

**WELCOME TO GTAC'S 2005 PUBLIC MEETING!**

Dear Colleague

Thank you for attending GTAC's 2005 public meeting: "**Demystifying Gene Therapy**".

In this Delegate Pack you will find some information on the work of GTAC, profiles of today's speakers, as well as summaries and printed copies of their presentations.

We have also provided you with a free copy of **GTAC's 11<sup>th</sup> annual report**, a summary of the Government's 2003 **White Paper on Genetics**, and some **CD-ROMs on Genetics**, all of which we hope you will find interesting.

We hope that you will enjoy the day. We have provided refreshments and a buffet lunch. Please feel free to chat to GTAC members.

Please would you fill in the **feedback form** and return to a member of the GTAC Secretariat. This will help us to organise next year's event and gives you the chance to **win some chocolate!**

With best wishes

Cathleen Schulte  
Monika Preuss  
Daniel Gooch

**The GTAC Secretariat**  
Department of Health

## WHAT IS GENE THERAPY?

The Government's **2003 "Genetics" White Paper: Our Inheritance, Our Future – realising the potential of genetics in the NHS**" says this about gene therapy:

"Gene therapy is the deliberate introduction of genetic material into patient's cells in order to treat or prevent a disease. As well as replacing defective copies of genes, a variety of sophisticated techniques are being developed that will allow the activity of genes to be turned up or down. Although this new branch of medicine is still at the research stage, we expect to see licensed gene therapy medicines within a decade. ... In the longer term gene therapy may become a cornerstone of modern medicine." **(Paragraph 1.25 & 1.26)**

"... [T]he Department of Health will invest up to **£3 million** to support gene therapy research into single gene disorders. Boosting research in this area now has the potential to benefit the estimated three-quarters of a million patients in this country with single gene disorders that are currently incurable." **(Paragraph 5.24)**

"... [T]he Department of Health will make available **£2.5 million** over 5 years to support gene therapy research for cystic fibrosis." **(Paragraph 5.25)**

"... [T]he Department of Health will invest up to **£4 million** to provide NHS and other public sector researchers with access to high standard gene therapy vector production facilities." **(Paragraph 5.27)**

"... [T]he Department of Health will fund research into the long-term safety of the use of gene therapy vectors which are designed to insert into human genetic material. This research should be invaluable in minimising the risks and maximising the benefits of gene therapy." **(Paragraph 5.28)**

The allocation of the **£3million** for single gene disorders, and the **£1million** for long-term safety work, were announced at last year's BSGT meeting. An announcement on the allocation of funding for the cystic fibrosis **£2.5million** was made in January 2005. The **£4million** for vectors is currently being implemented. All four of these commitments will help to support UK gene therapy and ensure that patients benefit by providing earlier access to promising new clinical trials.

## WHAT IS GTAC?

GTAC is the UK national research ethics committee for gene therapy clinical trials. Its main function is to provide advice to and receive proposals from doctors who wish to conduct gene therapy clinical trials in the NHS.

GTAC defines gene therapy as "**The deliberate introduction of nucleic acids into human somatic cells for therapeutic, prophylactic or diagnostic purposes.**"

GTAC's function is to:

## Demystifying Gene Therapy

- ◆ Consider and advise on the acceptability of proposals for gene therapy research on human subjects, on ethical grounds, taking account of the scientific merits of the proposals and the potential benefits and risks;
- ◆ Work with other agencies which have responsibilities in this field;
- ◆ Provide advice to UK Health Ministers on developments in gene therapy research and their implications.

GTAC's membership comprises the current Chairman, Professor Norman Nevin, who is a distinguished clinical geneticist, and 16 members who are drawn from a variety of professional backgrounds. The broad membership ensures that GTAC provides informed and balanced advice to health ministers. Just over half of the members have skills and experience in science and medicine. The others have skills and experience in genetic counselling, ethics, nursing, law, hospital management, industry, media, medical charities and patient welfare. Full details of the membership are given in the enclosed **GTAC 11<sup>th</sup> annual report**.

The work of the committee is supported by a secretariat of three, who coordinate and administer all GTAC business. GTAC meetings are usually attended by observers from the Health and Safety Executive (HSE) and the Medicine and Healthcare Products Regulatory Agency (MHRA).

## PROGRAMME

- 10:30 Registration (Tea and Coffee)**
- 11:00 Opening remarks**  
Prof Norman Nevin  
Chair of GTAC
- 11:10 Demystifying gene therapy clinical trials**  
Dr Christian Ottensmeier, Consultant and Cancer Research UK Senior Research Fellow  
Southampton University Hospitals
- 11:40 From molecule to market – developing a gene therapy drug**  
Dr John Ellis, Oncology Projects Leader  
ML Laboratories Plc
- 12:10 Break**
- 12:20 Research ethical issues in gene therapy**  
Dr Tuija Takala and Dr Lisa Bortolotti, Lecturers in Bioethics  
Centre for Social Ethics and Policy, Manchester University
- 12:50 The process of informed consent in gene therapy research**  
Mrs Deborah Beirne  
Senior Research Nurse, GTAC lay member  
St James' Hospital Leeds
- 13:20 Lunch**
- 14:00 Haemophilia gene transfer: solution to global treatment gaps**  
Dr Glenn Pierce  
World Federation of Hemophilia
- Haemophilia and Gene Therapy**  
Mr Adam Jones  
Severe haemophilia B patient
- 14:45 Awareness and involvement: BSGT, patients and the public**  
Mrs Renée Watson, British Society for Gene Therapy
- 15:00 Public involvement session**
- 16:00 Feedback**
- 16:30 Close**

