

Genetic and environmental risk factors for
melanoma:
translation into behavioural change

A
Network of Excellence
Project

Funded by the EC
Sixth Framework Programme



PRIORITY 1

Life sciences, genomics and biotechnology for health

Project Presentation

Foreword by the Scientific Coordinator
of GenoMEL



Professor Julia Newton Bishop

The Melanoma Genetics Consortium (now called GenoMEL) has been in existence for nine years. It started out as a relatively small cooperative of international research groups, but has grown to encompass over twenty participant centres from across the globe – ranging from the UK to Australia, and from Slovenia to Canada. I have chaired the Consortium throughout this time and it has been a real pleasure to see so many disparate groups and disciplines collaborating to the same ends.

Our recent success in obtaining a Network of Excellence grant from the European Commission has allowed GenoMEL to: establish a formal project management structure, to greatly increase our European activities and to enhance and extend our research. This presentation is intended to give an overview of the GenoMEL NoE and I hope you find it of interest.

If you would like to follow our efforts please take the time to visit our web site-

www.genomel.org

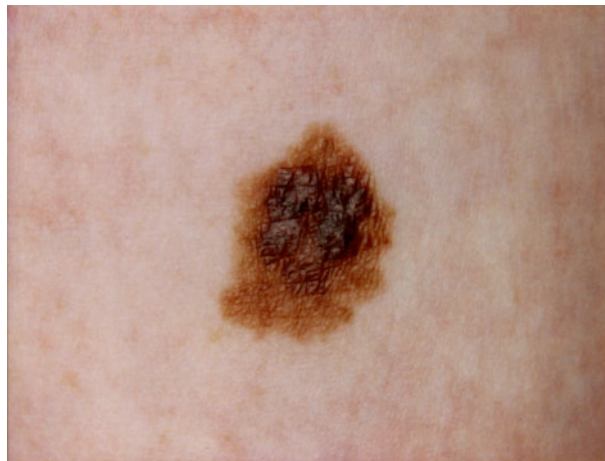
Thank you for your interest in our work.

Julia A Newton Bishop
Scientific Coordinator of GenoMEL
Leeds, 2006.

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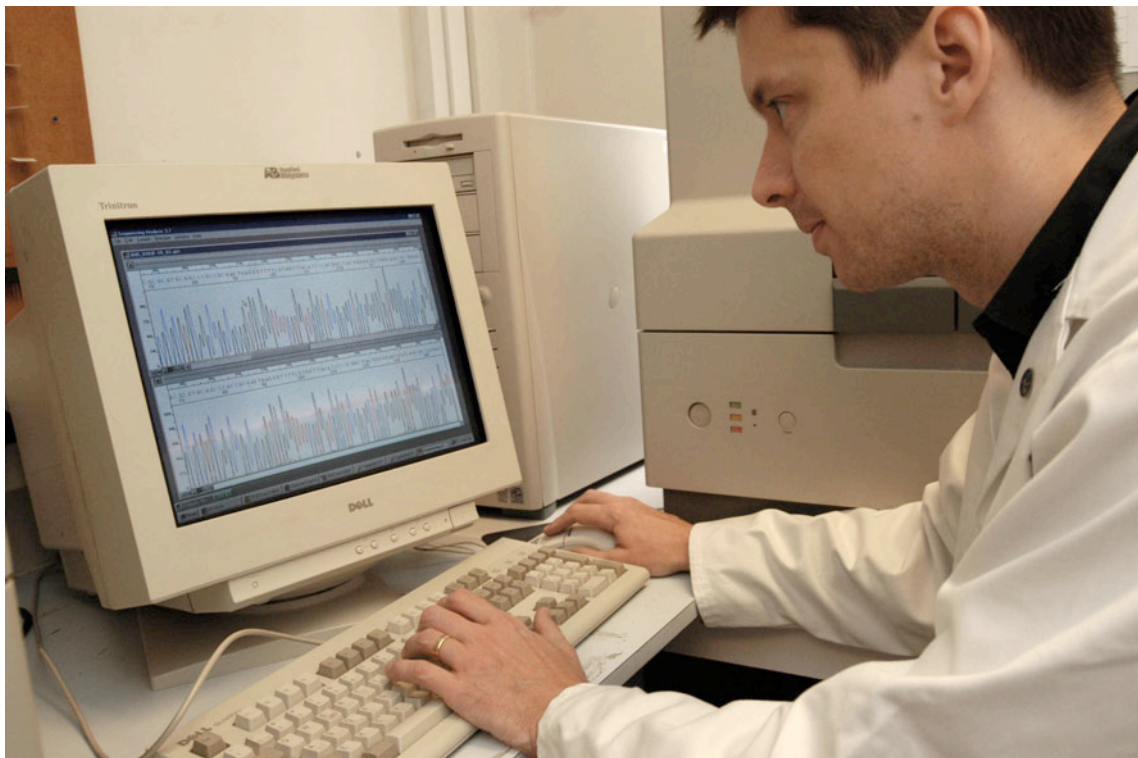
Malignant Melanoma –



