OXIDATIVE STRESS PATHWAY GENES, ENVIRONMENTAL TOBACCO EXPOSURE AND ASTHMA

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Background and aims. Studies on environment by gene interactions are challenged by multiple comparisons and contrasting findings from analyses conducted at the single nucleotide polymorphism (SNP) level. Until now, joint examination of several genes was performed at the functional level, but not at the pathway analysis level which consider protein interactions.

Methods. A four-step strategy is proposed:
1) Bioinformatic step based on **G**ene **O**ntology (GO) to define a) a list of genes with a given function (here response to oxidative stress) and b) the pathways in which these genes are involved (such as 'Metabolism of Xenobiotics by Cytochrome P450')
2) Selection step to choose candidate pathway(s) based on the biological knowledge of response to environmental hazard
3) Association analyses step performed at 1-the SNPs, 2-the genes and 3-the pathways levels
4) Validation of our findings in other epidemiological studies.

Results of steps 1 to 3 will be presented for 1900 subjects from the EGEA study, using genotypes from genome-wide data (Illumina 610quad, 2M imputed SNPs), and considering asthma, ETS and candidate pathways involved in response to oxidative stress.

Results.

Step 1: 190 genes were defined through GO browser (**GO** term 0006979) and 75 by literature search, corresponding to 285 different pathways according to Ingenuity Pathway Analysis software.

Step 2: 12 pathways (including 106 genes, 10-26 genes/pathway) were retained by taking into consideration biological knowledge regarding both the environment (ETS) and the disease (asthma), such as 'NRF2-mediated Oxidative Stress Response', 'apoptosis', ...

Step 3: Effect estimates for SNP allele dosage, ETS exposure and their interaction on asthma will be presented. Comparisons will be made between methods used for the gene/pathway approach (classical and the adaptive truncated product method to combine p-values).

Conclusions. Beyond collaboration between studies, interdisciplinary approach is needed to develop pathway approach in environmental epidemiology. (Supported by BIO_2NEA, IAGO.)