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.