



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

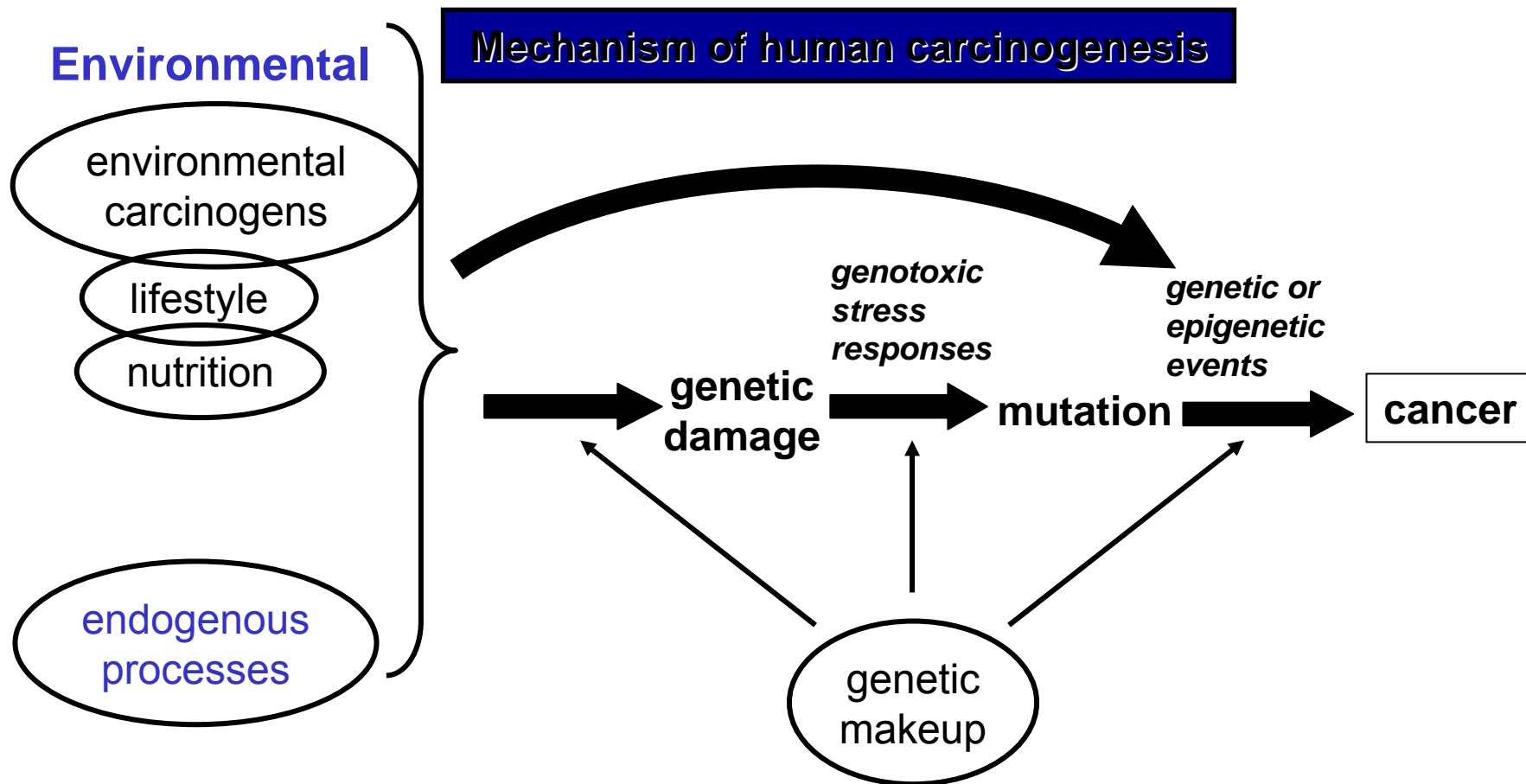
**Konrad Rydzyński
(on behalf of ECNIS partners)**



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



ECNIS Network of Excellence

- 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)



