Environmental Cancer Risk, Nutrition and Individual Susceptibility (ECNIS) Network of Excellence

Konrad Rydzyński
(on behalf of ECNIS partners)
Year 2003
in response to the European Commission’s Call for the 'expressions of interest’ to the 6th Framework Program of Research and Development (6th FP)

the Nofer Institute proposes to establish a Network of Excellence to deal with problems related to environment and cancer risk as modulated by diet and genetic disposition (ECNIS NoE)
Environmental (non-endogenous) factors: 70-90% of cancer risk
Gaps of knowledge on the environmental cancer risks

- Recently, any attempt to estimate the proportion of all cancers that might be avoided through the control of different environmental factors is still largely a guesswork.
- We are even more ignorant when we try to evaluate the effects of combined exposures (nutritional and environmental factors) in different genetically susceptible populations.
- Many of these gaps in knowledge may be filled in only by joint efforts of epidemiologists, toxicologists, food specialists and molecular biologists.
The proposal received high-grade assessment of the Commission and the topic was incorporated in the thematic list of 6FP

CALL

Food Quality and Safety

AREA

Environmental Health Risk (5.4.8)

TOPIC

Environmental cancer risk, nutrition and individual susceptibility – NoE T8.2
• Granted: fall 2004

• Funding from the European Commission – 11 mEu for 5 years + contribution of partners (ca 5mEu+)

• Negotiations with EC

• Project started May 1st 2005
Partners
NIOM (Poland) **(Coordinator)**
VUB (Belgium)
UCL (Belgium)
UC (Denmark)
FIOH (Finland)
DKFZ (Germany)
UM (Germany)
BIU (Germany)
NHRF (Greece)
FJOKK (Hungary)
ISI (Italy)
IRCCS (Italy)
Collegium Med. (Poland)
ICO (Spain)
KI (Sweden)
ULUND (Sweden)
UNIMAS (The Netherlands)
IRAS-UU (The Netherlands)
ULEIC (UK)
ICR (UK)
UNIVDUN (UK)
IARC (France)
Imperial College (UK)
## Number of researchers and doctoral students to be integrated

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1. To overcome the fragmented nature of research in areas related to carcinogenesis caused by diet, the environment, occupation, or lifestyle, as well as exposure assessment, within Europe
2. To integrate joint training and mobility programs in area of environmental cancer molecular epidemiology
3. To develop and validate existing and novel biomarkers of exposure, effect and susceptibility for environmental and occupational cancer risk assessment
4. To identify factors that modulate the environmental and occupational cancer risk resulting from nutrition and lifestyle factors
5. To develop hazard and risk assessment strategies based on mechanism of action of carcinogens
6. To disseminate of acquired knowledge to scientific community
7. To disseminate of acquired knowledge to external stakeholders
Integration activities

• Joint use of infrastructures
• Methodology standardisation
• Core facilities
• Knowledge Database on Molecular Epidemiology and Cancer (MEC)
• Videoconferencing network
Core facility

„virtual laboratory” conducting very specific studies in different location, but with fully integrated approach

- exchange of standards
- conduct of mini-trials amongst partners who routinely practice the same or similar methods (for example for comparison of analytical accuracy and reproducibility).
- quality indicators will be proposed to assist the assessment of results from the different protocols

Creation of core facilities will be based upon the inventories made during the first year, starting with a facility for synthesis of carcinogen-modified DNA and protein standards and producing antibodies
ECNIS Core Antibody facility

ECNIS group’s experience is largely from in-house production of both polyclonal antisera and monoclonal antibodies, principally to DNA adducts

- Antibodies offer distinct advantages over other techniques for assessing biomarkers of genotoxic insult.

- Immunohisto- and immunocytochemistry can localise biomarkers within tissues and cells.

**List of immunogens required**

1. Etheno-dA (polyclonal)
2. dTg (monoclonal)
3. Etheno-dC (monoclonal)
4. N2-ethyl-dG (polyclonal)

*From the Report on establishment of an ECNIS Core Antibody facility (WP1,6)  
July, 2007*
The ECNIS knowledge database on Molecular Epidemiology and Cancer (MEC)

Starting point for a re-evaluation of molecular epidemiology studies and for pooling ECNIS data with the results of other studies

MEC is currently accessible within ECNIS through its website
MEC incorporates:

(1) information on exposure, including nutrition and cancer chemoprevention
(2) biomarkers of exposure
(3) biomarkers of individual susceptibility
(4) cytogenetic and other genotoxic damage,

In the future is to be expanded by
(5) transcriptomics (DNA microarrays, SAGE etc), proteomics and metabolomics
**EPISAT** (Epidemiologic Information Storage and Analysis Tool)

Software for data import and conduction of pooled analyses available on ECNIS

Allows researchers to:
- store, maintain and retrieve epidemiologic information and databases
- analyze the content of the databases acquired
EPISAT provides a user-friendly interface based on a standard Internet browser to access the information stored in a database and to filter the data according to the user goals.

