



GABRIEL SUMMER 2007 NEWSLETTER

The First Year



The Annual Meeting, March 2007, at Imperial College London

We have had a productive first year, marred only by the sad premature death of Stephan Weiland. Stephan has made an extraordinary contribution to the epidemiology of childhood asthma, and we are privileged to be able to harvest the results of the goodwill and international co-operation which he built with such skill and gentle persuasion.

The advanced environmental studies have been successful, with the completed field testing of more than 10,000 schoolchildren in alpine and rural regions. We are awaiting the preliminary analyses of the results of this extraordinary study with real excitement. The way ahead is now clear for us to begin to dissect the environmental contribution to disease, with special attention on the

effects of the rich microbial environment that GABRIEL participants have already shown to protect against disease.

On the genetics side, we have carried out the first ever genome-wide association study for asthma, and found a new gene (or gene cluster) on chromosome 17q21 which predisposes to childhood asthma, and perhaps affects one third of children with the illness. In the year ahead we will extend our genetic studies to include adult and occupational asthma. Rapid advances in technology mean that we will by the end of this calendar year have completed a genome-wide survey of over 10,000 asthmatics. In the months to follow we expect genomic studies and our model systems to bring us closer to a true understanding of the cause of the mysterious disease of asthma.

Gratifyingly, our next year's budget has been approved by the EU, so we can continue to do the best science that we can, whilst continuing to enjoy each others' company in the wonderful shared culture that typifies Europe today.

William Cookson

c o n t e n t s

Editorial page 1 Stephan Weiland, a tragic loss page 2 GABRIEL publication page 2 Ethics in GABRIEL page 3 Fellowship Report page 4 GABRIEL's new partners page 5 GABRIEL Focus: Models page 6 Calendar and upcoming events page 8

Professor Stephan Weiland

Stephan Weiland was a highly talented and dedicated scientist and epidemiologist, who will be greatly missed. He was remembered on 27th July at a special Memorial Service in Ulm, his home town.



The sad news of Professor Stephan Weiland's sudden death, in March, came as a great shock to the whole GABRIEL Consortium, and to those who had known him and worked with him for many years, it was a painful tragedy. Colleagues, including Professor Erika von Mutius, who had worked with Stephan for many years, paid tribute to him in Ulm on 27th July 2007. In his honour and as a recognition of his contribution to science and to the work of GABRIEL, the Fellowship Programme offered by GABRIEL has been renamed "The Stephan Weiland Fellowship"

A full obituary is available on the GABRIEL website

GABRIEL Paper in Nature

The paper describes the genome-wide association (GWA) study that has been conducted and is a key component of the GABRIEL project, (work package 5.2) It is the first step in GABRIEL's aim to identify the important genetic factors underlying asthma. GABRIEL is already initiating the next phase to investigate the important findings from the GWA in the other cohorts and populations that have been collected over the years by the various GABRIEL partners.

The paper "Genetic variants regulating ORMDL3 expression contribute to the risk of childhood asthma" was published online in Nature, 4 July 2007, and in the print journal on 26th July 2007.

Dr Miriam Moffatt says : "This is a large study involving scientists and doctors from many countries, and we are confident that we have discovered something new and exciting about childhood asthma. These novel findings do not explain completely how asthma is caused, but they do provide a further part of the gene-environment jigsaw that makes up the disease. We and our colleagues are currently preparing even bigger studies to find other genes of smaller effect, and to relate these to environmental factors that protect against asthma. Our eventual aim is to be able to prevent the disease in susceptible individuals."



<http://www.nature.com/nature/journal/v448/n7152/full/nature06014.html>

ethics in gabriel

an overview of the issues

by Deirdre Madden



The GABRIEL Ethics Forum was established to provide a means by which the ethical issues raised by this research project can be discussed with the partners. As a first step the Forum would like to collate information regarding the consent procedures adopted in each partner country to enable us to analyse the divergences between partners on this important issue and to ascertain to what extent harmonisation is necessary or desirable in this context. This will help inform our research papers into best

practice on these issues which can be circulated in due course for electronic consultation, and subsequently at workshops. We would strongly encourage all partners to respond to the questions listed on the webpage to help us to get an accurate picture of the legislative framework within which their research is carried out, and any relevant professional or institutional guidelines in operation.

The Ethics work package of GABRIEL is examining the ethical, social and legal aspects of the participation of children in genetic research. Focus group work is currently being conducted to analyse the attitudes and expectations of children and their parents in relation to such participation. A legal and ethical literature review, which looks at issues such as the

rights of children who participate in genetic research and the law of consent, has now been completed and a draft report will shortly be disseminated to partners involved in the Ethics Forum for further discussion. Our plan is to synchronise this report with the results of the focus group work and to prepare recommendations for best practice in genetic research involving children. We would welcome comments in relation to any aspects of this work and have indicated some questions to stimulate discussion on the Ethics section of the GABRIEL website, (url below).

