is due to the geometrical error in the diode positioning. The GRD results were in good agreement with those from the Gafchromic film for almost all the collimators.
Conclusions: For the GRD output factor measurements in water of CK system. It is found that GRD is a useful dosimeter for circular collimators smaller than 10 mm diameter, in good agreement with a Gafchromic film. Future study will be devoted to investigate for possibility of using GRD for quality assurance audit program of stereotactic radiosurgery units.

5512 POSTER

Expression of NHEJ genes in head and neck squamous cell carcinoma is associated with tumor response to 5-fluorouracil and cisplatin-based induction chemotherapy

M. Pavon[1], M. Parreño[1], X. León[2], M.V. Céspedes[1], I. Casanova[1], L.C. Navas[1], M.A. Mangues[3], M. Quer[2], A. Barnadas[4], R. Mangues[1]. *[1]Institut de Recerca. Hospital de la Santa Creu i Sant Pau, Grup d'Oncogènesi i Antitumorals(GOA), Barcelona, Spain; [2]Hospital de la Santa Creu i Sant Pau, Department of Otorhinolaryngology, Barcelona, Spain; [3]Hospital de la Santa Creu i Sant Pau, Department of Pharmacy, Barcelona, Spain; [4]Hospital de la Santa Creu i Sant Pau, Department of Medical Oncology, Barcelona, Spain*

Expression of NHEJ genes in head and neck squamous cell carcinoma is associated with tumor response to 5-Fluorouracil and cisplatin-based induction chemotherapy.
Background: Concomitant chemoradiotherapy (CRT) or 5-Fluorouracil (5-FU) and cisplatin-based induction chemotherapy (IC), followed by CRT or radiotherapy (RT), are used to treat locally advanced head and neck squamous cell carcinoma (HNSCC). We studied the relationship between tumor expression of non-homologous end joining (NHEJ) repair genes (Ku80, Ku70 or DNA-PKcs) and their response to IC. The role of NHEJ in double-strand break (DSB) repair, genomic instability (HNSCC chromosomal rearrangements) and apoptosis suggests a possible role on tumor response to RT, 5-FU or cisplatin since all these agents induce DSBs.
Patients and Methods: In a Prospective Study, we evaluated the mRNA levels of Ku80, Ku70 and DNA-PKcs in 50 pre-treatment HNSCC biopsies by RT-PCR.
In a Retrospective Study, we evaluated Ku80 and Ku70 protein expression in pre-treatment HNSCC biopsies of an independent cohort of 52 patients by Immunohistochemistry (IHC) staining. Protein expression was assessed by morphometric image analysis, applying the HSI color model. This method makes it possible to measure the percentage of Ku80 and KU70 positive tumor cells present in a given tumor sample image.
To establish the relationship between Ku80, Ku70 and DNA-PKcs mRNA levels (or Ku70 and Ku80 protein expression) and response, we classified tumors in two groups according to response after IC. The responder group included patients with a reduction in tumor size higher than 50%, whereas the non-responder group included patients with an increase, stabilization or decrease in tumor size lower than 50%.
Results: Tumors included in the responder group had significantly higher mRNA levels for Ku80 ($p = 0.002$), Ku70 ($p = 0.005$) and DNA-PKcs ($p = 0.017$) than tumors in the non-responder group.
We also observed by IHC that the percentage of Ku80 and Ku70 positive tumor cells was significantly ($p = 0.021$, $p = 0.023$, respectively) higher in the responder group than in the non-responder group.
Conclusions: Ku80, Ku70 and DNA-PKcs expression in pre-treatment biopsies of patients with locally advanced head and neck squamous cell carcinoma is significantly associated with tumor response to 5-Fluorouracil (5-FU) and cisplatin-based induction chemotherapy.
In spite of these results additional independent studies will be necessary to validate the capacity of these genes to predict response to induction chemotherapy and to establish the best expression cut point.

5513 POSTER

Topical chemoprevention of skin cancer with dual inhibitors of 5-LOX and COX-2 via a microemulsion system

L.N. Feng, V. Mardirossian, Z. Wang. *Boston University school of medicine, otolaryngology, Boston MA, USA*

