of proficient *CYP1A1* genotype with deficient *GSTM1* variant would result in particularly elevated lung cancer (LC) risk, especially for squamous cell carcinoma (SCC).
Material and methods: In order to validate whether the *CYP1A1-C*^{3801} (*CYP1A1*2*) allele has an unfavorable significance alone and/or in combination with the *GSTM1* deficiency, we compared the genotype distribution in LC patients (n = 141), healthy donors (HD, n = 204), and elderly tumor-free smokers and non-smokers (ED, n = 246).
Results: *CYP1A1*2* allele carriers demonstrated a clear-cut association with SCC: the adjusted OR were 2.22 (95% CI = 1.06–4.63) and 2.27 (95% CI = 1.14–4.52) when HD and ED were used as referents, respectively. *CYP1A1*2(+)/GSTM1(−)* combined genotypes were overrepresented in the SCC patients (14/70, 20.0%) and underrepresented in the ED (19/246, 7.7%) as compared to the intermediate prevalence in the HD (26/204, 12.7%); the adjusted OR for SCC versus ED reached 3.85 (95% CI = 1.43–10.33).
Conclusions: In agreement with some literature data, our results support the concerted role of *CYP1A1* and *GSTM1* at-risk genotypes in SCC predisposition.

1178 PUBLICATION

Nuclear Factor-kappa B activation by TNF-alpha in mesothelial cells and expression in Malignant Mesothelioma

E. Jennions[2], W. Swain[2], D. Stewart[1], J. Edwards[1], K. O'Byrne[3], R. Walker[4]. [1]*Glenfield Hospital, Department of Thoracic Surgery, Leicester, United Kingdom;* [2]*University of Leicester, Department of Oncology, Leicester, United Kingdom;* [3]*St James' Hospital, HOPE Directorate, Dublin, Republic of Ireland;* [4]*University of Leicester, Department of Pathology, Leicester, United Kingdom*

Background: Nuclear Factor-kappa B (NF-κB) is a heterodimeric transcription factor central to cellular stress responses and protection against apoptosis, making it a potential target for novel anti-cancer therapies. The role of NF-κB in malignant mesothelioma (MM) is not clear.
Materials and Methods: We evaluated 1) the nuclear translocation of NF-κB in MET5A cells in response to TNFα by immunofluorescence and a nuclear protein factor p65 assay; 2) the degradation of IκBα in response to TNFα, with and without the administration of pharmacological inhibitors; 3) the expression of NF-κB by immunohistochemistry in 146 MM samples and its impact on survival. NF-κB expression was correlated with clinicopathological variables, tumour angiogenesis and necrosis and the expression of the Epidermal Growth Factor Receptor (EGFR). The impact of NF-κB expression on survival was determined.
Results: The pattern of NF-κB expression in untreated MET5A cells was cytoplasmic, with nuclear translocation occurring in response to TNFα administration. Significantly increased levels of nuclear p65 were noted at 8 and 24 hours. Degradation of IκBα was observed in MET5A cells in response to TNFα, but this was not altered by the administration of LY294002, U0126, SB20380, NS398, Iressa or vitamin E. Although cytoplasmic or membranous immunostaining was seen in the majority of tumour samples (96.5%), nuclear localisation of NF-κB was seen in only 11% cases. There was no significant correlation between the level of expression of NF-κB and standard clinicopathological prognostic factors. NF-κB correlated with the expression of EGFR ($p = 0.001$). Survival analysis showed that nuclear NF-κB expression was associated with reduced survival ($p = 0.04$), whereas cytoplasmic expression was not ($p = 0.7$).
Conclusions: NF-κB is activated in MET5A human mesothelial cells in response to TNFα. NF-κB expression is a common feature of MPM and may be a novel prognostic factor. NF-κB may play an important role in the carcinogenesis of MM. NF-κB may be a valid therapeutic target for novel therapies in MPM.

1179 PUBLICATION

EGFR mutation in lung cancers treated by Gefitinib in Thailand

T. Prempree, C. Wongpaksa. *Piyavate hospital, Oncology and gene Therapy center, Bangkok, Thailand*

Background: The sub-group analysis of IDEAL 1 and IDEAL 2 gefitinib studies interested us in that the objective response rate (ORR) of Japanese NSCLC patients fared better than that of Caucasian counterpart. We started our work in Thailand recently by using the mutation study of EGFR gene reported recently by Lynch et al and Paez et al. We ask two questions: 1) Do gefitinib responders of THAI Ethnicity have EGFR mutations as seen in other studies? 2) Is the EGFR mutation rate in THAI NSCLC patients with no gefitinib treatment higher than that of international standard ?
Materials: Fresh lung tumor tissues and or tissue paraffin blocks of six Thai NSCLC gefitinib responders were studied by DNA extraction followed by PCR and DNA Sequencing. Normal DNA pair of each patient was obtained from their own blood leukocytes. DNA from 4 NSCLC patients of our own study who have yet to start gefitinib treatment and 10 additional DNA samples from NSCLC Archives tissue paraffin blocks and from frozen tissue bank were studied for the baseline EGFR mutation rate.
Results:
1. All six gefitinib responders have EGFR gene mutations 6/6 (100%).
2. Deletions and point mutations were among the most commonly found events, however, the base insertions have also been found often in exon 21.
3. Our preliminary data of DNA from 12 NSCLC samples without treatment have mutation rate of 4 /14 (28.5%) in their EGFR genes, exons 19 and 21.

