# DEPARTMENT OF GENETIC ECOTOXICOLOGY

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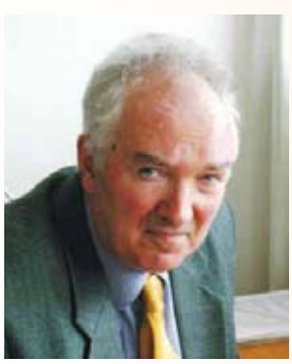

## LABORATORY OF MOLECULAR EPIDEMIOLOGY

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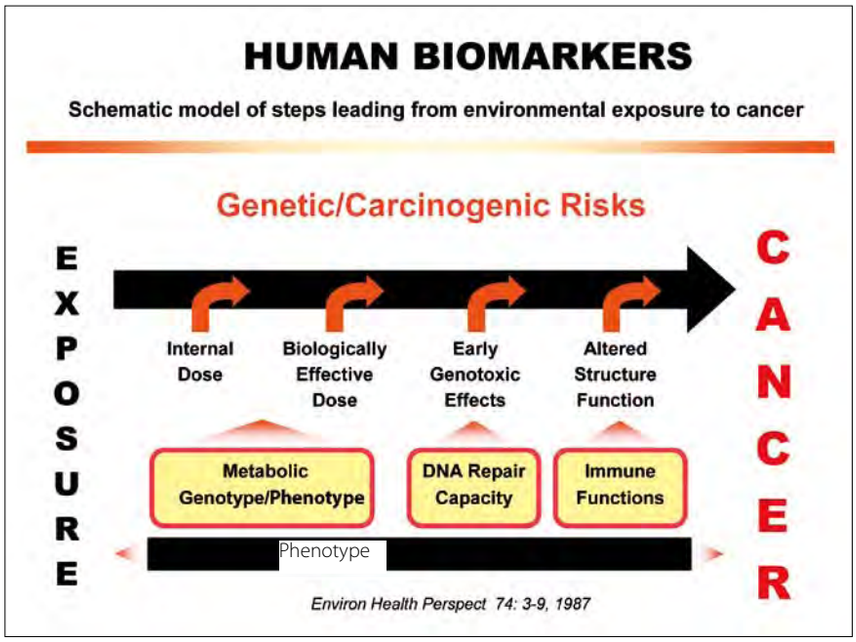
## RESEARCH TOPICS

The Department of Genetic Ecotoxicology (DGE) was formed from the Laboratory of Genetic Ecotoxicology, which in turn was founded in 1991 as a joint venture of the Institute of Experimental Medicine AS CR and the Regional Institute of Health of Central Bohemia with the aim of coordinating the international Teplice Program (1991–1999). This program, which studied the effect of air pollution on the health of the population living in the coal basin of Northern Bohemia, was carried out in collaboration with the U. S. Environmental Protection Agency and was supported by the EC program PHARE. This international collaboration helped to establish molecular epidemiology methods and to use them to assess the risk of exposure to air pollution.

The major findings included the fact that carcinogenic polycyclic aromatic hydrocarbons (c-PAHs) in the ambient air are responsible for most of the genotoxicity of complex mixtures and that exposure to c-PAHs in the early stages of pregnancy significantly increases intrauterine growth retardation (IUGR). Further, in polluted regions the relationship between c-PAHs exposure and DNA adduct levels, as well as the effect of genetic polymorphisms on DNA adducts, were studied.

The DGE participates in other international collaborative projects (EC, US EPA, HEI); among these, participation in the EC project EXPAH (Effects of PAHs in environmental pollution on exogenous and endogenous DNA damage, QLK4-CT-2000-00091) has been the most important.

Research in the DGE concentrates mostly on the effects of air pollution on genetic material, on the mechanisms of changes induced by environmental factors as well as modeling the relationships between individual factors (e. g. air pollution vs. life style), and the genetic damage caused by genotoxic and carcinogenic compounds, including polycyclic aromatic hydrocarbons, alkenes and other xenobiotics.



