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GenoMEL
Genetic and environmental determinants of melanoma: translation into behavioural change

Network of Excellence

FP6 Life sciences, genomics and biotechnology for health

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1. Project execution

Introduction

In 1997 the Melanoma Genetics Consortium was established. Starting out as a small cooperative of international research groups, it later secured funding from the US National Institutes of Health to conduct collaborative research. In 2005, using funding from FP6 as the GenoMEL Network of Excellence (NoE), it expanded to encompass over twenty participant groups and both broadened and deepened its research activities. GenoMEL's participant groups cover a variety of disciplines and are based across the globe.

The NoE established a formal project management structure and laid out a detailed work plan. Through a programme of jointly executed research it has:

- ✓ Achieved excellence in research.
  Over the last five and a half years GenoMEL has published 80 scientific papers, across a wide range of journals including several in the very highly rated journal *Nature Genetics*.

- ✓ Created an enduring structure for translational melanoma genetics research.
  GenoMEL now has a central database containing data on over 2000 families from around the world that have a strong predisposition to melanoma. There is also a central resource of biological material with one of GenoMEL's groups in the Netherlands. An annual meeting to discuss scientific progress and new directions is already planned for 2012, hosted in Leiden, the Netherlands.

- ✓ Increased institutional integration.
  GenoMEL has a truly international Steering Group with members based in the UK, Italy, Sweden, the Netherlands, Australia and the USA. The highly active GenoMEL Analysis Team (GAT) has members based in the UK, France and the USA. NoE member groups have also benefited from GenoMEL exchange activities and have used each other's specialist laboratory facilities.

- ✓ Sustained and increased international collaboration.
  GenoMEL has collaborated with other consortia based in the United States and Australia. It has also established a sister consortium called BioGenoMEL (www.biogenomel.eu) to examined the genetics of melanoma outcome.

GenoMEL's activities are grouped into four platforms. All of these platforms have achieved their major aims:

Platform 1: Developing shared resources and activities to increase efficiency and to improve the quality of control data.

Review bodies
Under the NoE, GenoMEL has created an appropriate management structure incorporating external review bodies and a successful website. Originally three bodies were planned – a patient advocacy board, a project ethics committee and a Scientific Advisory Board (SAB). It was quickly decided that the ethics committee and patient advocacy board had overlapping functions and were merged into the Joint Advisory Group (JAG).

At first there were problems with recruitment to the SAB – partly because many of the most eminent figures in the melanoma research field were already members of GenoMEL, but also because such people are typically extremely busy. However, the SAB gradually developed a good balance of expertise from across Europe, the US and Australia, encompassing leading figures in the world of melanoma research. The first task of the SAB was to help the Project Management Team (PMT) write the plan for Using and Disseminating Knowledge (PUDK). In GenoMEL's first review, the reviewer had only one comment concerning the PUDK - 'excellent'.

At every NoE annual meeting at least one member of GenoMEL's SAB has given a talk, and at the 2010 meeting three SAB members gave talks. This active involvement of the SAB at annual meetings has helped to keep the consortium vibrant and relevant. The SAB has also given guidance on GenoMEL's scientific direction and suggested ways of raising GenoMEL's public and scientific profile.

The JAG's first task was to write its own procedures. This was quickly followed by: reviews of research study protocols and questionnaires; the updating of the patient information on the GenoMEL website and a consultation on the issue of feeding back genetic test results. Later, the JAG undertook a major review of the ethical standards that GenoMEL requires of its participant centres based on the various consent forms used across the consortium. This was followed by a challenging review of the ethics of conducting an interferon study using historical samples and data without specific patient consent.

Throughout the NoE period, the JAG has provided valuable feedback on GenoMEL's website. For instance, when GenoMEL was developing its public position on the controversial area of vitamin D supplementation to avoid cancer, several successive versions of a summary were drafted based on JAG feedback and information received from relevant professionals, including endocrinologists. The JAG also played a key role in creating and reviewing two of GenoMEL's educational packages, the 'melanoma - dealing with the diagnosis' package and the 'dealing with the secondary diagnosis of melanoma' package. Finally, the JAG helped formulate a dissemination plan for the health psychology projects and reviewed GenoMEL's data protection statement.

The review bodies beyond the NoE

Both the JAG and SAB will continue beyond the grant period. GenoMEL's sister consortium, BioGenoMEL, is also considering adopting a similar review structure. However, sustaining GenoMEL's review bodies without specific management support will be challenging.

The website

The GenoMEL website has a Members' Section that acts as a secure depository for minutes and presentations. It now has over 200 presentations and other files for members to refer to. The public section of GenoMEL's website has information and resources for research participants, melanoma patients, clinicians, researchers and the public. It has achieved over 125,000 visitors and the British Medical Association (BMA) commended the GenoMEL patient information page in 2008. In 2010 the BMA highly commended GenoMEL's web based dealing with the diagnosis package. Greater detail concerning the GenoMEL website is provided under platform 4.

