Conclusions: This study reveals that the IL-1RN A2 allele seems to be involved in genetic susceptibility for the development of viral associated neoplasias. We assume that the mechanism trough which it increases the risk is by increasing the predisposition to shorter immune responses that predispose the host to develop easily viral infections. Therefore, oncogenic viruses can infect cells efficiently and promote cancer development.

106 Lung cancer risk and air pollution in an industrial region of Northern Spain: a hospital-based case-control study

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Background: Asturias, an Autonomous Region in Northern Spain with a large industrial area, registers high lung cancer incidence and mortality. While this excess risk of lung cancer might be partially attributable to smoking habit and occupational exposure, the role of industrial and urban pollution also needs to be assessed. The objective of this abstract was to ascertain the possible effect of air pollution, both urban and industrial, on lung cancer risk in Asturias.
Material and Methods: This study will be undertaken within the wider context of the Asturian Lung Cancer (*Cáncer de Pulmón en Asturias – CAPUA*) study, a hospital-based case-control study conducted in Asturias with the aim of ascertaining the influence of environmental and genetic factors on the development of lung cancer. This analysis included 626 lung cancer patients and 626 controls matched individually by ethnicity, hospital, age, and sex. Distances from the respective participants' residential locations to industrial facilities and city centers were computed. Using logistic regression, odds ratios (ORs) and 95% confidence intervals (95% CIs) for categories of distance to urban and industrial pollution sources were calculated, with adjustment for sex, age, hospital area, tobacco consumption, family history of cancer, and occupation.
Results: Whereas individuals living near industries displayed an excess risk of lung cancer (OR = 1.49; 95% CI = 0.93–2.39), which attained statistical significance for small cell carcinomas (OR = 2.23; 95% CI = 1.01–4.92), residents in urban areas showed a statistically significant increased risk for adenocarcinomas (OR = 1.92; 95% CI = 1.09–3.38). In the Gijon health area, residents in the urban area registered a statistically significant increased risk of lung cancer (OR = 2.17; 95% CI = 1.25–3.76), whereas in the Aviles health area, no differences in risk were found by area of exposure.
Conclusions: This study provides further evidence that air pollution, both urban and industrial, is a moderate risk factor for lung cancer, which varies according to histologic type and health area.

107 LNA™ based universal RT microRNA PCR system – a new generation high throughput QPCR platform optimized for development microRNA based molecular diagnostic assays on clinical FFPE and blood serum and plasma

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Background: Using a Locked Nucleic Acid (LNA™) based miRNA detection technology we have developed a high throughput QPCR system for genome wide detection of miRNAs in clinical paraffin-embedded tissue as well as blood derived plasma or serum. The use of the LNA™ bases adds critical specificity and sensitivity creating a more robust system for more rapid assay development in the clinical and diagnostic assay development.
Material and Methods: Blood derived serum or plasma are important bio-fluids that potentially hold critical biomarker information about disease diagnosis and prognosis. We have developed the advantages of our PCR system to provide a truly sensitive miRNA genome wide screening technology from extremely small volumes of blood derived serum or plasma. In addition the system is ideally suited for screening laser captured and macro-dissected tissue specimens allowing us to build extremely accurate and sensitive miRNA expression profiles from critical tumour biopsies.
Results and Conclusion: We have used the PCR system to screen miRNAs in colorectal cancer patient plasma samples and their matching tumour samples. We have been able to identify miRNAs in both the blood derived plasma and tumours that are differentially expressed between patients and healthy controls.