Dr Deirdre Madden is a Senior Lecturer in the Faculty of Law, University College Cork, Ireland, (Partner 14) and heads work package 2 in the GABRIEL Consortium.



www.gabriel-fp6.org/research/ethics/index.htm

fellowship report

immune mechanisms of *opisthorchis felinus* helminth infection and its relation to atopy

The GABRIEL Consortium offers two fellowships (workpackage 9) every year, each one lasting for three months. This gives researchers a valuable chance to work at another institution, often in a different country, where they may learn new techniques, acquire advanced skills, share knowledge, and build up international working relationships. In the first year, the Fellowships were awarded to Giovanni Malerba



Maria Vasilyeva

she was based at the Parasitology Department of Leiden University Medical Center (Partner 13) under the supervision of Professor Maria Yazdanbakhsh. She has received a 3-month training in cellular and molecular immunological techniques appropriate for the analysis of cell proliferation activity and immune system associated genes expression, and will now be able to use these methods for the project at the Central Research Laboratory of the Siberian State Medical University.

Maria Vasilyeva is a medical doctor with a specialization in Allergy and Immunology and a PhD in Oncology and Immunology. She works at the Central Research Laboratory of the Siberian State Medical University.

from the University of Verona, (Partner 31) and to Maria Vasilyeva, from the Siberian State Medical University in Tomsk (Partner 29). Dr Malerba will undertake his programme of work later this year, but Dr Vasilyeva has completed her fellowship and explains her work here.

Opisthorchis felinus helminth infection is very common in the Tomsk region (West Siberia, Russian Federation) and it appears to influence atopic disease prevalence in this region. Infectious background in conjunction with urban European-like and typical rural lifestyle give very good models of natural relationships between infectious and atopic diseases which are one of the major issues in the GABRIEL project. Immune mechanisms of opisthorchis infection and its relation to

atopy in urban and rural areas in the Tomsk region will be studied in the project of the Siberian State Medical University (SSMU, Tomsk, Russia) in conjunction with the Department of Parasitology of Leiden University Medical Center (LUMC, Leiden, Netherlands).



During Maria's GABRIEL Fellowship in the Netherlands

GABRIEL reaches beyond Europe with four new partners

GABRIEL continues to grow, and to expand its area of research, by including four new institutions as part of the EU Targeted Third Countries call.



The Microbiology Institute at the University of Quito, Ecuador (Partner 36):

This experienced group has an outstanding track record in the investigation of the interactions between geohelminth infection and asthma and allergic disease.

Dr Philip Cooper, who leads the group, is currently directing two cross-sectional studies and one birth cohort study that are examining gene-environment interactions in the development of asthma in rural and urban populations in tropical regions of Ecuador.

The Research Institute of Medical Genetics and Siberian State Medical University, Tomsk, Siberia (Partner 34):

The group will add to the main GABRIEL project by genotyping 200 families with multiple atopic asthma cases collected in the Tomsk region of Russia. The team has a long-term experience in collaborative investigation the molecular basis of atopic diseases with a strong record in atopic diseases management and epidemiology and genetic association study. The team is the leading one in genetics of atopic diseases in Russia. The team will contribute to the study of interaction between genes, infectious agents and atopic disease.

The Institute of Biochemistry and Genetics, Ufa Science Centre, Ufa, Russia (Partner 33):

The Institute carries out investigations in population genetics, evolution of anatomically modern humans, and the molecular genetic bases of hereditary and complex diseases. The Department has recruited a substantial case-control collection for the study of asthma. The asthma sample consists of 350 patients, the control group includes 303 unrelated nonasthmatic subjects with different ethnic origins (Russians, Tartars, Bashkirs).

The Chinese University of Hong Kong Partner 35):

The Department is the coordinating centre of the ISAAC program in the region. They have established a laboratory specialized in immunological and genetic research to determine the environmental and genetic determinants of asthma and allergies. The department has close collaboration with many major centers in Mainland China to determine the genetic and environmental factors for asthma and allergies

For a full description of the new partners and their work (work packages 3 & 4) please go to www.gabriel-fp6.org



Maxim Friedin and Valery Puzyrev of the Institute for Medical Genetics, Tomsk, Siberia



Drs Elza Khusnutdinova and Alexandra Karunas, Ufa Science Centre, Russia



The research group of Dr Gary Wong, at the Chinese University of Hong Kong, China



Philip Cooper (front) with his study group in Ecuador. Above left; field workers travel by canoe to reach the study group

GABRIEL Focus:

The work of the Models Group

GABRIEL MODELS GROUP (WP7)

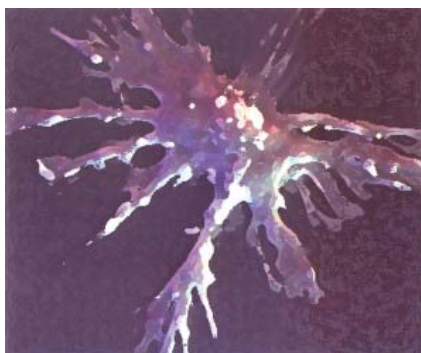
This work package has the task of developing validated models both using cell systems as animal models that can rapidly test the environmental samples from the epidemiological studies of GABRIEL with a strong protective effect against the development of allergic asthma.