Background: The cyclooxygenase (COX) and the 5-lipoxygenase (5-LOX) pathway have been suggested to play an important role in oral, colon, and other tissue carcinogenesis. However, it is unknown whether 5-LOX pathway contributes to skin carcinogenesis, and importantly whether combination of inhibitors of both pathways may have synergistic or additive effects of chemoprevention. In this study, we test topical combination application inhibitors of both pathways as a promising way for chemoprevention of skin cancer.
Material and Methods: Twenty four nude mice were intradermally inoculated with squamous cell carcinoma cells. Then these animals were divided into 3 groups (8 of each) to receive following treatments: (1) Celecoxib (a specific COX2 inhibitor); (2) combination of Zileuton (a specific 5-LOX inhibitor) and celecoxib; and (3) no treatment as a control. We investigated for the chemopreventive effects through topical application by a microemulsion system. Tumor growth continued to be measured for 15 days.
Results: The T50 (the time latency for the first 50% tumor to appear on all inoculated skin sites) were 3 days, 5days, and 6 days in control group, 6% celecoxib group, and 6% celecocib+6% zileuton group, respectively. Statistically, a significant difference of tumor growth was found between the control and two treatment groups. But the groups with the combined treatment had the best result, and showed an additive inhibitory effect on the incidence and growth of squamous cell carcinoma ($P < .001$).
Conclusions: The results clearly shows that both 5-LOX and COX2 play important roles in skin carcinogenesis, but a dual application of agents will significantly improve the results. We also found it would be a promising way to delivery celecoxib and zileuton through microemulsion system for topical inhibition of skin cancer. This is the first study for topical chemoprevention of skin cancer by combining inhibitors of 5-LOX and COX2.

5514 POSTER

Green tea extracts induce apopoptosis and inhibit in HGF-induced HNSCC progression in vitro

S.U. Kang, Y.R. Yoon, H.S. Hwang. *Ajou Univ. Hospital, Otolaryngology, Suwon, South Korea*

Purpose: Activation of hepatocyte growth factor(HGF) and its receptor, c-Met, has been known to be involved in many human cancer development and progression. During the search for an effective molecule inhibitor of HGF/c-Met signaling, we have found that Epigallocatechin-3-gallate(EGCG), the major bioactive polyphenol present in green tea, might inhibit HGF/c-Met signaling. Studies were performed to address whether EGCG inhibit HGF-dependent tumor proliferation and invasion in HNSCC.
Method: We performed RT-PCR and Western blot of HNSCC cell line. Proliferation assay, dispersion assay, wound healing assay, and invasion assay were performed in HGF 0, 10, 30 ng/mL HGF10+EGCG 1 μM, HGF10+EGCG10 μM, HGF30+EGCG1 μM, HGF30+EGCG10 μM. RT-PCR and zymography were performed to examine the roles of MMP-2 and MMP-9, as well as the relationship between HGF and MMPs in FaDu invasiveness. In addition, we confirmed HGF-mediated plasmin activation. We performed Tunnel assay, DNA fragmentation analysis, Annexin V staining, and FACS analysis for apoptotic effect of EGCG in HNSCC.
Results: Exogenous HGF significantly enhanced the growth of HNSCC cell and this phenomenon was inhibited by EGCG in dose-dependant manner. ($p < 0.05$) EGCG inhibited HGF-induced scattering of HNSCC cell. EGCG inhibited HGF-mediated migration and invasion of HNSCC cell in dose-dependant.($p < 0.05$). EGCG inhibits the HGF-Met-uPA-Plasmin network and MMP2, 9. We confirmed EGCG induced apoptotic phenomenon in Tunnel assay, Annexin V staining, DNA fragmentation analysis and FACS.
Conclusions: Inhibition of HGF/Met signaling by EGCG leads to decrease of proliferation and invasion in vitro, suggesting the possible use of EGCG in HNSCC associated with downregulation of HGF/Met signaling and the HGF-Met-uPA-Plasmin network and MMP2, 9.

5515 POSTER

Comparison of the efficacy and safety of miconazole 50 mg mucoadhesive buccal tablets to those of miconazole 500 mg gel in the treatment of oropharyngeal candidiasis: a prospective, randomised, single blind, multicenter, comparative, phase III trial in patients treated with radiotherapy for head and neck cancer

R.-J. Bensadoun[1], P. Attali[2]. *[1]Centre Antoine Lacassagne, Nice, France; [2]Bio Alliance Pharma Paris, France*

Background: Topical antifungal treatments are recommended as first line therapy for oropharyngeal candidiasis (OPC) in cancer patients. However, they are not used because of multiple daily dosing, bad taste and poor acceptance by patients. Miconazole 50 mg mucoadhesive buccal tablet (MBT) is a new delivery system that was reported to produce rapid and prolonged effective concentrations of miconazole in the mouth. Its pharmacokinetic profile is well suited to the treatment of OPC.
Patients and Methods: This prospective, single blind, randomised, comparative, multicenter trial was aimed at comparing the efficacy and safety of a 14-day treatment with MBT once daily to those of miconazole 500 mg oral gel (MOG) administered in 4 divided doses in head and neck cancer patients having undergone radiation therapy. Primary end point was clinical success at day 14. Secondary endpoints included clinical success at day 7, clinical cure, improvement in clinical symptoms, mycological cure, relapse rate and safety.
Results: A total of 282 were enrolled. Patients from both groups were not different at baseline, except for the extent of lesions and severely impaired