108 Association between FAS-670A/G polymorphism and ovarian cancer development

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Background: Apoptosis is an essential process in malignant cells elimination. One of the characteristics of malignant cells and of tumour development is tumoural cell evasion to apoptotic stimuli and alterations of the apoptotic pathways components.
FAS-670A/G polymorphism in the promoter region of *FAS* gene has been identified, it was proposed that *FAS-670* G allele may reduce Fas expression and might influence apoptosis activation. The aim of this study was evaluate if *FAS-670A/G* have a possible role in ovarian cancer development.
Methods: We performed Polymerase Chain Reaction – Restriction Fragment Length Polymorphism (PCR-RFLP) methodology, for *FAS* gene locus −670 genotyping. It was evaluated DNA samples from 428 women: 189 ovarian cancer patients and 239 healthy control female individuals.
Results: We found that the presence of GG genotype of *FAS-670* A/G represents a significant risk for development of grade III tumours (OR = 3.53; 95% confidence interval (CI): 1.30–9.58). Moreover, we found that individuals carrying *FAS-670* G allele had a higher risk of recurrence after first line chemotherapy with complete response (OR = 5.25; 95% CI: 1.51–18.2). Cumulatively, Kaplan–Meier function plots and probabilities analysis showed that *FAS-670* G allele carriers have a shorter recurrence free survival after first line chemotherapy with complete response (p = 0.017).
Conclusions: Our results indicate that *FAS-670A/G* may have an important role in ovarian cancer development; the study of this polymorphism could help selecting groups at progression risk.

109 Implementation of qPCR and sequencing for KRAS and EGFR mutation detection in Bulgarian patients with colorectal and lung cancer

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Background: Colorectal and lung cancer are among the most common human malignancies both in the United States and Europe. New targeted therapies have been developed in the past decade, such as monoclonal antibodies against epidermal growth factor receptor (EGFR) or KRAS oncogene. Genetic alterations of the intracellular effectors involved in EGFR related signaling pathways may have an effect on response to this targeted therapy Recent data now suggests a differential response to anti-EGFR antibody therapy based on mutational status of a major oncogene called KRAS and 18−21st EGFR's exons for patients with CRS and non-small cell lung cancer (NSCLC) respectively. The aim of this study was to introduce reliable methods for identifying of KRAS/EGFR mutational status in patients with CRC/NSCLC.
Methods and Results: In both groups DNA was extracted from paraffin embedded tissues. Twenty colorectal cancer patients were screened for KRAS mutations by qPCR based on Scorpions technology. Our results showed that five of those patients had mutations in the 12th codon of KRAS oncogene Two patients carried mutation 12 Asp, mutations 12 Ala, 12 Val and 12 Ser were found in the other three patients respectively. No mutations in the 13th codon of KRAS oncogene were found. Eight NSCLC patients were screened for EGFR mutations by qPCR based on high resolution melting technology and subsequent sequencing of aberrant profiles. Among these patients we found only 2 with mutations – one with a deletion (2236−2253del18) and the other a SNP(G719C) in 19th exon of EGFR.
Conclusion: Our study showed that HRM is reliable method for screening of NSCLC patients, however aberrant profiles should be sequenced in order to establish the exact mutation. Scorpion technology used for detection of KRAS status proved to be successful in all 20 patients.

110 Gastric adenocarcinoma development in patients with atrophy or/and intestinal metaplasia: the role of COX-2 polymorphisms in a Northern Portuguese population

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Background: COX-2 overexpression observed in 69% of gastric cancers (GC) and precancerous tissues is closely intertwined with key mechanisms of gastric carcinogenesis, namely inhibition of apoptosis, tumour growth, angiogenesis, invasion and metastasis. Genetic variations that modify6 the levels of COX-2 protein would be anticipated to have a substantial influence on disease phenotype. Hence, with this study we aimed at understanding the contribution of two functionally expected *COX-2* polymorphisms (−1195A>G and 8473T>C) in the development and progression of gastric lesions.
Material and Methods: A hospital-based case-control study was developed that gathered 134 patients diagnosed with gastric lesions (94 with GC and 40 with atrophy and/or intestinal metaplasia (AIM)) and 255 healthy individuals all from the Northern region of Portugal and recruited at Portuguese Institute

of Oncology, Porto. The −1195A>G and 8473T>C *COX-2* polymorphisms genotypes were characterized through PCR-RFLP and allelic discrimination techniques, respectively.