Annual meetings
GenoMEL has held a series of annual meetings to discuss progress and develop future projects. All of these meetings have given GenoMEL's younger researchers the opportunity to present their work. This has worked in combination with GenoMEL's exchange opportunities – the annual meeting providing an opportunity to network with potential research hosts, and a forum for disseminating their results. The exchange programme underpinning their new projects through travel and material funding and, for the final meeting, funding to attend and present.

The annual GenoMEL meetings in Italy, Sweden, Slovenia, the UK and Israel were all accompanied by parallel educational events. These events were aimed at local researchers and clinicians and gave them the opportunity to hear from subject experts of international standing. Rather than travelling to an international meeting, the speakers came to them, as it were. This was an excellent way of capitalising on the scientific expertise that GenoMEL meetings bring together. Typically these meetings were held in conjunction with a local organisation. In 2010 for example, the GenoMEL educational event was a joint GenoMEL-UK Melanoma Study Group meeting. In 2011 GenoMEL linked up with the Israel Cancer Association. In fact, the Israeli skin cancer awareness week was scheduled to coincide with the meeting and began with a joint press conference.

GenoMEL members in Genoa at the 2006 meeting

A 2012 GenoMEL meeting is already planned for Leiden in the Netherlands.

Shared biological resources – somatic samples
GenoMEL has also developed shared resources in terms of pooled biological samples. The University of Lund and the Karolinska Institute have gathered somatic samples from 135 familial primary melanomas and 52 matched primary sporadic melanomas from the GenoMEL centres. Laboratory work on these samples, looking at somatic *BRAF* and *NRAS* mutations, was presented at the 102nd meeting of the American Association for Cancer Research in 2011. The programme committee scored it in the top 2% of abstracts presented in the poster sessions. Submission of a related paper is planned for the coming months.

Shared biological resources – germline samples
In addition to somatic samples, GenoMEL has gathered germline DNA samples from thousands of research participants and sent them to Leiden in the Netherlands. These samples were used in GenoMEL's Genome Wide Association Studies (GWAS) and a project looking at the effect of additional inherited genes (modifier genes) on melanoma risk in families genetically predisposed to melanoma (see platforms 2 and 3). There are considerable quantities of residual samples and the GAT is considering their use in future collaborative projects. Some of the samples are already being transferred to the University of Leeds for follow up studies. In addition, the samples have been registered with the EC funded Biobanking and Biomolecular Resources Research Infrastructure (BBMRI) project. BBMRI has 50 plus members from over 30 countries and is intended as a pan-European biobank.

Joint training and new questionnaires
GenoMEL held specific training meetings in Genoa in 2005 and in Slovenia in 2006. These meetings enabled GenoMEL's new European groups and its centres in South America to familiarise themselves with the GenoMEL database which is maintained by the GenoMEL group at the University of Pennsylvania and is known as "the PENN database". They were also opportunities for the new groups to engage with GenoMEL's study protocols and questionnaires (which they subsequently translated). Sessions at all of the annual meetings were then dedicated to the PENN database and data entry progress.

As part of the NoE, a new questionnaire concerning smoking and the consumption of alcohol was developed and implemented across the consortium.

The GenoMEL exchange activities
As part of the NoE a formal exchange programme was created and managed by GenoMEL's participant group in Italy, the University of Genoa. The administrative challenges of supporting an exchange programme proved greater than anticipated. However, they were overcome and the financial management of the programme was moved to the Coordinating centre, the University of Leeds. At the end of each year the programme for the following year was revised with a view to encouraging further applications and to meet GenoMEL's commitments to integration and spreading excellence. Over the full period of the NoE approximately 144,000 Euros was awarded to exchange activities, supporting 28 successful applications:

- 10 applications for funding to attend meetings.
  For example, in June 2008 Dr Nadine Kasparian received funding to give talks at the 3rd International Genetics and Public Understanding Workshop and at the European Meeting on Psychosocial Aspects of Genetics, both in Barcelona.

- 9 applications to undertake 'long' (3 month) exchanges to other scientific groups.
  For example, in 2007 Dr Anton Puig Butille travelled to the GenoMEL group in Brisbane, Australia to undertake a molecular research project. He used their laboratory facilities to screening samples for novel familial melanoma genes.

- 5 applications for funding to host meetings.
  For example, Professor Cannon-Albright received funding to host an analysis meeting at a crucial time for GenoMEL's joint research projects into melanoma genetics.

- 3 applications to undertake short exchanges

For example, in 2009 May Chan undertook a short exchange to the PENN group to assist the database manager. Together they examined the integrity of the database, addressed data inconsistencies, revised procedures for data extraction/transfer and ensured compliance with security protocols.

