Decreased PM10 exposure attenuates age-related lung function decline : genetic variants in p53, p21, and CCND1 modify this effect

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 1196524
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Year 2009
Title Decreased PM10 exposure attenuates age-related lung function decline : genetic variants in p53, p21, and CCND1 modify this effect
Journal Environmental Health Perspectives
Volume 117
Number 9
Pages / **Article-Number** 1420-7
Keywords air pollution, cell cycle, cohort study, genes, respiratory function tests

BACKGROUND: Decreasing exposure to airborne particulates was previously associated with reduced age-related decline in lung function. However, whether the benefit from improved air quality depends on genetic background is not known. Recent evidence points to the involvement of the genes p53 and p21 and of the cell cycle control gene cyclin D1 (CCND1) in the response of bronchial cells to air pollution. OBJECTIVE: We determined in 4,326 participants of the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA) whether four single-nucleotide polymorphisms in three genes [CCND1 (rs9344 [P242P], rs667515), p53 (rs1042522 [R72P]), and p21 (rs1801270 [S31R])] modified the previously observed attenuation of the decline in the forced expiratory flow between 25% and 75% of the forced vital capacity (FEF(25-75)) associated with improved air quality. METHODS: Subjects of the prospective population-based SAPALDIA cohort were assessed in 1991 and 2002 by spirometry, questionnaires, and biological sample collection for genotyping. We assigned spatially resolved concentrations of particulate matter with aerodynamic diameter > or = 10 microm (PM(10)) to each participant's residential history 12 months before the baseline and follow-up assessments. RESULTS: The effect of diminishing PM(10) exposure on FEF(25-75) decline appeared to be modified by p53 R72P, CCND1 P242P, and CCND1 rs667515. For example, a 10-microg/m(3) decline in average PM(10) exposure over an 11-year period attenuated the average annual decline in FEF(25-75) by 21.33 mL/year (95% confidence interval, 10.57-32.08) among participants homozygous for the CCND1 (P242P) GG genotype, by 13.72 mL/year (5.38-22.06) among GA genotypes, and by 6.00 mL/year (-4.54 to 16.54) among AA genotypes. CONCLUSIONS: Our results suggest that cell cycle control genes may modify the degree to which improved air quality may benefit respiratory function in adults.

Publisher National Institute of Environmental Health Sciences
ISSN/ISBN 0091-6765 ; 1552-9924
edoc-URL http://edoc.unibas.ch/dok/A5843182
Full Text on edoc Available;
Digital Object Identifier DOI 10.1289/ehp.0800430
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/19750108
ISI-Number WOS:000269479900032

Document type (ISI) Journal Article