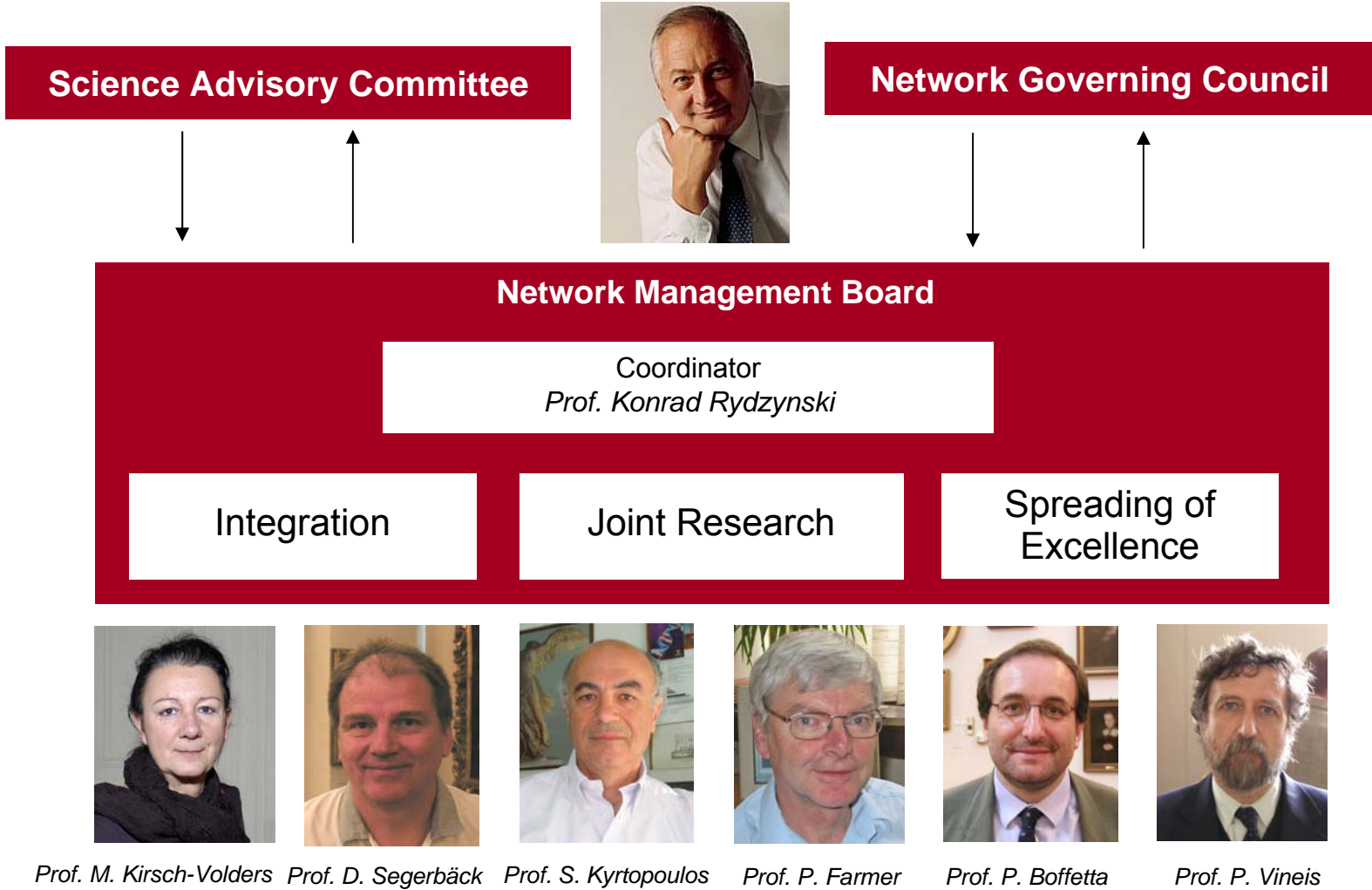
**Number
of researchers
and doctoral
students
to be
integrated**