- One application to support a public health initiative
  Professor Wilma Bergman received funding in 2008 to evaluate a new, pictorial strategy for increasing awareness of melanoma. This strategy involved innovative health promotion leaflets, which have proved so popular that the Dutch melanoma charity Stichting Melanoom has adopted them. Over 20,000 copies have been distributed so far and further print runs are planned.

The leaflet can be downloaded as a PDF file from:
www.melanoom.nfk.nl/content/140861/kunt_u_een_haai_van_een_dolfijn_onderscheiden

The sub-title translates as, 'Can you distinguish a shark from a dolphin?'

Project management
The PMT has played a prominent role in developing European Framework Programme (FP) manager networks. In 2006 the European Community Project Managers' Association (ECPMA) was established in the UK. The purpose of the ECPMA is to exchange information and share experiences of coordinating and managing FP projects. Both Project Managers in the UK are members of the ECPMA and the full time manager has been its secretary for most of its history. He has also written an article for the ECPMA website entitled, ''so you want to be the manager of an FP project?'' (Available from the ECPMA home page at www.ecpma.eu.) The ECPMA is chiefly composed of UK based managers but also includes managers from other countries including Germany, Greece, Spain, the Netherlands and Sweden.

The Leiden project manager is a founder member of the EU-Project Managers Association in the Netherlands (EUPMAN), and is part of its steering group. EUPMAN began in 2007 and quickly established a website (www.eupman.eu) and a large membership. Both EUPMAN and the ECPMA hold regular meetings to discuss a wide range of topics. Past themes have included proposal writing, collaborating with SMEs, dealing with exchange rate fluctuations, and the use of timesheets in FP6/FP7. Also, both groups have active member forums for online discussion. A combined meeting with members of both EUPMAN and ECPMA was held in Amsterdam early in 2010. Discussions are currently underway to establish closer collaboration, possibly with a shared website and a wider reach beyond the UK and the Netherlands.

Attendees at the joint ECPMA/EUPMAN meeting in 2010, Amsterdam (including two representatives from GenoMEL).

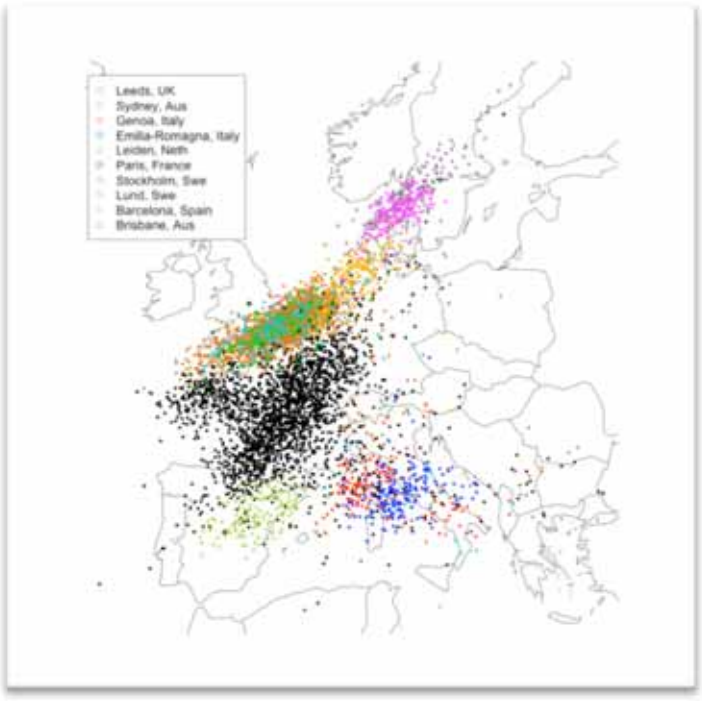
Platform 2: Identifying new susceptibility genes and understanding the role of these genes in tumours

The GenoMEL Genome Wide Association Studies (GWAS)
The first stage of the GenoMEL GWAS was completed in 2009 and resulted in a *Nature Genetics* publication in August of that year – 'Genome-wide association study identifies three loci associated with melanoma risk' *Nat Genet.* 2009;41:920-5. The genome-wide screen identified five regions with genotyped or imputed SNPs reaching $p < 5x10^{-7}$. Three regions were replicated in this study: 16q24 encompassing *MC1R*, 11q14-q21 encompassing *TYR*, and 9p21 adjacent to *MTAP* and flanking *CDKN2A* and *CDKN2B. MC1R* and *TYR* are associated with pigmentation and cutaneous sun sensitivity, well-recognised melanoma risk factors, while the 9p21 locus is novel for common variation underlying susceptibility to melanoma. Subsequently, we have conducted additional analyses showing that the chromosome 16 finding is due entirely to genetic variants in *MC1R*. We have also shown the chromosome 11 effect is entirely due to variants in the pigment gene, *TYR*. Thus this work confirmed the role of common inherited pigmented genes in melanoma susceptibility and the possibility of a new gene on chromosome 9.

