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Indoor risk factors for childhood respiratory diseases: development and application of non-invasive biomarkers

DURATION OF THE PROJECT
Phase 1: 01/01/2007 – 31/01/2009
Phase 2: 01/02/2009 – 31/01/2011

BUDGET
765.002 €

KEYWORDS
Asthma, allergy, children, biomarker, indoor pollution, biomonitoring

CONTEXT

Children's respiratory health is among the priorities of international environmental health programs (EU Environmental Health Action Plan, Budapest, 2004) and national programs such as Belgium's CEHAPE program.

Respiratory diseases are a major cause of illness in children of developed countries. Furthermore, asthma and allergies are increasing even up to 30% in certain age groups. Environmental factors are thought to affect a child's likelihood to develop these diseases; however the risk factors are largely unknown. The research will have the opportunity to focus on two types of risk factors namely on perinatal exposure which is relevant since respiratory organs are rapidly developing at that time, and secondly on indoor air quality which is also relevant since little children spend most of their time indoor.

PROJECT DESCRIPTION

Objectives

- to identify, standardise and design study protocols for non-invasive effect biomarkers of respiratory health.
- to evaluate the predictivity of these new non-invasive tests to respiratory health outcome
- to evaluate whether prenatal exposure and indoor exposure are environmental risk factors

Methodology

The project contains two parts:

Development of new non-invasive biomarkers and biomonitoring techniques.

Current methods to assess lung inflammation are invasive techniques which are less suitable to apply to children such as bronchial biopsies and bronchoalveolar lavage.
The network will focus on non-invasive approaches to study inflammatory processes. The VITO partner has experience with exhaled breath which is collected during normal breathing. E*xhaled breath condensate* (EBC) can be collected by cooling/freezing exhaled air. It contains proteins and lipid mediators which may be used as markers for the respiratory health status. E*xhaled breath gases* include volatile organic compound (VOC) and nitric oxide (NO), some of them have already been identified as markers for oxidative stress.
The UCL partner has developed recently a very simple and reproducible technique to collect *Nasal lavage* (NAL), this technique allows to collect proteins and other molecules (e.g. cytokines) that leak or are secreted at the surface of the nasal epithelium and may reflect inflammation or exposure to irritants (eg ozone).
The new markers will be compared to determinations of *NO (nitrix oxide)* in exhaled air which is a well-known indicator of deep lung/airway inflammation. The single-breath online technique is currently the "gold standard" technique, and will be compared to eNO measurements with recently developed mobile instruments. This may be practical for environmental health monitoring at different locations.

The proposed project will allow to optimize and standardize the sampling conditions (time, volume, reproducibility) for children. Determinants of individual and technical variability will be identified. This information is needed before the techniques can be applied in biomonitoring studies.

Child cohort studies:

The biomarkers described and optimized in the first part will be applied in an existing and a new child cohort. Children will also undergo a lung function test (spirometry and provocation test) and a clinical examination to diagnose their respiratory health status. The studies will be conducted after the approval of the Ethic Committees and written approval of the parents.

Part of the children enrolled in the Flemish environmental health birth cohort initiated in 2002 will receive a second follow-up at the age of 5 or 6.
Following associations will be studied: 1. **Biomarkers of effect with respiratory outcome**: this will allow to evaluate the predictivity of the biomarkers. At the age of six diagnosis for asthma and respiratory health status is more reliable than at the first moment of follow up (age of three). 2. **Biomarkers of**

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effect with exposure markers: the biomarkers of effect will be related to concentrations of Pb, Cd, HCB, pp'-DDE, dioxine-like compounds and PCBs that have been measured in cord blood at birth. It has been shown that normal prenatal development is essential for normal lung development. Environmental pollutants may interfere with this development. Other data on childhood exposure will be further collected by questionnaires eg housing conditions (dampness, mold), cleaning behavior, heating,…), pet exposure, day care/school attendance, swimming pool attendance, food consumption, …

A **new child cohort will be initiated** including schoolchildren aged 5-6 years. The focus in this cohort will be primarily on indoor environmental risk factors. Two groups (each of 100 boys and 100 girls) will be considered based on their exposure to trichloramine in air due to swimming pool attendance. Information on other exposures such as to plasticers in building materials, frequent use of chemical household products will be obtained by questionnaires.

INTERACTION BETWEEN THE DIFFERENT PARTNERS

The VITO partner has extensive experience with biomonitoring and with development of biomarkers for respiratory sensitization. The UCL partner has experience with development of biomarkers to measure lung membrane integrity. However the use of non- invasive techniques is for both partners a new approach which will be developed in the presented project. The clinical experience of the UA partner will be of great help to evaluate predictivity of the new biomarkers.

EXPECTED RESULTS AND/OR PRODUCTS

General public: an information sheet on outcome of study with respect to environmental risk factors will be made available at the end of the study
Stakeholders : a workshop will be organized at the end of the project
Scientific community: the results will be published in peer reviewed international journals.

PARTNERS - ACTIVITIES

Partner 1(VITO): the core expertise of the VITO partner is on biomarker development using molecular markers. This technology is applied for development of *in vitro* tests and for biomonitoring. VITO has coordinated the Flemish human biomonitoring campaigns on environmental health (2002-2006) and leads a workpackage on biomonitoring and environmental health surveillance in the EU-ESBIO project and on bimonitoring and risk assessment in the EU-INTARESE project.

Partner 2 (UCL): the expertise of UCL focuses on the development and use of new non – invasive biomarkers, in particular on biomarkers related to nephrotoxicity and respiratory toxicity. UCL has developed the concept of investigating the integrity of the lung epithelium by lungproteins present as biomarkers in blood samples. UCL has commercialised a bioassay based on the Clara cell protein. UCL has a long term experience with epidemiological studies and environmental exposure (eg. dioxins, heavy metals, ozone, chlorination byproducts). UCL has coordinated three EU framework projects, and particpated in five other EU projects related to environmental health. The UCL partner has developed the hypothesis of chlorine byproducts as an additional risk factor for childhood asthma in Western countries.

Partner 3 (UA): Prof.Dr.K. Desager is since 1993 connected as paediatrician to the Department of Paediatrics and Respiratory Medicine of the Antwerp university Hospital and University of Antwerp. She is involved in research projects on epidemiology and respiratory function in childhood asthma and allergy.

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Follow-up Committee

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