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Title: Microsatellite alterations at 3p and 19q in EBC/DNA of smokers: Are they reversible after smoking cessation?

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Body: Microsatellite alterations (MAs) at 3p and 19q are early targets for cigarette smoke and markers of genetic susceptibility to lung cancer. Several susceptible genes modulated by smoking have been found to return to baseline years after smoking cessation. Although great interest has been devoted to the classification of smoke-related genetic alterations as reversible or irreversible, as it seems to influence the different biological functions, none have yet focused on MAs at 3p and 19q. The aim of this study was to analyse MAs at 3p and 19q in exhaled breath condensate (EBC)/DNA and WB/DNA of smokers after 12 months from smoking cessation. The 63 smokers enrolled in the study participated in a multidisciplinary smoking cessation program with a genetic study. All the subjects enrolled underwent EBC and whole blood (WB) collection at baseline. The 28 smokers (20 M, 53±8.5 yrs) who stopped smoking followed up and repeated sample collection after 12 months. All subjects had allelotyping analysis of DNA from EBC and WB from of a selected panel of seven microsatellites located in 3p and 9q. MAs at 3p and 19q resulted higher in EBC/DNA than in WB/DNA and dose-dependent from cigarette smoking. These somatic alterations both in EBC/DNA and in WB/DNA resulted as being not modifiable after 12 months from smoking cessation. In conclusion we demonstrated for the first time that MAs at 3p and 19q are not modifiable in short term from smoking cessation, although a longer follow-up is needed to better classify MA at these loci. Furthermore, we supported the usefulness of smoking cessation programs based on the information on genotype for its potential ethical consideration.