The same edition of *Nature Genetics* contained another GenoMEL paper. We collaborated with a team based at Kings College London (part of the FP7 ENGAGE project and also funded by the Wellcome Trust and the UK National Institute for Health Research) and validated their findings concerning variants of the *MTAP* and *PLA2G6* genes. Together we showed that these variants are associated with increased naevus counts and melanoma risk. This paper was entitled, 'Genome-wide association study identifies variants at 9p21 and 22q13 associated with development of cutaneous nevi' Nat Genet. 2009;41:915-9.

The second stage of the GenoMEL GWAS study involved a further case-control analysis of 1200 cases and 1200 controls, with the results being merged to produce a combined genome-wide study. Additional GenoMEL funds also supported genotyping on a further sample set. This genotyping focussed on regions identified in the course of this study as containing susceptibility loci. 800 cases and 800 controls were genotyped with the customized 220k Illumina SNP array (produced by the EU FP7 COGS Consortium) to identify with more precision the critical SNP variants in the *CDKN2A*/*MTAP* region, around *TERT* and around *CASP8* (the first detailed mapping of these regions). Phase 2 of this work therefore identified entirely new melanoma susceptibility genes such as *CASP8* whose role in melanoma carcinogenesis will now be explored.

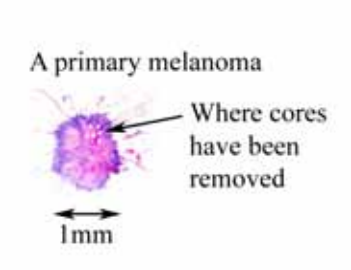
A manuscript based on the second stage of the GWAS is under second review at *Nature Genetics*. We have also collaborated with two other consortia and combined information to identify further susceptibility genes. A manuscript from these collaborations is also under review at *Nature Genetics*. In total, we have now identified 10 loci associated with melanoma susceptibility: many in pigmentation genes, others in genes associated with nevogenesis and others in novel biological pathways.



This image is from the first *Nature Genetics* paper and shows an estimation of where sample donors come from based on a principal components analysis, which distinguishes populations based upon a small number of genes, which differ between them. In this case the genes included HLA, lactase and a pigment gene which determines eye colour.

Studying somatic mutations

GenoMEL's extensive GWAS projects look at susceptibility and inherited genes. They involve DNA samples extracted from blood or cheek cells. However, GenoMEL is also researching changes in the tissue that cause particular melanomas to develop, and relating this to inherited genetic variation. These studies involve samples of genetic material taken from actual tumours. Primary melanoma tumours are very small and working with such small quantities is technically challenging. GenoMEL is a pioneer in this area and has produced reliable results using techniques such as coring of paraffin embedded tumours, micro-dissection and DASL arrays.



This image (not to scale) demonstrates the challenge of taking cores from melanoma tumours. GenoMEL also uses laser micro-dissection techniques that can remove a single cell.

Somatic mutations in *CDKN2A* gene carriers

It is well known that particular alterations of the *CDKN2A* gene can increase susceptibility to melanoma. GenoMEL's online database was used to identify samples for a collaborative study on tumours from carriers and non-carriers of these mutations. GenoMEL's groups gathered almost 200 tumour samples together and looked to see if there were different, additional mutations in the actual tumours between carriers and non-carriers, and between

familial melanoma and sporadic melanoma. The researchers looked for mutations in genes that code for particular proteins, the *BRAF* and *NRAS* genes. There was no significant difference in the frequency of *BRAF* mutations between familial melanomas with *CDKN2A* mutations and those without *CDKN2A* mutations. Similarly, the frequency of *NRAS* mutations did not differ when tumours from patients with and without *CDKN2A* mutations were compared. In no case were *BRAF* and *NRAS* mutations found to coexist in the same tumour. In conclusion, a comprehensive investigation of somatic genomic events in *CDKN2A* mutated melanomas has been performed. GenoMEL's Swedish researchers, at Lund University and the Karolinska Institute, are currently integrating genetic data (*BRAF* and *NRAS*) and genomic data for a manuscript that will be submitted to a leading journal.

Platform 3: Investigation of genotype/phenotype interaction, gene/gene interaction and gene/environment interaction for known susceptibility genes

The GenoMEL PENN database

As part of the NoE, a new, online database at the University of Pennsylvania has been created. This resource builds on an existing consortium database, but gives groups online access to their own data and enables the database manager to generate reports and resolve queries. The database currently holds information on 16,251 individuals (from 2,146 families), with over 5,000 melanoma patients. Information is available from 3,828 questionnaire modules on family history and 2,830 questionnaires on sun exposure. The database also contains information about cancers other than melanoma, *CDKN2A*/*CDK4* mutation status and nevus phenotype information.