Results: The −1195A>G *COX-2* polymorphism did not appear to modulate the susceptibility for the development of gastric lesions in normal individuals (OR = 0.764; 95%CI:0.448–1.303 and OR = 1.823; 95% CI: 0.926–3.588 in −1195AG+GG genotypes carriers for GC and AIM onset, respectively). However, once the precancerous lesions were installed the −1195G allele was associated with a decreased risk for GC onset in AIM patients (OR = 0.419; 95% CI: 0.193–0.911). This protective effect in G allele carriers increased when we included the age and gender as covariates in a multivariate analysis (OR = 0.194; 95% CI: 0.075–0.499). Antagonically, for the 8473T>C genetic variation a 2.4-fold increased predisposition for AIM progression was reported in C allele carriers in the adjusted analysis.

Conclusion: The −1195A>G and 8473T>C *COX-2* polymorphisms emerged as susceptibility markers for AIM progression into cancer. The incorporation of genetic biomarkers in gastric cancer risk models might be of relevant importance as at this point there are no guidelines for the follow-up of individuals diagnosed with gastric precancerous lesions that ultimately may contribute to an early diagnosis of GC.

111 VEGF, VEGFR1 and bFGF gene polymorphisms and chronic lymphocytic leukemia

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Background: B-cell chronic lymphocytic leukemia (B-CLL) is a heterogeneous disease with a highly variable clinical outcome. Recent studies have documented that a number of different molecular prognostic markers have been identified (including mutational status of the *IgVH* gene, ZAP70 and CD38 expression) allowing to discriminate between patients in prognostic subgroups, but with no implications in the treatment beginning. Different expression patterns of *VEGF*, *VEGFR1* and *bFGF* have been related with the patient treatment requirements. We have analyzed the polymorphisms: *VEGFR1* −710 C/T, *VEGF* 936 C/T rs 833052, rs 1109324, rs 3025039, rs 1547651 and *bFGF* 223 C/T in order to determine possible relations with clinical prognosis.

Methods: Peripheral blood samples from 182 patients with CLL and 280 controls were genotyped using probes TaqMan® SNP Genotyping Assays (7900 HT Fast Real Time PCR System; Applied Biosystems). Samples were providing from the Hospital Clinic of Valencia. Four SNPs in the VEGF gene, one SNPs in the bFGF gene and one SNP in the VEGFR1 gene were evaluated. Statistical analysis was performed using SNPStats program (Catalan Institute of Oncology).

Results: We have observed an increased frequency in the T allele of bFGF 223 C/T (rs1449683) in our LLC-B patients when compared to control subjects [Fisher's exact p-value = 0.066; OR 1.70 (95% CI: 0.97, 2.98)].

Conclusion: This preliminary data indicate an increased frequency of the T allele of polimorfismo bFGF 223 c/t which possibly account for the individual supsceptibility to the develop of B-CLL. Further studies regarding the role of pro-angiogenic markers in CLL would be beneficial to help elucidate pathogenic pathways in this disease.

112 The importance antioxidant, antiangiogenesis and immune enhancement supplements in cancer

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Antioxidant, antiangiogenesis and immune enhancement treatments may facilitate current classical treatments in fighting cancer. There are an increasing number of scientific publications that show nutritional supplements play important roles in counteracting the formation and propagation of cancer. These supplements include the following: Acetyl L-Carnitine (ALC), Alpha Lipoic Acid (ALA), Coenzyme Q10 (CoQ10), Curcumin with Peperine, Genistein, Lentinan, N-AcetylCysteine (NAC), Resveratrol, selenium, Vitamin B Complex, Vitamin C, Vitamin E and zinc. These ingredients have been demonstrated, either individually or collectively, to have antioxidant, anti-angiogenesis, and immune stimulation properties. Furthermore, the scientific literature supports direct cancer cell cytotoxicity for Curcumin, Geinstein and NAC. The Formulation component activities are supported by over 13,000 references in the scientific literature (PubMed.com) and over 1,200 clinical trials (clinicaltrials.gov). From the literature there is evidence that some of the antiangiogenesis components affect the majority if not all pathways of angiogenesis when used in combination. Furthermore, Curcumin, Genistein and NAC actually stimulate the *in vivo* production of natural antiangiogenic compounds which include Angiostatin, Endostatin and Thrombospotin 1. All of the above components play a role in serving as either water or lipid soluble (able to cross the blood-brain barrier) antioxidants. Curcumin, Genistein, Resveratrol, Lentinen, NAC, zinc, selenium and the B and C vitamins all stimulate the immune system. Except for ALC and CoQ10, the other components show anti-inflammatory activity. ALC, Resveratrol along with the B and C vitamins are helpful in treating fatigue. The components that help protect the brain and promote nerve regeneration include ALA, CoQ10, Resveratrol, NAC, selenium, zinc and the B and C vitamins. Limited clinical studies with the supplements have resulted in positive outcomes in late stage disease patients. In conclusion, effective prevention and treatment for diseases such as cancer, heart disease and immune deficiency will require multiple compounds. The safety and efficacy of these components on an individual component basis are the targets for a number of clinical trials. However, treating them as nutritional supplements may allow a multicomponent approach for the prevention and complementary treatment of cancer.

