Materials and Methods: To determine the prevalence of *IDH1* and *IDH2* mutations in Bulgarian patients and their impact on prognosis, 31 glial tumours, including astrocytomas and oligodendrogliomas of various grades, were examined by sequencing for mutations in exon 4 of *IDH1* and *IDH2* genes.
Results: *IDH1* carried genetic alterations in 8 (26%) tumour samples. All mutations were G to A changes at position 395 which caused amino acid substitution R132H. Mutations in *IDH2* were not detected. Genetic alterations in *IDH1* were found in younger patients of all grades (median age 35.5 vs 53 in non-mutated cases; p = 0.003) and were associated with an increased overall survival (median survival 32 months vs 5.5 in non-mutated cases; p = 0.018).
Conclusions: *IDH1* genetic alterations may be used as a specific marker for prognosis prediction in Bulgarian patients with glial tumours.

891 TP53 binding protein-1 and mutated in Ataxia-Telangiectasia gene variants affect TP53 mutations in lung cancer

S. Zienolddiny[1], V. Skaug[1], A. Haugen[1]. [1]*National Institute of Occupational Health, Chemical and Biological Work Environment, Oslo, Norway*

Background: Lung cancer is a major cause of cancer-related deaths in the world. Cigarette smoking, environmental and occupational exposures are major etiological factors. The TP53 protein is a key player in DNA damage, repair and cell-cycle checkpoints. Alterations in the *TP53* gene are important events and occur early during lung carcinogenesis.
Material and Methods: We have investigated polymorphisms in the TP53 pathway genes including *TP53*, *TP53BP1*, *P73*, *ATM, DDB-2, GADD45a* and *XRCC1* in 272 Non-small cell lung cancer patients and analyzed the data in relation to the frequency, pattern and spectrum of somatic tumour-associated mutations in the *TP53* gene.
Results: Here we report significant association between *TP53* mutations with the variant genotypes of *TP53BP1*and *ATM* genes. For the *TP53BP1* homozygote variant Asp353Asp carriers were less likely to have a mutated *TP53* in the tumour compared to carriers of the common Glu353 allele (P = 0.008). Presence of the Asp353Asp genotype had a significant protective effect on occurrence of tumour-associated *TP53* mutations (odds ratio 0.24; 95% CI, 0.07–0.83). The number of lung cancer cases with a variant A allele of the *ATM* (rs664143, G>A) gene and a tumour-associated mutation in the *TP53* gene was significantly higher than cases with the common G allele (P = 0.009). This was associated with increased odds of harbouring a *TP53* mutation in the tumour (OR 2.60; 95% CI, 1.14–5.91). We also analyzed the pattern and spectrum of the *TP53* mutations in hot spot codons in relation to the *TP53BP1* and *ATM* genotypes. The *ATM* variant genotype was associated with a higher frequency of mutations affecting the hotspot codon 273. Furthermore, there was an overload of G to T transversions in subjects carrying at least one A variant allele of the *ATM* gene.
Conclusion: The results suggest that the genotypes of *TP53BP1* and *ATM* genes may modulate the frequency as well as mutational pattern in lung tumours.