As part of the NoE, a new questionnaire concerning smoking and the consumption of alcohol was developed and implemented across the consortium in a study designed to determine if smoking and alcohol consumption "explains" an increased risk of pancreatic cancer in some melanoma families. The database now contains information from this questionnaire on over 3,800 individuals. Preliminary analyses from the database were presented at the 2011 annual meeting and papers are currently being drafted. The PENN team have undertaken to support the database for the foreseeable future.

Screening for modifier genes

Mutations in the *CDK4* and *CDKN2A* genes are known to increase susceptibility. GenoMEL has been using single nucleotide polymorphism (SNP) arrays to screen for other genes that could modify the effect of these mutations. We looked for an effect on the penetrance of these mutations, the risk of other cancers and an influence on a person's nevus phenotype. Our research suggested a role for genes involved in pigmentation and nevus susceptibility, and we identified a set of 30 SNPs covering the known pigmentation variation and the nevus count variation. The samples were successfully screened for the selected SNPs using the Sequenom platform based at Leiden University Medical Center. The results of this research are not yet ready for public release. However, a manuscript is currently being drafted. Also, further data are being sent to us from the GenoMEL groups in Australia who performed a similar analysis on their own samples. The analysis of the combined dataset and the manuscript are expected in the next two months.

Platform 4: Attitudes to risk of melanoma and behavioural modification

Overview
As part of the NoE, GenoMEL has expanded its remit to include new scientific fields. Previously the consortium had focussed on understanding the genetics of melanoma susceptibility with scientific publications seen as the prime method of dissemination. However, it was clear that there was a need to engage with the world in a wider sense and to optimise the use of our scientific findings. So the NoE expanded the consortium's genetic and epidemiological research and combined it with information technology and health psychology expertise. This enabled GenoMEL to undertake an ambitious programme of online research and dissemination.

The public GenoMEL website
When the Melanoma Genetic Consortium was applying for the NoE it was clear that the consortium had to greatly increase its public profile and its engagement with clinicians, patients, and study participants The consortium's first website was established in 2005 and the NoE has revised and expanded this site beyond all recognition over the last five years. The website has three aims: to enable research; to increase scientific dissemination/integration, and to offer feedback to study participants. Currently the website is divided into sections aimed at the public/patients, physicians and the scientific community. It contains a mixture of text, images, downloadable PDF files, online tutorials, video, audio and other educational material.

Over the period of the NoE the website has achieved over 125,000 visitors –

Year	Unique Visitors
2005	952
2006	14,823
2007	33,154
2008	30,763
2009	32,989
2010	9,741
2011	2,583(up to the end of July)

Visitor numbers greatly increased in the middle of the NoE when the online questionnaire aimed at the public was recruiting participants. 'Unique visitors' represent the number of unduplicated (counted only once) visitors to the website over the course of a particular year. The number of visitors was determined using 'cookies' (first with Statcounter, subsequently with Google Analytics). GenoMEL's website privacy policy covers this automated collection of data. The privacy policy can be found at www.genomel.org/#js_privacy

Health psychology questionnaire aimed at the general public
Led by researchers from the Karolinska Institute, GenoMEL devised a series of online questionnaires. With the assistance of the PMT, the SME New Knowledge Directorate (NKD) turned these questionnaires into online packages. The first online questionnaire was made available in ten different languages and over 8,000 members of the general public took part.

Based on the results, Dr. Richard Branstrom presented a well-received abstract at the World Melanoma Congress in 2009. This was followed in 2010 by papers in the *European Journal of Cancer Prevention* and in *Cancer Epidemiology, Biomarkers and Prevention*. The first paper was entitled, 'Melanoma risk factors, perceived threat and intentional tanning: an

international online survey' (Branstrom et al. *European Journal of Cancer Prevention* 2010, 19: 219-26). The second was entitled, 'Predictors of Sun Protection Behaviours and Severe Sunburn in an International Online Study' (Bränström et al. *Cancer Epidemiology, Biomarkers and Prevention* 2010, 19:2199-210). As part of our commitment to dissemination, plain language summaries of these papers were written and added to the GenoMEL website at www.genomel.org/patient_information.php#js_laysummaries
Study participants were also informed by email that summaries were available –thousands of the participants volunteered email addresses for feedback.

Briefly, the first paper looked at why people seek a tan and how tanning is related to different melanoma risk factors. Overall, 70% of people reported some degree of intentional tanning during the past year. Perhaps surprisingly, 38% of respondents who reported a previous diagnosis of melanoma had also intentionally tanned. Preference for a dark suntan seemed to be the strongest reason for intentional tanning even amongst those with a previous melanoma. People from different countries generally gave more weight to their desire for a tan than to their risk of developing melanoma. The 'take home' message was that we should look at ways of influencing this drive to sunbathe if we want to reduce the number of melanomas being diagnosed.

