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Alkyladenine-DNA glycosylase (AAG) and alkylguanine-DNA alkyltransferase (MGMT) repair activity in peripheral blood mononuclear cells (PBMC) from lung cancer cases and cancer free controls

P A J Crosbie¹, A J Watson¹, P V Barber³, R Agius², A C Povey², G P Margison¹

¹Carcinogenesis Group, Paterson Institute for Cancer Research, Manchester, United Kingdom; ²Centre for Occupational and Environmental Health, Manchester University, Manchester, United Kingdom; ³North West Lung Centre, Wythenshawe Hospital, Manchester, United Kingdom

DNA damage, caused by tobacco smoke carcinogens, is a critical step for lung cancer development. Differences in the ability to repair DNA damage may make some individuals more susceptible to lung cancer. To explore this we investigated the activity of two DNA repair functions, AAG and MGMT that repair respectively alkyladenines and O⁶-alkylguanines, DNA damage that is induced by alkylating agents such as the tobacco-specific nitrosamines present in cigarette smoke.

Repair activity was determined using two [³²P]-based oligonucleotide cleavage assays in PBMCs collected from 42 incident lung cancer cases and 77 cancer free controls. AAG activity was detected in all samples (range 1.37 – 8.43 fmole/μg DNA / hr) and MGMT in 114 / 119 samples (range 0.4 – 13.37 fmole/μg DNA). AAG and MGMT repair activities were significantly correlated ($R^2 = 0.24$, $p = 0.0001$).

Repair activity of either protein was not related to age or gender. MGMT activity was also unrelated to smoking or case status whereas there was evidence that AAG activity was greater in current and former smokers when compared to never smokers ($p=0.06$ and 0.07 respectively). AAG activity was significantly higher in cases than controls ($p=0.02$); when stratified by smoking status, only current smoking cases were significantly higher than controls ($p=0.04$).

The increased expression of AAG, by as yet unknown mechanism/s, may be a factor in smoking-related lung cancer induction.