Melanoma is an important health issue within the European Community because of its increasing incidence in many member states.

Introduction to GenoMEL

GenoMEL is an international research consortium working on the genetics of melanoma. At its core are most of the world's leading melanoma genetics research centres. As part of the Network of Excellence (NoE) programme, the network has been expanded to include many complementary centres and disciplines. For example, new members have been found in the diverse fields of psycho-oncology, multi-media design and medical ethics. A partnership has also been formed with a commercial, molecular genetics company to assist in the identification of new melanoma genes.



A GenoMEL researcher at work

Our Mission Statement



A GenoMEL researcher in the laboratory

The mission of the Melanoma Genetics Consortium is to develop and support collaborations between member groups to:

- Identify melanoma susceptibility genes
- Assess the risk of melanoma and other cancers related to variations in these genes
- Evaluate gene-environment interactions

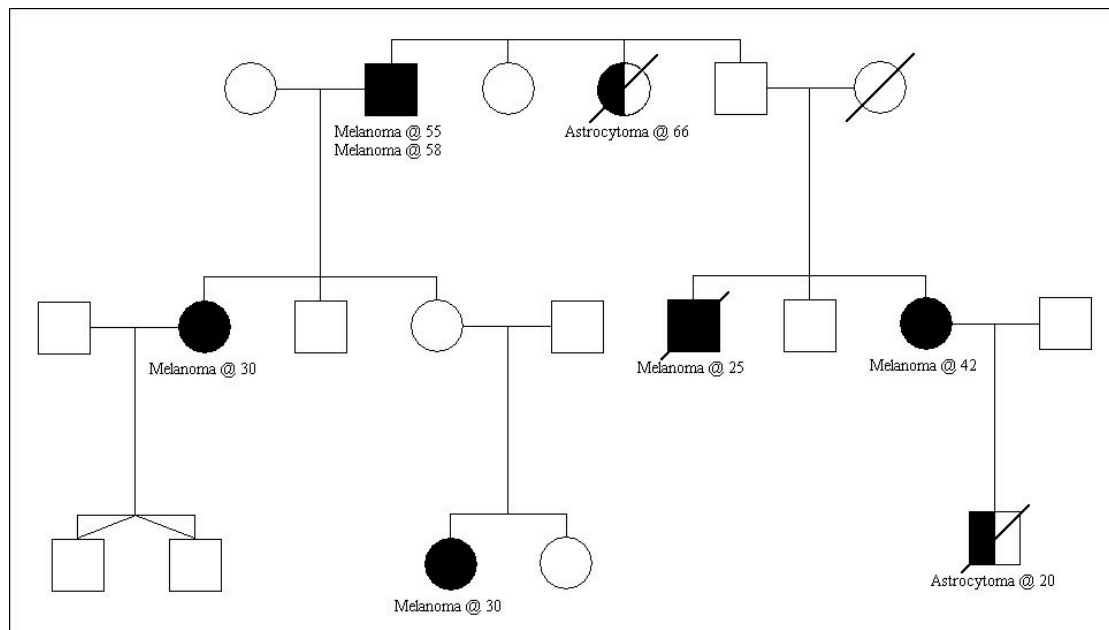
The GenoMEL NoE participants

University of Leeds, UK
Leiden University Medical Centre, the Netherlands
Queensland Institute of Medical Research, Australia
Westmead Institute of Cancer Research, Australia
Hospital Clinic I Provincial de Barcelona, Spain
INSERM, France
Dipartimento di Oncologia, Biologia e Genetica - Università degli Studi di Genova, Italy
Department of Oncology-Pathology, Karolinska Institute, Sweden
ServiceXS B.V., The Netherlands
Kings College London, UK
Departments of Oncology and Surgery, University Hospital, Lund, Sweden
University of Pennsylvania, USA
University of Utah, USA
University of Toronto, Canada
Tel Aviv University, Israel
Naked Design Consultancy, UK
Biomedical Research and Study Centre, University of Latvia
Institut Gustave Roussy, France
VU Medical Centre, The Netherlands
Institute of Oncology, Ljubljana, Slovenia
Pomeranian Medical University, Poland

