perceptions of oneself, one's social relationships, and one's life priorities) in 50% to 90% of patients. However less is known about the temporally trajectory of PTG and its correlates, because off the cross-sectional design of studies.
Material and Methods: A longitudinal study was conducted with a group of 53 cancer patients currently in the treatment and management phase of their illness. Data were collected by means of a written questionnaire, at two time points (T1 and T2) that were 24 months apart.
Post-traumatic growth was assessed by the Post-traumatic Growth Inventory. Intrusion and avoidance symptoms was measured by the Impact of Events Scale.
Results: Analysis showed that neither PTG levels neither avoidance symptoms change during the 24 months. On the contrary, intrusion symptoms increased significantly ($t = -2{,}02$, $df = 52$, $p < 0.05$). Further, both intrusion and avoidance symptoms was strongly related with PTG at t2 (respectively, $r = 0.37$; $r = 0.47$).
Conclusions: Data highlighted the temporal stability of the growth process that seems to be related to a cognitive engagement processes. From a clinical point of view data suggest the crucial role of meaning making process in fostering psychological adjustment to cancer illness and treatment.

1086 POSTER

Identification of the Receptor Tyrosine Kinase AXL as a New Target for Prostate Cancer Therapy

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Axl is a receptor tyrosine kinase of the family of TAM receptors (which includes TYRO3 and MER) and plays roles in different types of cancer. It is highly expressed in sarcoma, metastatic colon carcinoma, gastric and certain types of breast cancer. As Axl is upregulated in several metastatic cell types it may play a role during invasion and metastasis. Tyrosine kinases (TKs) represent a major class of proto-oncogenes and are involved in tumour growth, progression and metastasis of cancer cells. TKs are being actively studied as targets for therapeutic intervention and several of them have shown efficacy in clinical trials. Prostate cancer (PCa) is the most common solid cancer in older men and is one of the most frequent causes of deaths. Although androgen ablation therapy, surgery and radiation therapy are effective for the treatment of local PCa, there is no effective treatment available for patients with the metastatic androgen-independent disease. In this work we demonstrated the role of Axl in PCa progression and identified Axl as a potential target for PCa therapy. Using real time PCR to assess the level of tyrosine kinase receptors' expression in PCa cell lines and human tissue, we observed that Axl has consistent over-expression across cell lines and human prostate tumour tissue, providing a model for testing the targeting of Axl. Our data shows a significant increase in Axl expression in metastatic PCa cells and clinical samples (48% of adenocarcinomas of prostate compared with normal prostate tissue). Blockage of Axl gene expression using lentivirus encoding siRNA against Axl inhibits proliferation, migration and invasion of PCa cells. Our pilot studies in a xenograft subcutaneous model demonstrate that inhibition of Axl reduces tumour formation by 50%. Moreover, microarray analysis in addition to pathway analysis of Axl knockdown cells show that some survival pathways are inhibited, but strikingly all members of the NF-kB pathway are down regulated. To establish an alternative for PCa treatment we tested different inhibitors of the NF-kB pathway. Treatment of PCa cells with these drugs reduce proliferation and induce apoptosis. Furthermore, treatment of Axl knockdown cell lines with these drugs enhances their effects. Finally, in order to develop a specific inhibitor for Axl, we are evaluating a library of natural compounds from the African and Asian continents. We have found a compound that reduces proliferation and induces apoptosis in PCa cell lines and reduces Axl levels, thus representing a good candidate for future tests. Taken together our data demonstrates that Axl plays a role in migration, invasion and tumour development and can be used as a marker for invasive and metastatic tumours highlighting it as a target for drug therapies.

1087 POSTER

The Synergic Effect of CKD-516 to Conventional Chemotherapy

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Background: Tubulin polymerization inhibitors had emerged as one of promising anticancer therapeutics because of their dual mechanism of action, i.e. apoptosis by cell-cycle arrest and VDA, vascular disrupting agent. VDAs are believed to be more efficient, less toxic, and several of them are currently undergoing clinical trials.
CKD-516 is a vascular disrupting agent (VDA) that attacks only tumour vessels inhibiting microtubule assembly. CKD Pharmaceuticals is conducting a phase I study of CKD-516 in patients having refractory solid cancers in Korea.
The clinical success of VDA inhibitors depends on their combination with other conventional therapeutic agents. In search for new therapeutic modalities to target NSCLC, we investigated the effect of CKD-516 as a single treatment or in combination with the established therapeutic agents such as carboplatin and paclitaxel.