Conclusion:
1. For Non small cell lung cancer, EGFR gene mutations at the Tyrosine Kinase Domain appeared to be required for objective gefitinib response.
2. Our preliminary data, even still small in number, appeared to suggest the high mutation rate in NSCLC in Thai Ethnic patients. Perhaps, this could explain the high success rate of gefitinib treatment in Asian countries. Further study is needed to substantiate our findings.

1180 PUBLICATION

The role of TTF1 as prognostic factor in stage III non-small cell lung cancer (NSCLC)

T. Berghmans[1], C. Mascaux[1,2], B. Martin[1], J.P. Sculier[1]. [1]*Institut Jules Bordet, Intensive Care Unit and Thoracic Oncology, Brussels, Belgium;* [2]*FNRS, Research Fellow, Brussels, Belgium*

Background: The 1997 International Staging System (ISS) separated stage III NSCLC patients into IIIA and IIIB. Stage III NSCLC represents a heterogeneous group and the ISS remains unsatisfactory in term of prognosis prediction. In a previous study, we observed that survival was better predicted when unresectable NSCLC patients were classified into stages IIIβ (T3–4N3) and IIIá (other TN stage III). The aim of the present study was to determine the role of a biological factor, TTF1 (thyroid transcription factor 1) as prognostic factor in stage III NSCLC in addition to stage and other known clinical factors.
Material and methods: All stage III NSCLC patients treated in our hospital were retrieved and searched for biopsy specimens. TTF1 was assessed by immunohistochemistry (Novocastra SPT24).
Results: Between 01/1987 and 07/2003, 108 assessable stage III NSCLC patients, for whom biopsies were available, were included in the study. Their principal characteristics were: median age 64 years (range 37–83), male/female 81/27, squamous/non squamous 52/56, IIIA/IIIB 44/64, III/III 89/16, median Karnofsky PS 80 (range 20–100). They were treated according to the following modalities: chemotherapy alone 44, radiotherapy alone 15, surgery alone 3 and combined treatment 46. Forty-four patients were positive for TTF1 (squamous 25.0% vs non-squamous 55.4%; $p = 0.007$). Nineteen patients were alive at the time of analysis (05/2005). In univariate analysis, good PS, surgery, normal platelet count were found good prognostic factors for survival ($p < 0.05$). In multivariate analysis, including all variables with a p value less than 0.2 in univariate analysis, only 3 factors were statistically significantly associated with better survival: good PS ($p = 0.005$), surgery ($p = 0.004$) and creatinine level ($p = 0.02$). When the analysis was restricted to adenocarcinoma or to non-squamous histology, TTF1 was found a potential prognostic factor for survival in univariate analysis ($p < 0.05$).
Conclusion: In stage III NSCLC patients, good PS, resectability and low creatinine level but not TTF1 are prognostic factors for survival. Nevertheless, TTF1 appears a potential prognostic factor for survival in adenocarcinoma.

1181 PUBLICATION

Bcl-2 family proteins and lymph node metastasis in bronchopulmonary carcinoid tumors

D. Trufelli[1], L. de Matos[1], J. Pereira[2], A. Santos[3], J. Sander[4], V. Capelozzi[3], R. Souto[5]. [1]*School of Medicine – ABC's Foundation, Santo Andre, Brazil;* [2]*Georges Pompidou European Hospital, Thoracic Surgery, Paris, France;* [3]*Hospital das Clínicas – School of Medicine – University of Sao Paulo, Pathology, Sao Paulo, Brazil;* [4]*School of Medicine – ABC's Foundation, Pathology, Santo Andre, Brazil;* [5]*School of Medicine – ABC's Foundation, Biochemistry, Santo Andre, Brazil*

Apoptosis or programmed cell death is a regulated process responsible for deletion of single cells in normal tissue turnover, allowing the organism to tightly control cell numbers and tissue size. The Bcl-2 family of proteins, which has a crucial role in intracellular apoptotic signal transduction, is composed by pro-apoptotic (Bax) and anti-apoptotic (Bcl-2) members. The objective of this study was to survey the occurrence of apoptosis in