Once the studies have been selected, EPISAT can:
(a) show general information, such as study design,
(b) give summary information on the variables the user is interested in,
(c) allow to download different kinds of files, including datasets or parts of them, and results in different formats (pdf, csv, jpg),
(d) summarize the results and
(e) automatically perform meta-analyses.
### EpiSAT project

#### Databases

**Name**: MEC - knowledge database
- Principal investigator: admin
- Total subjects: 1994
- control: 1306
- case: 688
- Dataset included: 2

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- **Notes**: sample dataset of adducts
Joint Research

- Formulation of common research strategy
- Priorities agreed:

1. Validation of biomarkers in inter-laboratory studies
2. Development & validation of phenotypic biomarkers
3. Development of novel nutritional biomarkers
4. Studies on cancer induction mechanism for better prediction and prevention
5. Integration of biomarkers into risk assessment

- Development of ethical rules in biomarker research
  WP12 and Ethical Review Panel
Collaborative research projects
(1st Call – February, 2006):

1. Validation of NNOC-related DNA adducts and assessment of their determinants in the general population
2. Towards consensus for the measurement of urinary 8-oxo-7,8-dihydro-2’deoxyguanosine.
3. Use of lymphoblastoid cell lines for the identification of at risk genotypes: validation of cell lines for the DNA repair response
5. Molecular dissection and potential cross-talk of the biological and genetic pathways affected by benzo[a]pyren (BaP) and dioxin (TCDD)
6. Induction of oxidative stress by polycyclic aromatic hydrocarbons and its modulation by food components
7. Short-term effects of selenium on global gene expression in humans using selenium-rich milk and different selenium supplements
8. Genetic and epigenetic alterations in plasma DNA of healthy and cancers subjects as biomarkers of exposure or tumorigenesis.
9. A Mendelian randomization study of cruciferous vegetables and lung cancer within the EPIC cohort study
10. Is PPARs the “fat sensor” that mediates the promotion of intestinal cancer by high fat diets?
Collaborative research projects
(2nd Call – November, 2006):

1. Biomarker-based assessment of alcohol-related cancer risk
2. Early changes in immunological markers in Non-Hodgkin’s Lymphomas; Development and validation of multi-analyte platforms.
3. Integration of biomarkers in the estimate of cancers attributable to environmental and dietary factors in Europe
4. Method development and validation of acetaldehyde induced DNA damage as a biomarker of alcohol intake
5. Improving the throughput and efficiency of the 32P-postlabelling assay
6. Assessment and reduction of comet assay variation in relation to DNA damage and DNA repair phenotype
7. Contribution of diet, cell turnover and DNA repair to production of urinary DNA damage products: validation of biomarkers of DNA damage and repair
8. Development and validation of phenotypical nucleotide excision DNA repair (NER) assays for use in molecular epidemiology
9. Assessment of general population exposure to PAHs in northern Iran, a high risk area for esophageal cancer
ECNIS ETHICAL REVIEW PANEL

• Görman Ulf (Sweden) - chairman of the ERP
• Sekeris Constantine (Greece)
• Casteleyn Ludwine (Belgium)
• Dumez Birgit (Belgium)
• Whittaker Peter (UK)
• Polańska Kinga (Poland)
ECNIS ETHICAL REVIEW PANEL responsibility

- Collect and store the copies of ethics permit forms from all parties.
- Examine ethical issues which may be raised by the ECNIS NoE or the partners.
- Advise on postgraduate education on research ethics for PhD students within the NoE.
- Represent the ECNIS NoE on ethics issues in appropriate bodies within the EU organisation.
- Review annually the achievements of ECNIS to advise research teams with a view to ensure that ethical considerations have been giving full attention in accordance with EU socio-ethical values.
- Check if novel ethical questions in the field of interface of environmental cancer/nutrition/ genetics arise.
• **Spreading of Excellence**

- Reviews on the state of science
- Personnel mobility, fellowship schemes for young researchers
- Meetings, courses and workshops
State of the Art Reviews

- **Vol 1.** Biomarkers of carcinogen exposure and early effects
  *Edited by Peter B. Farmer, Jean M. Emeny*

- **Vol 2.** Dietary vitamins, polyphenols, selenium and probiotics: biomarkers of exposure and mechanism of anticarcinogenic action
  *Edited by Björn Åkesson, Per Mercke*

- **Vol 3.** Epidemiological concepts of validation of biomarkers for the identification/quantification of environmental carcinogenic exposures
  *Edited by Paolo Vineis, Valentina Gallo*

- **Vol 4.** State of validation of biomarkers of carcinogen exposure and early effects and their applicability to molecular epidemiology
  *Edited by Peter B. Farmer, Soterios A. Kyrtopoulos, Jean M. Emeny*

330 articles by ECNIS partners on website www.ecnis.org
Exchange fellowships

Awarded to doctoral and post-doctoral students and junior scientists from a laboratory member of ECNIS to visit another laboratory member of ECNIS, to work on a joint ECNIS-related project. Two calls are issued each year. **Fifteen of these fellowships awarded so far.**

Training fellowships

Awarded to doctoral and post-doctoral students and junior scientists from a non-ECNIS laboratory including students from non-European countries to visit an ECNIS member laboratory. Two calls are issued each year. **Five of these fellowships awarded so far.**

Training fellowships for ECNIS scientists in non-ECNIS institutions ECNIS

Awarded to junior and senior scientists from an institute member of ECNIS to visit another centre non-member of ECNIS, with the aim of acquiring specific skills and methodologies that could be then implemented within ECNIS projects. Applications can be submitted at any time. **Three of these fellowships awarded so far.**
• Events for public organizations and policy makers

• Biomarkers and their potential in human biomonitoring and environmental health surveillance, Luxemburg, November 2006

• Integration of Biomarkers in Cancer Risk Assessment, Utrecht 2006

• Biomarker of Exposure and Cancer Risk: DNA Damage and DNA Adduct Detection, Heidelberg 2006
• Dissemination of knowledge through the website (www.ecnis.org) and its "Science Portal"
Newsletters
Thank you for your attention
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