

Global and gene-specific promoter methylation changes and micronuclei levels in construction workers exposed to environmental carcinogens.

Isana Rodrigues-Silva (Molecular Oncology Research Center, Barretos Cancer Hospital, Brazil), Manoela C.A.S Ramos (Molecular Oncology Research Center, Barretos Cancer Hospital, Brazil), Fernanda Cury (Molecular Oncology Research Center, Barretos Cancer Hospital, Brazil), Lidia M.R.B Arantes (Molecular Oncology Research Center, Barretos Cancer Hospital, Brazil), André V.H Lengert (Molecular Oncology Research Center, Barretos Cancer Hospital, Brazil), Fernando Barbosa Jr (Laboratório de Toxicologia e Essencialidade de Metais, Departamento de Análises Clínicas, Toxicológicas e Bromatológicas, Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP, São Paulo, Brazil) and Henrique C.S Silveira (Molecular Oncology Research Center, Barretos Cancer Hospital, Brazil).

BACKGROUND: Construction sector has a large representation in the Brazilian economy and social importance. The workers have long working hours and are exposed to various environmental and occupational factors that can lead to the development of diseases such as cancer. It is estimated that about 2% to 8% of cancers worldwide occur as a result of occupational exposure to carcinogens, with the most common is lung cancer, which is responsible for 70% of cases. The exposure of construction workers to materials containing asbestos, silica, metals and solar radiation, are factors that can be affecting the genomic stability and promote epigenetic alterations.

HYPOTHESIS: Thus, our aim was to evaluate through biomarkers, the association of potential risk of cancer in construction workers with occupational exposure to carcinogens. For this, it was determined the methylation status of tumor suppressor genes APC, RASSF1A, CDKN2A, MLH1, MGMT and repetitive sequences ALU and LINE-1 in construction workers and compared with a group of workers without exposure, using pyrosequencing methodology. Furthermore, to determine the genomic instability we evaluated the micronuclei frequencies in lymphocytes and buccal cells in both groups. Furthermore, we were assessed the metal components in blood of construction workers.

METHODS: We recruited 59 construction workers and 49 workers of administrative sector. A questionnaire was used to collect detailed information on lifestyle and occupational history. The both groups showed an age average of 35 years and all individuals were no smokers. The peripheral blood leukocyte (PBL) samples were extracted the DNA and submitted to bisulfite conversion and the methylation profiles of the samples were assessed by pyrosequencing methodology. The frequency of micronuclei in exfoliated buccal cells and peripheral blood lymphocytes was determined in both groups. Indeed, the metal components were measured through multi-elemental analysis performed by means of inductively coupled-plasma mass spectrometer (ICP-MS).

RESULTS: The questionnaire analysis was verified that construction workers group showed a mean age of 39 years and the control group of 32 years. It was verified that the case group has more frequent exposure to sand, concrete, wood dust and ultraviolet radiation. The pyrosequencing analysis demonstrated statistically significant means for the CDKN2A, MLH1, APC genes and LINE-1 repetitive sequence in construction workers compared to the control group. Confounding factors, such as drinking habit and passive smoke have no influence on methylation levels of genes. Agents found in the construction environment, like concrete and silica seem to influence the methylation status of MLH1 gene and LINE-1 repetitive sequence, respectively. The frequency of micronuclei was higher in the construction workers and no statistical differences were established metal components. In conclusion, it was verified alterations in methylation status of CDKN2A, MLH1, APC genes and LINE-1 repetitive sequence in construction workers compared to the control group. Furthermore, it was found higher frequencies of micronuclei in construction workers group. These findings suggest that the construction environment can influence the methylation profile of genes involved in the carcinogenesis and can also lead to changes in genomic instability.