Four groups are members of GenoMEL but are not part of the NoE. These groups are:

1. The National Cancer Institute Melanoma group led by Dr Peggy Tucker
2. The University of Glasgow group led by Professor Rona MacKie
3. The Massachusetts group led by Dr Hensin Tsao
4. The North Eastern Italy Melanoma Families Group led by Dr Maria Teresa Landi

These groups contribute data and/or samples to GenoMEL projects but do not receive direct funding from the NoE.



An example of a 'pedigree' or family tree, used to examine the incidence of melanoma in a single family.

Purpose of the NoE

The consortium's previous research has been very successful in understanding susceptibility genes and developing joint data collection for gene/environment interaction studies. In order to continue its proactive role, GenoMEL has established a multidisciplinary European platform, directed towards:

- Developing shared resources and activities.
- The identification of new susceptibility genes and understanding the role of these genes in tumours.
- The investigation of genotype/phenotype interaction and gene/environment interaction for known susceptibility genes.
- The investigation of attitudes to risk of melanoma in Europe, and translation of that risk perception into behavioural change.
- Spreading excellence by creating a widely accessible web-based Content Management System (CMS) to address prevention, early detection, dealing with the diagnosis of melanoma and genetic counselling.

Through GenoMEL's jointly executed research, groups will support the network's goals in maintaining excellence in research, increasing institutional integration and creating an enduring structure of translational melanoma genetics research in Europe and other countries. European integration will enhance dialogue, disseminate expertise and resources, provide training and allow mobility of scientists within Europe.

Platform 1:

Developing shared resources and activities to increase efficiency and to improve the quality control of data

GenoMEL has been successful in creating a cooperative network. Its continuation and growth are dependent upon the creation of structures that facilitate cooperation without damaging the trust that exists between its member groups.

A supportive management structure is being developed to increase the efficiency of collaborative projects through centralised pooling of data and resources. These structures include:

1. External review schedules to promote better focus of research activities incorporating both Scientific Advisory and Patient Advocacy Boards.
2. A project specific ethical committee to review protocols and interfaces with the general public.
3. Administrative support for GenoMEL in the form of activity managers.
4. Improved communication within GenoMEL by further development of the GenoMEL web site and regular video/web conferencing.
5. Broadening of the scope of GenoMEL by funding post-doctoral student and researcher exchange programmes and the strengthening of link to new centres.
6. Developing a DNA/cell line/tumour resource. This will be particularly important in support of doctoral students and will strengthen collaborations between Western and Eastern Europe.
7. Organise centralised mutation screening/genotyping of samples where this will improve efficiency and including samples from new centres not yet able to process samples rapidly.
8. Enlargement of the number of groups collecting the same data set from melanoma families using a common questionnaire and a shared database with remote data entry.

Platform 2:

Identifying new susceptibility genes and understanding the role of these genes in tumours

- GenoMEL is already exploring genetic linkage approaches to the identification of new high penetrance genes, in cooperation with Dr Jeff Trent of TGen. We now propose to use SNP chip technology to identify medium to high penetrance susceptibility genes associated with a family history of melanoma, young age of onset or multiple primaries. This project will be carried in two phases over the first 4 years of the grant. During the first phase in year 1, a GenoMEL screen will be carried out by Service XS, using a 250K chip. In phase 2, Illumina bead arrays will be developed, to explore Single Nucleotide Polymorphisms (SNP's) of interest identified in phase 1 and a series of coding SNP's from candidate gene families as are being identified currently by the Sanger Centre in Cambridge. The choice of chip remains an area for discussion as the technology is evolving rapidly.
- In the third year of the grant, GenoMEL will use the phase 2 Illumina bead arrays to identify genes modifying phenotype in families with germ line mutations in susceptibility genes if funding remains to do this.
- Classic tumour suppressor genes often play a crucial role as somatic mutations in sporadic tumours. GenoMEL will investigate the role of genes at the CDKN2A locus in carcinogenesis by studying somatic events in tumours removed from patients with germ line mutations and in those without.