The second paper looked at whether people reported using shade and clothing to protect their skin from the sun, as well as about other behaviours such as wearing sunscreen. Half of them reported at least one severe sunburn, during the previous 12 months. Perhaps surprisingly, 27% of those with a previous melanoma also reported at least one severe sunburn during the previous 12 months. Use of protective clothing and shade, as well as avoiding midday sun exposure, were more strongly related to reduced risk of sunburn than sunscreen use. Unsurprisingly, those who considered sun protection to be difficult and impractical, and those who reported a positive attitude towards suntans, were less likely to protect themselves.

Despite public health messages about the importance of sun protection, many people, including some with a previous melanoma, were not protecting themselves effectively resulting in severe sunburn. If we want to reduce the number of people getting sunburnt we should target the practical, social, and psychological barriers to practising sun protection.

A third paper is currently under review with the journal *Archives of Dermatology*.

Following publication, numerous queries have been received from other researchers interested in using the questionnaire items and/or the questionnaire images. GenoMEL has subsequently shared these materials with other researchers based in the UK, Switzerland, Australia, Croatia, Canada, New Zealand, Germany and the USA.

Health psychology questionnaires aimed at members of families with a predisposition to developing melanoma
As a follow up to the first questionnaire two further questionnaires were developed for individuals in the PENN database (from melanoma families and who therefore have an increased risk of melanoma). The first of these was an adapted version of the first questionnaire looking at behaviour in the sun, and the second examined attitudes to genetic testing and genetic research.

Collection of data for these questionnaires was time consuming. Several groups who participated in promoting the first questionnaire did not have enough participants with a family history of melanoma to warrant taking part in this study. Also, it was found that many

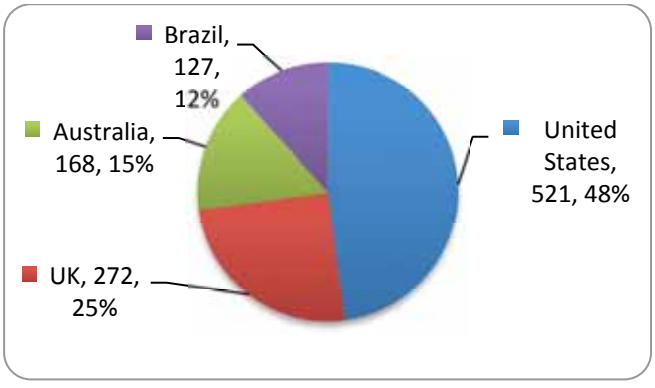
individuals who had taken part in the familial melanoma studies did not have ready access to the Internet to complete the questionnaire. Several groups therefore used postal questionnaires to increase participation. Over 400 participants were eventually recruited. This figure was relatively disappointing, as this number was a small proportion of the individuals recruited to the GenoMEL studies overall, but one of the aims of the health psychology questionnaires was simply to see whether it was possible to conduct a study in this way. The first questionnaire showed that it certainly is possible when your target audience are users of the Internet. The other questionnaires suggest that Internet use is probably not yet sufficiently widespread when targeting an existing cohort of research participants.

Results from the second and third questionnaires were presented to the GenoMEL membership at the Tel Aviv meeting in May 2011. These findings are now being written up for submission to journals later this year. It would therefore be premature to publish the full results of the two questionnaires here. However, a large proportion of the participants considerably underestimated their own risk of developing melanoma. Perhaps not surprisingly, given their previous study participation, they were supportive of genetic research. Similarly the participants were also receptive concerning genetic testing, but the results indicated that negative test results might be misinterpreted and lead to less preventive behaviours.

GenoMEL's web tutorials and other educational packages
During the NoE GenoMEL has produced a suite of educational packages and other health promotion materials. The amount of time and other resources that these required was greatly underestimated in the first version of the Joint Programme of Activities. However, the consortium in general, and the PMT and NKD in particular, devoted additional attention to these activities with impressive results. These packages are also an excellent example of GenoMEL's integration, involving subject experts from the Netherlands, Spain, the UK, Sweden, Australia and the USA.

GenoMEL's educational packages – the dermoscopy tutorial
Dermoscopy is a technique that can improve the early recognition of melanoma. In 2009 GenoMEL released an online tutorial (www.genomel.org/dermoscopy) aimed at educating healthcare professionals concerning dermoscopy. Over 600 CD versions of the tutorial were distributed at the Congress of the International Dermoscopy Society Congress in Barcelona. The attendees, from 43 different countries, gave positive feedback on the tutorial.

