



**2<sup>nd</sup> GENSUT Workshop**  
**September 14-17, 2000**  
**Venue: Emmanuel College, Cambridge, UK**

**Programme**

**Thursday, Sept. 14**

Arrival of participants dinner

19:30 *Dinner* (there is no late dinner available)

**Friday, Sept. 15**

8:00 *Breakfast*

**Session 1: *From exposure to mutation***

Chair: H.M. Bolt

8:30 T. Kauppinen, N CAREX: occupational exposure matrix  
9:30 H. Autrup, DK Traditional exposure assessment  
vs. biomarkers

10:15 *Coffee Break*

10:45 R. Thier, D Environmental vs endogenous mutagens  
11:30 N.G.J. Jaspers, NL Relevance of DNA-repair for mutagenesis

12:30 *Lunch*

**Session 2: *Ongoing activities at national level***

Chair: I. Cascorbi, Greifswald

13:30 Pi\*S and Pi\*Z Alpha 1 antitrypsin polymorphism and blood hydroxyproline as biological markers for occupational exposure to asbestos.

**A. Lafuente Flo**

13:45 Genetic Polymorphisms in relation to DNA Adducts

**F.J. van Schooten**

14:00 The global repair phenotype, assessed by the COMET assay, as a measurement of susceptibility

**M. Kirsch-Volders, N. Touil, M. De Boeck**

14:15 Genetic polymorphisms with possible influence on cancer susceptibility:  
outcome of the disease or treatment response  
**V. Nedelcheva Kristensen**

**Session 3: Susceptible groups and genetics**

Chair: R. Wolf, Dundee

14:30 A. Futreal, UK Genome-wide searches for new cancer genes

15:30 *Coffee Break*

16:00 D. Easton, UK Future of familial and candidate gene studies to  
investigate susceptibility to cancer

17:00 M. Bobrow, UK Ethical issues associated with the  
identification of susceptibility genes

18:00 Predinner Debate: *Summary of day 1*  
Moderator: H.M. Bolt, Dortmund

*Topics:* Will a candidate gene approach to identify susceptibility genes ever work?  
- Single vs multiple exposure scenarios  
- Physiological methylation of DNA  
- Spontaneous vs exposure dependent mutation spectra  
- .....

19:30 *Special dinner at the library of Emmanuel College*

**Saturday, Sept. 16:**

8:00 *Breakfast*

**Session 4: Epidemiology**

Chair: F. Cambien, Paris

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|-------|---------------------|---|
| 8:30  | P. Vineis, I        | Structure and requirements for an internet database of susceptibility genes                                   |
| 9:15  | A.J. McMichael, UK  | Environmental factors and development of cancer (significance / height of exposure)                           |
| 10:15 | <i>Coffee break</i> |   |
| 10:45 | H.E. Wichmann, D    | Environmental factors and development of asthma (significance / height of exposure)                           |
| 11:45 | E. Taioli, I        | Update of the international pooled analysis of studies of genetic susceptibility to environmental carcinogens |
| 12:30 | <i>Lunch</i>        |   |

**Session 5: Updates of network research**

Chair:

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|-------|--|--|
| 14:30 | Update on GenEPIC<br><b>F. Canzian</b>   |  |
| 14:45 | Metabolic polymorphisms in oral cancer patients and in the general population in Italy.<br><b>A.M. Rossi</b> |  |
| 15:00 | Updates of the role of myeloperoxidase and CYP1A1 to cancer susceptibility<br><b>I. Cascorbi</b>             |  |
| 15:15 | BIOMODEM - Biomarkers for Occupational Diesel Exhaust Exposure Monitoring<br><b>L. Knudsen</b>               |  |
| 15:30 | <i>Coffee break</i>  |  |

## **Session 6: Working groups**

16:00 Introductory remarks of the organisers of the 4 workshops

16:30 Working groups

a) Guidelines for minimum requirements for studies and the collection of unpublished data (questionnaire).