Participant no	Participant short name	Number of researchers to be integrated			Number of doctoral students to be integrated in the network		
		Female	Male	Total	Female	Male	Total
1	NIOM	2	6	8	4	1	5
2	DKFZ	2	3	5	0	0	0
3	UC	2	4	6	6	3	9
4	KI	1	5	6	4	0	4
5	ISI	2	4	6	0	0	0
6	NHFR	1	5	6	0	0	0
7	ULEIC	2	5	7	2	0	2
8	FJOKK	2	1	3	0	0	0
9	Collegium Med.	0	4	4	3	2	5
10	GRI	3	1	4	2	0	2
11	JOGU	5	2	7	6	0	6
12	FIOH	1	2	3	3	1	4
13	VUB	2	1	3	5	1	6
14	ULUND	2	6	8	5	2	7
15	UCL	1	1	2	3	0	3
16	ICR	2	3	5	1	1	2
17	UM	0	5	5	5	2	7
18	BIU (SME)	0	1	1	1	0	1
19	ICO	1	3	4	2	0	2
20	IRAS-UU	0	5	5	1	1	2
21	UNIVDUN	2	6	8	6	3	9
22	IARC	0	4	4	0	0	0
23	NETIX (SME)	0	2	2	0	0	0
24	Leocordia AB (SME)	0	10	10	0	0	0
Total		33	77	114	59	17	76



The overall objectives of ECNIS

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



Prof. M. Kirsch-Volders

Prof. D. Segerbäck

Prof. S. Kyrtopoulos

Prof. P. Farmer

Prof. P. Boffetta

Prof. P. Vineis



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



EPI SAT (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 Molecular Epidemiology toolkit site - Mozilla Firefox

File Modifica Visualizza Vai Segnalibri Strumenti ?

Adesso: Nebbia, 8° C Mar: 12° C Mer: 13° C

http://localhost/phplabdb/projects/?computation=40&id_project=1

Vai gsec status

Projects Language Logout

EpiSAT
project

- EpiSAT Home
- Databases
- Dataset manager
- DNA Repair
- Project manager
- Administration
- About

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

Name	Notes	Unique ID
<input type="checkbox"/> Bladder	Bladder Cancer dataset	1
<input type="checkbox"/> Adducts - sample	sample dataset of adducts	372525

Name	Cases	Aggregation Type	Control Type
road	control: 221 case: 124	No	No
psm_now	control: 221 case: 124	Yes	No
psm_work	control: 221 case: 124	Yes	No
ralpos	control: 221 case: 124	Yes	No
ERCC2/XPD_23591	control: 221 case: 124	No	No
ERCC2/XPD_35931	control: 221 case: 124	No	No
PCMA	control: 221 case: 124	No	No

Completato

Apri blocco note

Episat Molecular Epidemiology toolkit site - Mozilla Firefox

File Modifica Visualizza Vai Segnalibri Strumenti ?

Adesso: Nebbia, 8° C Mar: 12° C Mer: 13° C

http://localhost/phplabdb/gexpdb/index.php?computation=40&id_dataset=372525

Vai gsec status

Projects Language Logout

EpiSAT
project

- EpiSAT Home
- Databases
- Dataset manager
- DNA Repair
- Project manager
- Administration
- About

Name [Adducts - sample](#)

Date of storage **02/16/2007**

File [pooled3.csv](#)

Link

Notes **sample dataset of adducts**

Case/Control vs Smoker

	former smoker	current smoker
control	593	492
case	298	265

control

former smoker

case

former smoker

Completato

Apri blocco gote

Episat Molecular Epidemiology toolkit site - Mozilla Firefox

File Modifica Visualizza Vai Segnalibri Strumenti ?

http://localhost/phplabdb/gexpdb/index.php?computation=40&id_dataset=372525

Errore di connessione

EpiSAT Home
 Databases
 Dataset manager
 DNA Repair
 Project manager
 Administration
 About

Name [Adducts - sample](#)
 Date of storage **02/16/2007**
 File [pooled3.csv](#)
 Link
 Notes **sample dataset of adducts**

Case/Control vs Smoker

	never smoker	former smoker	current smoker
Control	528	447	109
Lung cancer	221	201	54
Leukemia	33	20	10
Bladder cancer	14	10	2

Completato

Apri blocco note

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**
4. **Development of methods for determination of tobacco-smoke related collagen adducts in human lung – possible biomarkers of long-term exposure**
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
- Organisation of events in the context of major international conferences (EEMS2005, 2006, 2007; EUROTOX 2005, 2006, 2007; ISEE Congress 2006, IUTOX 2007, AACR, EACR – July 3-8, 2008, Lyon, France)

State of the Art Reviews

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



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



ECNIS Fellowships

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"

ECNIS (Environmental Cancer Risk, Nutrition and Individual Susceptibility) is a Network of Excellence operating in the context of the 6th EU Framework Programme for Research and Development (FP6).

