investigated. We analysed methyltransferase gene expression in workers exposed to high levels of metal-rich particles, and its relationship with the DNA methylation of nine inflammatory and tumour suppressor genes.

Methods We recruited 63 healthy male foundry workers. Individual exposure to arsenic and other metals was estimated based on metal components in PM10 collected in each work area (by coupled-plasma mass spectrometer) and on time spent in different areas by each worker. Methyltransferase gene expression was measured by real-time PCR in blood leucocytes DNA. Gene-specific DNA methylation was measured trough bisulfite PCR-pyrosequencing. Multivariable linear regression models adjusted for age, BMI, smoking and drug consumption, were applied to assess the association between exposure and methyltransferase expression and, in turn, between methyltransferase expression and gene-specific methylation. Geometric mean ratios (GMR) were used to express results of log-transformed variables.

Results Enhanced methyltransferase (DNMT3B) gene expression was associated with increased exposure to arsenic (GMR=1.52, 95% CI: 1.06 to 2.20) and to other contaminants (Cu, Mo, Sn, Sb). DNMT3B expression was in turn associated with hypermethylation of the RASSF1A tumour suppressor gene (β=0.54, 95% CI: +0.15 to +0.94) and with hypomethylation of the Et-1 and IL-6 genes.

Discussion Our preliminary data suggest the possible role of methyltransferase gene overexpression in the pathway linking metal exposure to oncogene regulation. In particular, we found an increased DNMT3B expression in arsenic-exposed workers, that resulted also in hypermethylation (down-regulation) of RASSF1A. Interestingly, RASSF1A is a tumour suppressor gene involved in the development of cancers related to As exposure (bladder, lung).

134 PKC θ-MEDIATED CA^{2+}/NF-AT SIGNALLING PATHWAY MAY BE INVOLVED IN T-CELL IMMUNOSUPPRESSION OF COAL-BURNING ARSENIC-POISONED POPULATION

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Introduction Arsenic poisoning is a worldwide endemic disease that affects thousands of people. Growing evidence from animal, cell, and human studies indicates that arsenic has deleterious effects on immune systems, but its specific mechanism needs to be further explored.

Methods This is a population-based study that observed the changes in the proliferation of human T cells, IL-2, and INF-γ mRNA expression of coal-burning arsenic-poisoned population and control population. In addition, the intracellular calcium index, expression of PKC θ and phosphorylated PKC θ, and the DNA binding activity of NF-AT in PBMCs were analysed.

Results In the exposure group, and the mild, moderate, and severe arsenic poisoning groups, the stimulation indexes of the T cells, the mRNA expression of IL-2 and INF-γ significantly reduce in comparison to the control group. A correlation analysis shows a clear correlation between PKC θ/NF-AT signalling, (Intracellular calcium index, PKC θ, *p*-PKC θ and the activity of the NF-AT binding DNA) T cell proliferation, and inflammatory factors (IL-2 and INF-γ).

Conclusion Coal-burning arsenic can cause T cell immunosuppression in the population, and participates in the occurrence and development of arsenic poisoning. In addition, the PKC θ-mediated Ca^{2+}/NF-AT signalling pathway may be involved in the T-cell immunosuppression of the coal-burning arsenic poisoned population. The study provides important research data towards a mechanistic understanding of endemic arsenic poisoning. The next step should be to verify the results of this research *in vitro* and with a larger cohort.

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1367 THE ASSOCIATION BETWEEN PARKINSONISM AND QUALITY OF LIFE IN SOUTH AFRICAN MANGANESE MINE WORKERS

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Introduction Manganese is an essential micronutrient but excessive levels are harmful, and have been associated with parkinsonism. We sought to confirm the association between parkinsonism and quality of life (QoL), previously described in manganese-exposed welders, in a cohort of manganese mine workers, thereby also testing the usefulness of a tool originally designed for use in clinical settings.

Methods The study population comprised 418 manganese mine workers in South Africa. Parkinsonism was defined as a Unified Parkinson Disease Rating Scale motor score (UPDRS3) >15. The 39–item Parkinson Disease Questionnaire (PDQ-39) was used to assess miners' health status and/or QoL – our primary outcome. For this analysis, violation of the constant variance assumption led to a 'square root' transformation of the outcome variable. We used Mann-Whitney and Pearson's Chi-Square (or Fishers exact) tests to compare participants' parkinsonism status regarding baseline continuous and categorical characteristics. Multiple linear regression modelling was used to quantify associations.

Results The mean age of participants was 41.5 years; 97.6% were male. The prevalence of parkinsonism was 29.4%. QoL sub-scores and total scaled PDQ-39 score means were higher in mine workers with parkinsonism, relative to the rest of the cohort. Age (β=−0.48, p=0.031) and parkinsonism (β=0.63, p=0.004) were strong predictors of QoL. QoL was negatively associated with age; and parkinsonism predicted poorer QoL and/or health status.

Conclusion We found a strong association between parkinsonism and QoL abnormalities in manganese mine workers, confirming previous reports in manganese–exposed welders. The PDQ-39 proved to be a robust tool for assessing QoL in these workers.