Organisation: F. Nyberg, Stockholm

b) Development of an internet database (published and unpublished data) of susceptibility genes

Organisation: P. Vineis, Torino

c) Network of blood/DNA banks: technology and data involved, discovery of new genes, etc.

Organisation: P. van Bladeren, Zeist

d) Critical elements of ethical issues (in preparation of the 3<sup>rd</sup> GENSUT workshop, 2001)

Organisation: K. Husgavfel, Helsinki

19:30 *Dinner*

## **Session 7 (evening): Summary of workshop**

Chair: F. Canzian, Lyon

20:30 Presentation of group results (a,b,c,d)

21:30 General discussion and conclusions

## **Sunday, Sept. 17:**

8:30 *Breakfast*

9:00 Internal GENSUT Coordination Committee Meeting  
(Chairman and organisation: H. Autrup)

GENSUT - An ESF Scientific network on “Genetic susceptibility to environmental toxicants – impacts for human health.

## ANNUAL REPORT - 2000

### Background:

The network was initiated in January 2000 at a meeting in London. The principal objective of the network was to better understand host factors contributing to varying levels of individual risk. To reach this objective, a multidisciplinary approach involving laboratory scientists and epidemiologists is required. The network members represent experience in epidemiology, molecular biology, genetics, toxicology and occupational health.

### Activities:

The 2<sup>nd</sup> GENSUT workshop took place at the Emmanuel College, Cambridge, UK September 14-17, 2000. The meeting was attended by 27 persons representing 12 different European nations (appendix 1). Fifteen of the participants had also attended the 1<sup>st</sup> workshop in Rungsted, Denmark.. Information about the network meeting was mailed directly to participants in the 1<sup>st</sup> meeting, and to people who had expressed interest in joining the network. In addition, the meeting was announced through the scientific societies, EEMS and EUROTOX , that have established interest groups in molecular epidemiology and genetic susceptibility, respectively. The meeting was placed “head to tail” with the EUROTOX2001 congress in London, but this did not increase the number of participants from this target group. The steering group has not been effective in promoting the Network activities in other scientific societies.

The program for the 2<sup>nd</sup> workshop is enclosed as appendix 2. The key session was on “Search of new susceptibility genes”, and the presentations were given by scientists not linked to the network.. It became clear that it is a massive undertaking, both economically and in infrastructure, to identify new susceptibility genes. The aspect of ethical issues was raised by one speaker, but the subject will be covered more extensively in the 3<sup>rd</sup> workshop. Other key scientific sessions covered the subjects “From exposure to mutation”, and “Epidemiological problems”.

One of the key activities of the 2<sup>nd</sup> workshop was an update of on-going activities at the national level by the network participants. A total of 8 presentations were selected, including new projects e.g. alfa-antitrypsin as a risk factor in lung disease in Spain, link between genotype and DNA adduct levels, and effect of metabolic genotype on response to treatment.

At the 1<sup>st</sup> network meeting different areas were identified as being problematic for the continued development of this interdisciplinary research area. Four different subject areas were identified – resources, ethical issues, standardised information and data bases. The four working group presented their conclusions in plenum, but no final recommendations could be made.

## Resources:

This session was chaired by B. Van Omen. There was a general consensus that centralised high-throughput facilities for general genotype analysis should be established. In addition, reference material for the different allelic variants should be made available to researchers for quality control and method validation. It was recommended to establish biobanks for future molecular epidemiology studies using the experience from earlier biobanks concerning storage of biological material and proper information about exposure, and to facilitate an easy transfer of biological material and information across borders. And, at the European level the links between genomic structure, gene function, gene polymorphism and human diseases

## Ethical issues:

This session was chaired Kirsti Husgafvel-Pursiainen.

### *Background* for the discussion:

Interaction between genes and exogenous exposure is central in the concept of genetic susceptibility. In this context, studies on structure and function of genes encoding for enzymes involved in the metabolism of xenobiotics, have revealed a growing number of genetic polymorphisms. Many of those, as well as a number of other genes involved in the development of chronic diseases, have been shown to carry multiple allelic variants. Subsequently, genotyping (and phenotyping) assays for those are increasingly being used as in studies focused on increased susceptibility.