Launched in May 2005, ECNIS brings together some of the best European research groups active in the area of environmental cancer and its modulation by nutrition and genetic makeup, into a durable network of [partners](#) to conduct high-class research on cancer causation and prevention.

Nearly one in three Europeans develops cancer at some time during his or her lifetime, resulting in more than 2.9 million new cases and 1.7 million cancer deaths every year in the European Union. Environmental factors, nutrition and lifestyle play a major role in cancer causation, while genetic makeup affects the susceptibility to cancer of different individuals. It is obvious that cancer constitutes a major public health problem, which affects most people directly or indirectly, and that a great need to achieve a reduction in cancer burden exists.

Mechanism of human carcinogenesis

```
graph LR
    subgraph Environmental
        A[environmental carcinogens]
        B[lifestyle]
        C[nutrition]
    end
    subgraph Endogenous
        D[genetic damage]
        E[genetic makeup]
    end
    A --> D
    B --> D
    C --> D
    D --> F[mutation]
    E --> F
    F --> G[cancer]
```

Current highlights

- ECNIS Review NEW ISSUE
- Novel Biomarkers 13 Dec 2007 London
- 2nd year Review Meeting

Visitors: 109533

• Newsletters

ecnis new
ENVIRONMENTAL CANCER RISK, NUTRITION AND INDIVIDUAL SUSCEPTIBILITY
EU Network of Excellence

2008 No. 2

The Annual International Congress of ECNIS

Two meetings are reported in this newsletter. In July ECNIS had its Annual International Congress in Prague. The Prague-meeting contained many symposia, workshops and lectures under the general heading: "From Genes to Molecular Epidemiology".

See pages 8-9



The Heidelberg Workshop
In September a workshop was held in Heidelberg at the German Cancer Research Center together with GDM (Gesellschaft für Umwelt- und Molekularbiologie) entitled "Biomarker of Exposure and Cancer Risk".

See page 10



ECNIS - From cell to society

The course "Genes to Cancer Risk", summer, has 7 different...

Gene-Env was the title graduate or by one part from Hung...

Cancer risk

Do you wonder about your risk to develop... cancer, diabetes, heart disease, osteoporosis or stroke? Are you interested in risk factors and what you can do to reduce the risk?

Go to: www.ecnis.org
On the right side bar, press "my cancer risk". Modify your answers and you can see how much it affects your risk to develop disease.

Biomarkers in Cancer Epidemiology

Fundamental Topics include:
• Biomarkers and their validation
• Design of epidemiological studies
• Biomarkers of nutrition
• Proteomics
• Exposure assessment with biomarkers
• Gene-environment interactions: theory and examples
• Biomarkers of genotoxicity
• Metabonomics
• New biomarkers and their development

See page 10

Is there an environment for the development of cancer?

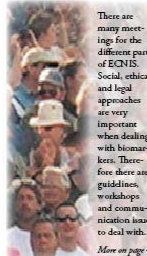
Why are there certain geographical patterns where uterine cancer is found?

- This is the case in certain areas of Romania, Croatia, Serbia and Bulgaria. Even between villages there can be great differences in the cancer risk. Is this risk food related, and if so, can biomarkers be used to verify the connections? Further, is this also related to herbal medicine and inflammation?



See the full

ECNIS Meetings



There are many meetings for the different parts of ECNIS. Social, ethical and legal approaches are very important when dealing with biomarkers. Therefore, there are guidelines, workshops and communication issues to deal with.

More on page 6



ECNIS - From cell to society

Broccoli, Toen and Selenium

What is the common factor that binds these three matters together? It could be ECNIS, which it is, but also that this newsletter has short articles on these three subjects.

• Broccoli seems to have protective effects for certain forms of cancer. Read about the background and practical advice. (page 9)

• Toenails, is something different. It is a tool for epidemiologists to collect DNA. Material from 90,000 subjects, which is a treasury! (page 11)

• Selenium is a common food additive, which is considered to be protective for cancer. Easy to understand - or very complicated? (pages 14-15)

Cancer risk

Do you wonder about your risk to develop... cancer, diabetes, heart disease, osteoporosis or stroke? Are you interested in risk factors and what you can do to reduce the risk?

Go to: www.ecnis.org
On the right side bar, press "my cancer risk". Modify your answers and you can see how much it affects your risk to develop disease.