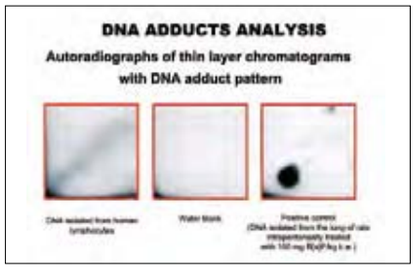

## THE RESEARCH IS ORGANIZED IN SEVERAL LEVELS

- Model studies on human cell cultures;
- molecular-epidemiological studies on model populations using biomarkers of exposure, effect and susceptibility;
- reproductive epidemiology – the effect of the environment on pregnancy outcomes (the involvement of genetic material, genetic polymorphisms, gene expression, and oxidative stress);
- the effect of air pollution on upper respiratory diseases in children and the modulatory effects of genetic polymorphisms on childhood morbidity.

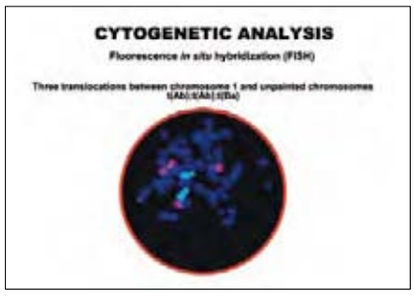
Currently, molecular-epidemiological studies are being conducted on volunteers in Prague and Ostrava, reproductive epidemiology studies in Prague and České Budějovice, and epidemiology studies on respiratory morbidity in children from the Teplice, Prachatice and Ostrava regions. As far as respirable particulate matter and c-PAHs are concerned, the Ostrava region is considered the most polluted EU area.

# Laboratory of Molecular Epidemiology

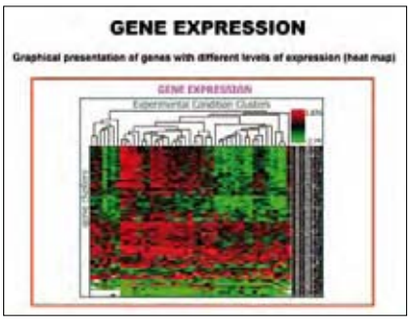
The Laboratory of Molecular Epidemiology conducts molecular epidemiological studies, including the risk assessment of mutagen and carcinogen exposure, using biomarkers of exposure, effect and susceptibility (DNA adducts,