NKD also created a prototype iPhone dermoscopy 'app'. After testing it was released for download on the iTunes website. Users in 49 countries have since downloaded it several thousand times. The countries with the highest number of downloads are the US, the UK, Australia and Brazil (see below).



Downloads	
US	521
UK	272
AU	168
BR	127

This was the media company NKD's first iPhone app and they have subsequently capitalised on the experience by creating other apps. Thus GenoMEL has promoted the development of European small companies.

GenoMEL's educational packages – the early diagnosis tutorial
In early 2009 GenoMEL published an interactive tutorial to assist primary healthcare workers and specialists in training with early diagnosis of melanoma – such early diagnosis is crucial to promoting better outcomes for melanoma patients. The package contained text, photographs, diagrams and videos and a self-assessment section. As well as an online version a CD version was recreated and over 1,500 copies were distributed at international meetings including the World Melanoma Congress in Vienna.

The early diagnosis tutorial was been well received by the medical community. The Royal College of General Practitioners reviewed the tutorial and gave us positive feedback –

"…an excellent educational tool for all doctors training or established in general practice."

"…pictures are of excellent quality and the variety of examples used the best our commentator has come across."

In 2010 a major review of the package took place and a revised version was launched in February 2011. The early diagnosis tutorial can be found at www.genomel.org/WP_3.3/wp3.3.html

GenoMEL's educational packages – the genetic counselling tutorial
Clinical genetic testing for patients with familial melanoma is a controversial area. In 2009 GenoMEL's Utah group led an effort to establish selection criteria for possible testing. This resulted in a paper in the *Journal of the American Academy of Dermatology* (2009, 6:677). Writing this paper to encompass opinion from across the world was a major challenge and demonstrated the need for clearer guidance in this area.

In 2010 GenoMEL produced an online tutorial to assist health care professionals involved in counselling patients about possible genetic testing for familial melanoma. This involved consulting widely with the GenoMEL membership to ensure the package encompassed differing opinions across Europe, the US and Australia. The tutorial was promoted at the spring meeting of the Association of Genetic Nurses and Counsellors in Belfast, April 2011. It was subsequently presented at international meetings and versions of the tutorial have been distributed on USB memory 'sticks'. This tutorial is an excellent example of how GenoMEL has sought to disseminate its scientific findings and improve melanoma care.

GenoMEL's educational packages – the dealing with a diagnosis of melanoma
GenoMEL's Leeds group created a package to help patients deal with a diagnosis of melanoma in 2004. It featured video interviews with patients discussing their experiences and was initially produced only as a CD-ROM. This package was taken as a model for the GenoMEL packages, and as part of the NoE it was extensively revised and remodelled. In 2010 it was highly commended in the British Medical Association Patient Information Awards.

GenoMEL's educational packages – the dealing with a secondary diagnosis of melanoma
To follow on from GenoMEL's first patient package, a second presentation was created concerning a secondary diagnosis of melanoma. This package was optimised for the web and featured audio interviews and photographs rather than videos. The quality of the audio was also greatly improved in comparison to the original package. This production has been entered into the BMA 2011 Patient Information Awards.

Other dissemination via the GenoMEL website
The GenoMEL website has a number of other dissemination strands. It has a monthly news section updated via a blog (http://genomel.blogspot.com), a podcast section (www.genomel.org/#js_podcasts) and a series of patient and clinician information pages. For example, there is a page specifically for people who have a family history of melanoma. The wealth of website content is a testament to the progress and commitment of the consortium.

The future
GenoMEL is already planning future meetings and has a host of on going research projects. The University of Leeds and NKD have agreed to maintain the website in the short to medium term and the University of Pennsylvania will support the PENN database for the foreseeable future. However, dedicated management support and development of these resources will be dependent on successful future funding applications.

2. Dissemination and use

How to disseminate knowledge from an FP project via the web – the GenoMEL experience

In the 21st Century many Europeans first turn to the Internet when they need information. To be taken seriously an organisation therefore needs an online presence. The GenoMEL website www.genomel.eu was created in 2004 to promote the Melanoma Genetics Consortium. It carried descriptions of the consortium partners, lists of their scientific papers, and an overview of existing/proposed studies. Under an FP6 Network of Excellence (NoE), it has under gone two major reorganisations, numerous minor revisions and switched its focus to disseminating the outputs of the project. It has now received over 125,000 visitors.

Original features of the website
The website began with two sections. A public section and a password protected members' section. The public section contained descriptions of the individual groups, a description of the overall project and specific pages aimed at patients and clinicians. However, the group descriptions provided most of the content.