Generation and use of genetic data, the nature of which is many times considered to be distinct from other types of personal data, have raised ethical concerns and implications. These relate to the role, meaning and relevance of the genetic markers used. In addition, ethical accountability is underscored in studies on genetic material or genetic traits. The ethical principles valid for health-related studies in general, i.e. respect for autonomy, doing good (beneficence), doing no harm (non-maleficence) and social justice, should strictly be applied in studies on human genetic material.

There are multiple ethical guidelines and declarations launched by various international bodies such as the Council of Europe, UNESCO, European Commission as well as a number professional codes of ethics. In addition, many organisations funding and supporting research pay growing attention to bioethics and conduct of ethical research, national funding bodies and European Science Foundation being such organisations. Recently, the European Commission has established a European Group of Ethics in Science and New Technologies (EGE) as an advisory body.

Most importantly, national, regional and local ethics committees, commonly based on governmental legislation, are increasingly aware of the unique features of genetic information. All these bodies are, however, mostly advisory in nature. The importance of ethical issues is further emphasised as the recent advances in technology, referred to as high-throughput technologies, like DNA microarray techniques, make large-scale genetic screening an option readily available and at use. On the other hand, despite all concerns, it is important to secure future research in this field.

### *Points for discussion for the next meeting*

- Biobanks based upon the report from the European Group on Ethics. Ethical aspects of human tissue banking. Opinion of the European Group on Ethics in Science and New Technologies to the European Commission (No 11). July 1998 and Sorsa M, Eyfjörd J, eds. Human Biobanks – Ethical and social issues. Nordic Committee on Bioethics. Nord 1997:9.
- Use of genetic markers, their relevance, informed consent based upon
- Schulte, PA, Lomax GP, Ward EM, Colligan MJ. Ethical issues in the use of genetic markers in occupational epidemiologic research. J Occup Environ Med 41, 639-646, 1999 and Hunter D, Caporaso N. Informed consent in epidemiological studies involving genetic markers. Epidemiology 8, 596-599, 1997.
- Use of high throughput technologies and genetic screening based upon Henn W. Genetic screening with the DNA chip: a new Pandora's box. J Medical Ethics, 25, 200-203, 1999 and Rawbone RG. Future impact of genetic screening in occupational and environmental medicine. Occup Environ Med 56, 721-724, 1999.

### **Standardised information:**

This session was chaired by Fredrik Nyberg. It was stressed that in order to get valid information about exposure and confounding factors, a standard form for these information would more easily facilitate the development of meta-analysis. A minimal questionnaire will be prepared by F. Nyberg, and it will be distributed to the network participants prior to the next meeting, where it will be subject to discussion.

### **Data bases:**

This session was chaired by F. Canzain. A grant application will be prepared for the World Cancer Research Foundation coordinated by Professor P. Vineis and involving several of the network participants. A full application will be submitted to the EU 5<sup>th</sup> framework programme.

It was decided that sessions covering each of the subjects should be arranged at the last network meeting in 2001 and that recommendations reached at this meeting should be made available in the scientific literature e.g. meeting report in a scientific journal.

### **Future activities:**

The next meeting is scheduled to take place in September 2001, i.e. Garmisch-Partenkirchen in connection with a German-US meeting on gene-environment interaction, but the final decision has not been made.

### **Outcome of the network activities up to date:**

Network participants are collaborating in a number of new EU-supported projects funded in 2000. New project proposals, involving network participants, will be prepared and submitted to EU for the Key action 4 Environment and Health March 2001 deadline

An application for an EuroSCO conference will be submitted for the 2001 deadline in order to continue the interdisciplinary collaboration established through this network.

Recommendation for research activities in the EU 6<sup>th</sup> framework programme.

## List of Participants

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