ECNIS Evaluation

"We would like to compliment the project consortium for the completeness of the reports. The documents have been submitted on time and are clear and easy to read. We would, also, like to compliment the consortium for the participation to the review meeting and the given presentations. The information provided both in the written reports and answers as well as in the oral presentations, was complete and realistic. The achievements of each workshop and of the Network as a whole were clearly described. Based on this evidence, it is considered that ECNIS is a good project even if has not fully achieved all its objectives and expectations after first year; the first year has served as the foundation of the activity of the project and progress in the year to come".

More on pages 14-15

ECNIS Works

ECNIS organises a workshop on November 25 "Biomarkers and their environmental health and members of ECNIS will discuss those matters".

See page 10 for more

ECNIS Courses

An advanced course on Epidemiology is reported

www.ecnis.org

Editorial.....	2	Broccoli.....	9
Advanced course.....	3	Luxembourg.....	10
Ethics.....	4	Epidemiology.....	11
Imperial College.....	5	Research priorities.....	13
Publications.....	5	Selenium.....	14
Biomarker validation.....	7	Aim/Partners.....	16



www.ecnis.org

Editorial.....	2	Prague.....	8
Sci. Adv. Com.....	2	ECNIS goes ethical.....	10
Gender Aspects.....	3	Course on Biomarkers.....	10
Course report.....	4	Urothelial cancer.....	11
Student exchange.....	5	ECNIS fellowship.....	15
Heidelberg.....	6	Aim/Partners.....	16



ecnis news

ENVIRONMENTAL CANCER RISK, NUTRITION AND INDIVIDUAL SUSCEPTIBILITY
EU Network of Excellence

2007 No.1 (4)

Exchanges, meetings and courses

There are many activities within ECNIS dealing with exchange of knowledge, research and methods. On page 3 there is a personal experience told by a Hungarian young scientist visiting the German Cancer Research Center. Page 4 shows a report published in Management based on a meeting held in Heidelberg. The System (Growth) course is summarized on page 15.

On page 5 the coming Stockholm course on "Oxidative Stress - Diseases, Methods and Concepts" is presented. The course will take place June 10-15 at Karolinska Institute. At the time of printing this newsletter there is a possibility to accept a few more participants. More information to be found at "ecnis.org".



ECNIS - From cell to society

Ethical aspects I

In this issue of the newsletter there are two articles on ethical issues. The Ethical Review Panel (ERP) explains why they care, what they do and their experiences so far. It is obvious that there are rather simple rules to follow that many scientists are aware of, but there are also very complicated matters regarding information, the influence by the donor's decisions, how specific data are presented regarding rare diseases for instance, and the very complicated issue with different ethical legislations in different EU-countries.

Continued on page 6

Ethical aspects II

One of the ECNIS scientists, Pauls Viteris, comments on the subject "Why should we be interested in ethics?" Further, what are the roots of ethics in different regions, what is "dignity" and do we need philosophy in ethics?

Continued on page 11

Cancer risk

Do you wonder about your risk to develop... cancer, diabetes, heart disease, osteoporosis or stroke? Are you interested in risk factors and what you can do to reduce the risk?

Go to: www.ecnis.org
On the right side bar, press "my cancer risk". Modify your answers and you can see how much it affects your risk to develop disease.



Luxembourg November 2006

ECNIS organized a stakeholder meeting in Luxembourg November 29, 2006. The meeting was co-organized with DG Research and DG Environment. Members of ECNIS, NewGenetics and ESHO presented.

Continued on page 9



Stavros Kyriopoulos presents ECNIS Network of Excellence in Luxembourg

Maastricht February 2007

ECNIS Annual Meeting was held in Maastricht February 25-28, 2007. It was an intensive meeting when 15 work packages were presented together with posters and many meetings to plan further collaborations.

Continued on page 10



www.ecnis.org

Editorial.....	2	Maastricht Feb 2007.....	10
Exchange from Hungary.....	3	Ethics.....	11
Individual susceptibility.....	4	System Course Oct 2006.....	13
Ethical Review Panel.....	6	IARC Monographs.....	14
Luxembourg Nov 2006.....	9	Aim/Partners.....	16





Thank you for your attention

What we have:	N. of studies
Dietary data in healthy subjects	12
Dietary data in cancer studies	20
Diet and DNA adducts	11
Diet and DNA repair	5
Diet and oxidative damage	5
Diet and MN	3
Diet and other markers	20