The members' section contained: a directory of members; a slideshow; a notice board; a meeting minutes area; a members' messaging service; a who's who area; a calendar; GenoMEL policy statements and a resources area. Many of these facilities were under utilised by members who generally preferred to communicate by email. However, the resources area proved popular, with folders containing presentations from previous meetings and a wide range of other documents. By mid 2011 the resources area contained over 200 presentations and other files.

Expansion of the website
Gradually the clinician pages and patient information pages were revised and expanded. In 2008 the GenoMEL patient information web page was commended in the British Medical Association (BMA) Book Competition Awards.

A major output of the project was a series of Content Management Systems (CMSs). Two of these were placed on the patient information page and were specifically aimed at melanoma patients with a diagnosis of melanoma. A major component of both these packages were interviews with actual patients, talking about their experiences and how they have dealt with melanoma. Subsequently, the dealing with the diagnosis CMS was highly commended in the 2010 BMA Patient Information Awards.

Three CMSs were created for healthcare professionals. The first was a tutorial aimed at encouraging clinicians to diagnose melanomas at an early stage improving outcomes for melanoma patients. This CMS contains many clinical photographs, video, animations, diagrams, a series of case studies and assessment exercises. The early diagnosis tutorial was well received by the medical community. In 2009 the Royal College of General Practitioners reviewed the tutorial and gave us positive feedback, "... an excellent educational tool for all doctors training or established in general practice... pictures are of excellent quality and the variety of examples used the best our commentator has come across." The early diagnosis of melanoma tutorial was extensively revised in February 2011.

A second tutorial was added to the physician page in 2009. This CMS promoted the use of

dermoscopy in the early diagnosis of melanoma. It was subsequently released as an ‘app’ on the iTunes store. The third tutorial concerned genetic counseling for melanoma and was launched in late 2010. This CMS also contained photographs, video, animations, diagrams and assessment exercises. Promotion of this CMS continues.

Health psychology questionnaires
As part of the NoE, GenoMEL launched a series of online questionnaires on the website. The first was available in ten different languages and garnered over 10,000 responses. This questionnaire was aimed at the general public and examined behavior in the sun. The second and third questionnaires were aimed at people who were already participating in GenoMEL’s melanoma studies. As a result of these questionnaires two scientific papers have been published, a third has been accepted for publication and more are likely to follow.

News and meetings
The website home page has a news section; this is updated on a monthly basis via a blog. A list of relevant national and international meetings was also maintained during the project but this has now been discontinued to reduce the amount of updating that the website requires.

Languages
The original intention was to have the website available in four or five languages to increase its appeal to a European audience. Many of the web pages were translated and were available in Dutch, Swedish, Spanish, Latvian and Russian. However, every new page, and every revision of an existing page, required translation and the amount of work required quickly mushroomed. The possibility of computer-assisted translation was investigated but would still have required specialist input. Rather than have a patchwork of translations of varying dates it was decided to concentrate on a single language, English, but to strive to make the text as clear as possible. This also enabled the consortium to concentrate on translation of the online questionnaires.

Visitor numbers and locations
Since the NoE began the website has achieved over 125,000 visitors.

Year	Unique Visitors
2005	952
2006	14,823
2007	33,154
2008	30,763
2009	32,989
2010	9,741
2011	2,583(so far)

Map overlay, visitors to the website since the major revision in September 2009
There were 24,186 visits from 2,877 cities

Conclusions

The Internet provides an excellent opportunity to publicise your project and disseminate your research findings. In particular, it can reach large segments of the European population, enabling your project to establish a public profile. However, creating an effective project website is a major undertaking. Many researchers underestimate the work required, especially in terms of maintenance. Out of date information can be worse than no information at all because it reflects badly on the commitment of the project partners. Proper resourcing and planning can avoid these problems.

Key questions for project websites

Before creating your site

- Is the domain name short, relevant and memorable? (Preferably a .eu name.)
- What is the consortium's key message?
- How is that message going to be communicated?
- Who will build the site? What sites have they previously created?
- What colours, fonts, pictures, etc. are needed for a unified look?
- How much effort will be required to maintain the site?
- Who will be maintaining the site?
- Are other languages necessary?
- Is a secure, members' only area required?

When creating your site

- Is the site clear and simple to look at?
- Who will proof read the text?
- Is the text as easy to read as the subject allows?
- Is a tracking tool, such as Google Analytics or Statcounter, necessary to monitor usage of the site?
- What links to other sites are needed?
- Have the funders been acknowledged with appropriate text, logos and web links?
- Has a privacy policy been included?
- Have terms and conditions of use been included?
- Are there creation dates on the individual web pages?

When maintaining your site

- Is the site disseminating the consortium's latest findings (if appropriate)?
- What other sites should link to this one?
- Are the existing links up to date?
- Is the original 'message' still relevant after one year?
- Has the whole website been formally reviewed in the last two years?
- Are there revision dates on the web pages?
- What will happen to the site when the funding period ends?