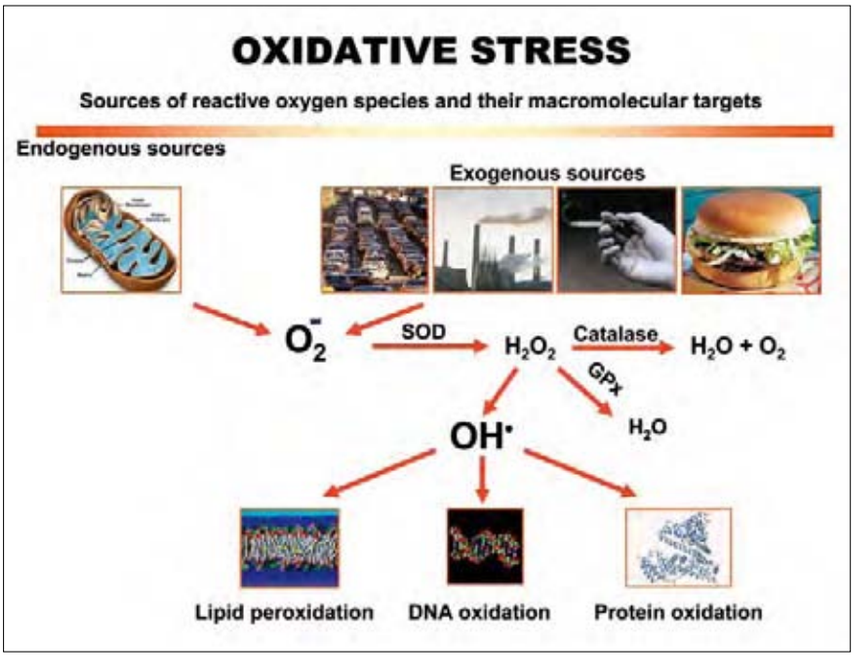

chromosomal aberrations,

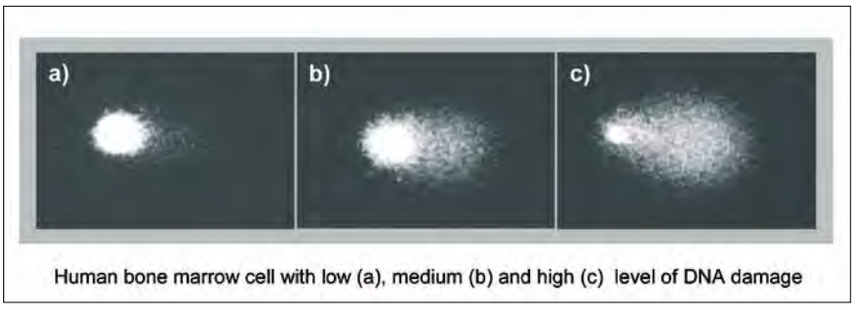


micronuclei, oxidative damage to DNA, proteins and lipids)




analyses of genetic polymorphisms and RNA expression profiles, studies of the effect of the environment on pregnancy outcomes, and the effect of the environment on children's health. DNA instability in patients with myelodysplastic syndrome is also studied.




Human bone marrow cell with low (a), medium (b) and high (c) level of DNA damage

# Laboratory of Genetic Toxicology

The Laboratory of Genetic Toxicology concentrates on the genotoxic effects of xenobiotics and oxidative damage to DNA, proteins and lipids in cell cultures (the hepatoma cell line HepG2, human diploid embryonic fibroblasts). The laboratory also studies the effect of environmental pollutants on the mechanisms underlying prostate cancer induction and progression.

# Laboratory of Genomics

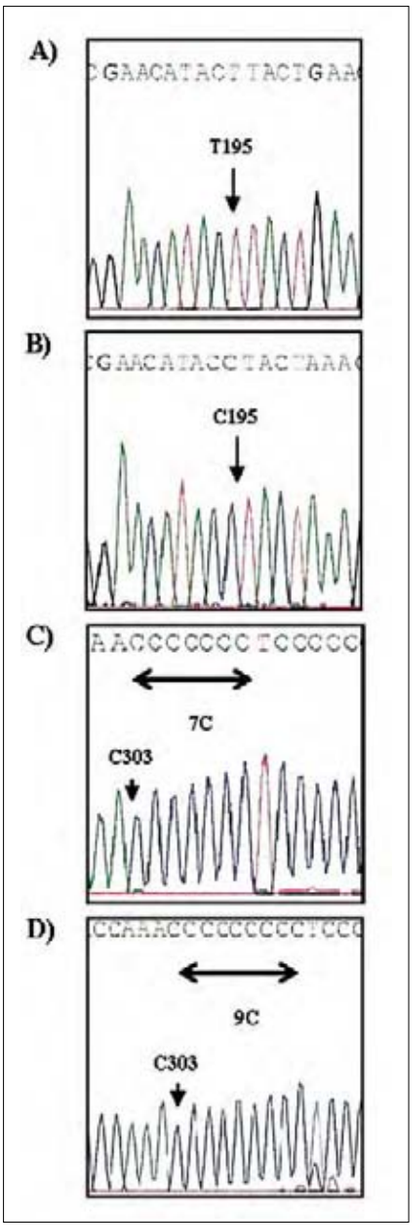
The Laboratory of Genomics studies gene expression profiles in populations exposed to air pollution, tobacco smoke and other factors. It also concentrates on the analysis of single nucleotide polymorphisms affecting the metabolism of xenobiotics, DNA repair, immune responses and other biological processes. The Laboratory of Genomics is a joint venture of the Institute of Experimental Medicine AS CR, v.v.i. and the Institute of Hematology and Blood Transfusion.