Clinical cancer literature and trial references to each component

Formulation components	Total articles	2009–2010	Cancer trials
ALC	14	3	4
ALA	52	2	4
CoQ10	65	1	4
Curcumin	732	53	24
Genistein	1290	44	19
Lentinan	159	6	3
NAC	572	31	47
Resveratrol	711	49	8
Selenium	1885	69	41
Zinc	2800	102	13
B Complex	203	14	572
Vitamin C	2192	49	272
Vitamin E	2752	87	199

113 ADH3 Ile349Val polymorphism influence on genotoxicity biomarkers frequency in workers occupationally exposed to formaldehyde

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Formaldehyde (FA) is a highly water soluble gas when inhaled, reacts rapidly at the site of contact and is quickly metabolized by enzymes in the respiratory tract and in the red blood cells. Genetic polymorphisms in enzymes involved in the metabolism are very important and can make changes in the individual susceptibility to disease. Alcohol dehydrogenase class 3 (ADH3), also known as FA dehydrogenase dependent of glutathione, is the major enzyme involved in the FA oxidation, especially in the buccal mucosa. The polymorphism in study is a substitution of an isoleucine for a valine in codon 349 of ADH3. The goal of this study was to investigate the possibility of an association between the ADH3 Ile 349 Val and the mean of micronucleus (MN) in lymphocytes and mucosa buccal cells, nucleoplasmic bridges (NPB) and nuclear buds (NBUD) in occupationally workers exposed to formaldehyde.

The study was carried out in Portugal in a sample of 56 workers occupationally exposed to FA in pathology anatomy laboratories and in 85 non-exposed subjects. The evaluation of genotoxic effects was conducted by applying cytokinesis blocked micronucleus assay (CBMN) in peripheral blood lymphocytes (PBL) and the MN test in exfoliated cells from buccal mucosa. The data were analyzed statistically using Logistic Regression.

The mean of all genotoxicity biomarkers in study was higher compared with controls, a statistically significant difference (Mann-Whitney test, $p < 0.001$).

Exposed and controls carrying the Val/Val genotype were found to have higher mean in MN in PBL (4.75 vs 3.81 and 2.00 vs 0.65) and in NBUD (1.50 vs 0.44 and 0.11 vs 0.06), respectively.

Both groups, exposed and controls, had lowers means of MN in buccal mucosa cells with the heterozigotic genotype and NPB in the controls. Multiple regression analysis indicated that the exposure to FA was an important variable affecting the genotoxic response, but the polymorphism ADH3 Ile 349 Val was not found statistically significant, with the exception for MN in PBL.

The lower enzymatic activity of ADH3 has probably an impact against the stress caused by FA exposure, especially in tissues with direct contact like oral epithelium. It was not observed in this study association between ADH3 polymorphisms and MN in buccal mucosa cells. However, a protective association between the ADH3 heterozygotic genotype and PBL MN was found. This result is showed in some studies, concluding that heterozigotic alleles have a protective role.