Platform 3:

Investigation of genotype/phenotype interaction, gene/gene interaction and gene/environment interaction for known susceptibility genes

To further study the environmental determinants of melanoma, GenoMEL has already developed a common questionnaire to measure sun exposure using latitudes of residence to compute exposure levels. These data are stored on a server at the University of Pennsylvania. The questionnaire is concerned essentially with personal and family history of cancer, and sun exposure. The complete data set is comprised of these exposure data, phenotyping data (naevus count, hair colour, freckling) and results of mutation screening of a blood sample. These data will be used to perform genotype/phenotype and gene/environment interaction studies. The statistical power of these studies will be very significantly increased by this NoE as a result of the large increase in the size of the data set and by the recruitment of groups from very different latitudes, and with genetically diverse populations.

Whilst most families develop melanoma alone, early data suggest that families are at increased risk of cancers related to exposure to smoking, such as pancreatic cancer. GenoMEL is therefore introducing a one-page supplementary questionnaire that will be used to collect data on smoking and alcohol intake. It is possible that modifier genes affect the expression of the CDKN2A locus and therefore the effect of known genes, such as variants in the MC1R receptor on penetrance, will be studied and new modifier genes will be sought.

Platform 4:

Attitudes to risk of melanoma and behavioural modification

It is GenoMEL's hypothesis that health education designed to prevent melanoma will be more effective if directed towards those at increased risk. This hypothesis will be tested by questionnaire studies in families and in general European populations by correlating estimation of self-risk with reported behaviour. The literature will then be surveyed in order to design a computer-based tool to be used by family members and the general population to estimate risk and this tool will be evaluated. Finally this risk estimation tool will be linked to a multi-media package mounted on the GenoMEL web site in which appropriate sun protection strategies and early detection strategies are linked to the estimation of risk.



Sun protection strategies are an important part of melanoma prevention.

Activities to Spread Excellence

GenoMEL is in a strong position to spread scientific excellence. There is great enthusiasm for, and commitment to, research within new member states. It is proposed to encourage the development of these groups through the facilitation of exchange programmes for post doctoral students, by providing access to centralized screening of samples (where necessary), data analysis, web based information and scientific meetings.

GenoMEL will contribute to economic development in Europe by involving Small to Medium sized Enterprises (SME's) in:

- The development of content management systems (CMS), tools that enable the production of text, data or graphics within a coherent and validated website, and
- 'SNP chip' projects looking for new genes and the screening of samples for mutations.

GenoMEL has also recruited two new groups from new member states and allocated funds to our Spanish participant to support data collection in Latin America. All of these new centres will benefit from shared resources and the existing expertise of the consortium.

GenoMEL also intends to develop educational strategies for melanoma families, the general public, melanoma patients and health care professionals via

www.genomel.org, which carries the first CMS aimed at patients newly-diagnosed with melanoma. This package was developed with the SME, Naked Design.

GenoMEL will evaluate this system by analysis of questionnaires completed by users of the web site, and will adjust the content accordingly. If the analysis is positive, then similar CMS's for patients addressed to metastatic disease and familial melanoma will be developed.

GenoMEL will also develop CMS's aimed at health care professionals, which address:

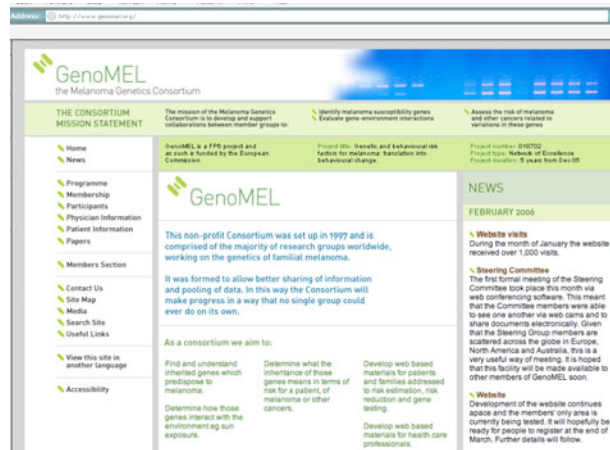
- Early diagnosis (for physicians in primary health, and dermatologists/plastic surgeons in training).
- Genetic counselling/risk assessment for dermatologists and clinical geneticists.
- The management of melanoma.

Clinicians in European countries will also be invited to one-day educational meetings held in conjunction with GenoMEL scientific meetings.



The city of Genoa in Italy – site of the 2006 GenoMEL meeting.

Further information



For further information please visit the GenoMEL web site at:

<http://www.genomel.org/>

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