## CURRENT GRANT SUPPORT

EU 6th FP, 044232, ENVIRISK, Assessing the risks of environmental stressors: contribution to the development of integrating metodology, 2008–2009.

EU 6th FP, 018385-2, INTARESE, Integrated assessment of health risks of environmental stressors in Europe, 2006–2009.

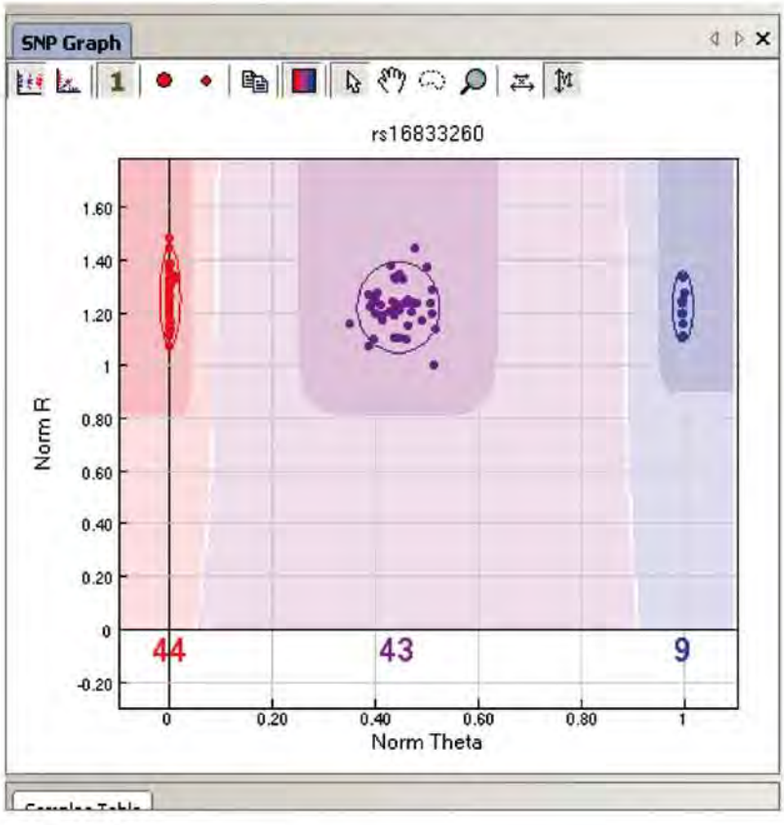
Ministry of Environment, SP/1b3/8/08, Study of the health consequences of polluted air in the Ostrava region with the use of genomics, AIRGEN, 2008–2010.