Samples

The structural characterization of active compounds will be conducted at Research Center Borstel under supervision of Professor Otto Holst. The group has a strong track record in characterization of microbial compounds using cutting edge technologies.

The microbiological assessment of the environmental samples will be undertaken at the University of Franche-Comté Besançon under supervision of Professor Piarroux. The laboratory has considerable experience in the typing of the environmental microflora and isolation and culture of microorganisms.

The participation of EMC microcollections in the model group, will allow access to synthetic molecules from bacteria that have been found in dust collections from farms and are thought to be protective against the development of asthma.



From Leiden University Medical Centre, (Partner 13) from left, Franca Hartgers, Bart Everts, Yvonne Kruize, Maria Yazdanbakhsh and Alwin van der Ham

Environmental factors and epithelial cells (WP7.1)

The group of Professor Ian Adcock at the National Heart and Lung Institute in London (Partner 1) will, in search of environmental factors with the ability to prevent the development of allergic inflammation, investigate the action of compounds on epithelial cell cultures and primary cells from patients with airway diseases.

Environmental factors and dendritic cells and T cells (WP7.2)

Candidate compounds (dust extracts and bacterial extracts) will be tested by the group of Professor Maria Yazdanbakhsh at Leiden University Medical Center on cell activating capacity using dendritic cells. Dendritic cells are known to induce different regulatory immune responses and can be used to test potential ability of candidate compounds to act pro allergic or anti allergic.

Early life events are important in setting the stage for the development of allergic disorders. The

group of Dr. Bianca Schaub, at University Children's Hospital at Ludwig Maximilians Universität München will study the immune responses of cord blood cells to stimulation with different dust and bacterial extracts. The identification of compounds that have strong regulatory effects on cord blood cells might be important for selection of those that might be included in early allergy prevention strategies.

Environmental factors and murine models (WP7.3)

Dr. Marcus Peters in the group of Professor Albrecht Bufe at Bochum University, has developed an ovalbumin model of allergic asthma in the mouse. The group will test the available compounds in this model to determine the effect that a farming environment might have on the development of asthma. By using genetically different mice, it will be possible to understand in a mechanistic way how any identified compound suppresses allergic inflammation.

Animal models of house dust mite-induced allergic asthma used at the GRIAC institute [Groningen Research Institute for Asthma and COPD] target specifically the effect that (maternal) smoke exposure has on the development of asthma and its interaction with genes. Dr. Machteld Hylkema, Dr. Gerard Koppelman,

Prof. Antoon van Oosterhout and Prof. Dirkje Postma are collaborating on how asthma genes and tobacco smoke interact with dust and bacterial extracts to modify asthma outcome.



Members of the Models group at Groningen University (Partner 20): back row from left, Machteld Hylkema, Dirkje Postma, Benoit Piavaux, Marike Boezen, front row, Anton van Oosterhout, Henk Koning, Anne Blacquiere, Gerard Koppelman

Asthma documentary underway



Professors Bill Cookson and Erika von Mutius on location during the making of the documentary about asthma.

Filming of a new documentary about asthma took place in and near Munich in July, and will be shown on television and in over 1000 schools and colleges. Professor William Cookson, Dr Miriam Moffatt and Dr Markus Hilty travelled from the UK to participate in field studies on Bavarian farms, which will be featured in the film, along with members of the team from Munich University, led by Professor Erika von Mutius. The film, made by Visions Unlimited Media GmBH, and co-ordinated by Paul Pechan, is part of the EU EMRS (European Media Repository of Science) Project.

A feat of logistics: field studies accomplished in Germany



A huge undertaking, the field studies in Germany have demanded a level of organisation and coordination that defies belief.

More will be written about this extraordinary undertaking in the next issue, and on the website. Thousands of questionnaires were sent out, to hundreds of schools, and families, and then followed up by field workers and doctors collecting samples which then had to be transported back to Munich and stored ready for analysis. The hard work of the team at Munich and all the helpers and field workers is very much admired and appreciated by everyone in GABRIEL.

Preparations for sending out the questionnaires to hundreds of schools in Bavaria, Ludwig Maximilian Children's Hospital, Munich

GABRIEL Calendar 2007-2008

Meetings

GABRIEL Annual Meeting

14-15th February 2008
Maison del la Chimie, Paris
Reserve these dates!
More information to follow

Workshops

10-12 October 2007 University Medical Centre Groningen:
Introduction to family-based and population-based genetic research and data analysis. contact c.alen@imperial.ac.uk to register.

19-22 November 2007 Leiden University Medical Centre:
Immunological methods for epidemiological studies with specialized analysis for immunological data.
contact Claudia Alen on c.alen@imperial.ac.uk

Full details on www.gabriel-fp6.org



If you would like your workshop or meeting advertised in the next issue of the GABRIEL Newsletter, or on the website, please send all details to Dana Finch d.finch@imperial.ac.uk