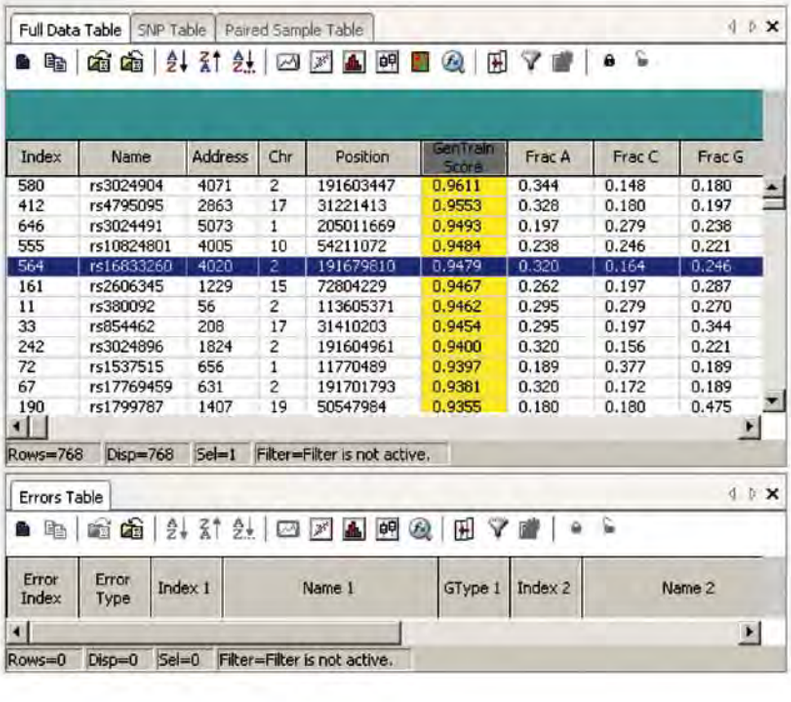



*Single nucleotide polymorphisms of HVRII mtDNA in children associated with respiratory morbidity: T195 allele(A); C195 allele (B); 7C 303 allele (C); 9C 303 allele(D).*

# ANALYSIS OF GENETIC POLYMORPHISMS

## Clusters representing samples with different combination of alleles




Ministry of Environment, SP/1b3/50/07, The effects of genome variability on the interaction between the human organism and the environment, ENVIRONGENOM, 2007–2011.

Ministry of Education, 2B08005, New approaches to study the toxicity of air pollution and their contribution to assess limits for selected pollutants,AIRTOX, 2008–2011.

Ministry of Education, 2B06088, Application of toxicogenomics to study mechanisms of the action of environmental pollutants on human health, ENVIRONGEN, 2006–2011.

Ministry of Education, 2B06150, Modulation of anti-PAH-antibody levels in relation to smoking and lung disease (cancer/noncancer) and the increase of PAH-resistance of the organism by immunization, 2006–2011.

GA CR, 310/07/0961, The role of environmental pollutants in the mechanisms regulating the development of prostate carcinoma, 2007–2010.

IGA of the Ministry of Health, NS9804-4/2008, Genetic databases, their structure and application, 2009–2011.

## SELECTED RECENT PUBLICATIONS

**1.** Binková B, Šrám RJ. (2004) the genotoxic effect of carcinogenic PAHs, their artificial and environmental mixtures (EOM), on human diploid lung fibroblasts. Mutation Res (Fundam.) 547(1-2): 109–121.

**2.** Šrám RJ, Beskid O, Binková B, Chvátalová I, Lněničková Z, Milcová A, Solanský I, Tulupová E, Bavorová H, Očadlíková D, Farmer PB. (2007) Chromosomal aberrations in environmentally exposed population in relation to metabolic and gene polymorphisms. Mutation Res (Fundam.) 620: 22–33.

**3.** Binková B, Chvátalová I, Lněničková Z, Milcová A, Tulupová E, Farmer PB, Šrám RJ. (2007) PAH-DNA adducts in environmentally exposed population in relation to metabolic and DNA repair genes polymorphisms. Mutation Res (Fundam.) 620: 49–61.

**4.** Van Leeuwen DM, Pedersen M, Hendriksen PJM, Boorsma A, van Herwijnen MHM, Gottschalk RWH, Kirsch-Volders M, Knudsen LE, Šrám RJ, Bajak E, van Delft JHM, Kleinjans J. (2008) Genomic analysis suggests higher susceptibility of children to air pollution. Carcinogenesis 29: 977–983.

**5.** Švecová V, Rössner P Jr., Dostál M, Topinka J, Solanský I, Šrám RJ. (2009) Urinary 8-oxodeoxyguanosine levels in children exposed to air pollutants. Mutation Res (Fundam.) 662: 37–43.

**6.** Schmuczerová J, Brdička R, Dostál M, Šrám RJ, Topinka J. (2009) Genetic variability of HVRII mtDNA in cord blood and respiratory morbidity in children. Mutation Res (Fundam.) 666: 1–7.