# **Speakers' Profiles**

**Professor Norman C Nevin OBE**

Chair of GTAC



Norman C. Nevin is Emeritus Professor of Medical Genetics, Queen's University of Belfast and Head of the Northern Regional Genetics Service. He has held the positions of secretary, vice-president and president of the UK Clinical Genetics Society as well as serving on various national and international committees notably the Human Genetics Advisory Commission. He is a member of the European Concerted Action for congenital abnormalities. Professor Nevin was a founder member of the UK Gene Therapy Advisory Committee (GTAC) and is currently Chairman. His research interests have resulted in over 300 peer reviewed publications on various aspects of genetics, especially single gene disorders and congenital abnormalities. In 2003 he received an OBE for his services to gene therapy.

**Dr Christian Ottensmeier**

Southampton University Hospitals



Dr. Christian Ottensmeier obtained his medical degree in 1986 at the University of Münster, Germany. Until 1991 he trained in medical oncology/haematology. He then took up a postdoctoral research fellowship at the Dana Farber Cancer Institute, Harvard, Boston, USA before moving to the University of Southampton in 1994. At Southampton he completed his specialist training in medical oncology and became the first Cancer Research UK research fellow. He gained his PhD in Southampton in 1999 and since 1999 holds a Cancer Research UK senior research fellowship. He is currently Senior Lecturer and Medical Oncologist at the University of Southampton. His academic interests focus on DNA vaccination for B-cell malignancies and solid tumours and he has published widely in both medical and scientific journals.

**Dr John Ellis**

ML Laboratories Plc



I gained my PhD at the University of Birmingham and worked for 6 years as a post-doctoral fellow at the CR UK Inst for Cancer Studies in Birmingham. I subsequently worked in the commercial biotechnology sector developing novel molecules for cancer therapy. In my current role, I am responsible for the pre-clinical and clinical development of gene therapy applications for cancer.

## **Dr Tuija Takala**

Centre for Social Ethics and Policy, University of Manchester



Tuija Takala, MSc (soc) (Helsinki, Finland), LicSc (soc) (Turku, Finland), PhD (Turku, Finland) is Lecturer in Bioethics at the University of Manchester, U.K. and Adjunct Professor in Practical Philosophy at the University of Helsinki, Finland. Dr. Takala's research interests lie in the philosophical analysis of bioethical arguments and concepts, and she has a special interest in issues related to genetic information, consent, autonomy and paternalism. Her publications include contributions to *Bioethics*, *Cambridge Quarterly of Healthcare Ethics*, *Journal of Medical Ethics*, *Journal of Medicine and Philosophy*, *Medicine, Healthcare and Philosophy*, *Perspectivas Bioéticas*, *Theoretical Medicine and Bioethics*, *Western Journal of Medicine* and the book *Scratching the Surface of Bioethics* (ed. with M. Häyry) (New York and Amsterdam: Rodopi, 2003). Dr. Takala is the chair of the editorial board of the *Cambridge Quarterly of Healthcare Ethics*, co-editor of the *Values in Bioethics* special book series (Rodopi) and member of the editorial board of the *Theoretical Medicine and Bioethics*.

**Dr Lisa Bortolotti**

Centre for Social Ethics and Policy, University of Manchester



Dr Lisa Bortolotti is Research Associate and Honorary Lecturer in Bioethics at the Centre for Social Ethics and Policy, School of Law, University of Manchester. Her research interests are in philosophy of mind, philosophy of science, philosophy of psychology and applied ethics. She has written papers on rationality, theories of interpretation, delusions, animal cognition and the ethics of stem cell research and reproduction. She works on the EC funded project EURECA on delimiting the concept of research and the nature of research activities.

**Mrs Deborah Beirne**

Cancer Research UK Clinical Centre, St James' Hospital, Leeds



Debbie Beirne is a practicing nurse within the field of medical oncology research. She has previous experience in medicine, surgery, renal dialysis and transplantation and haematology nursing. During this time she has successfully undertaken a Bachelor of Science degree in Health Studies, and more recently a Masters degree in Health Care Ethics at the University of Leeds.

Her work currently involves coordinating a portfolio of clinical trials primarily in renal cancer and malignant melanoma, with an emphasis on biological and gene therapy approaches. She has direct contact with patients and their families in both a supporting and counselling role as well as carrying out the necessary monitoring and direct administration of 'novel treatments' within the context of a clinical trial.

Debbie Beirne has been a GTAC lay member since 2002.

## **Dr Glenn Pierce**

World Federation of Hemophilia



Glenn Pierce, Ph.D., M.D., has served as Vice President, Research and Clinical Development, of Avigen, Inc., a San Francisco Bay area gene therapy company, since November 2002. At Avigen, he has conducted clinical gene transfer preclinical and clinical research in hemophilia and Parkinson's disease. Before joining Avigen, Dr. Pierce was Vice President, Therapeutic Product Development, at Selective Genetics, a San Diego gene therapy company he helped found in 1998. While there, he initiated clinical studies in diabetic leg ulcers using a growth factor gene. From 1994-1998, he served as Vice President, Preclinical Development at Prizm Pharmaceuticals, a start-up biotechnology company. Prior to that, Dr. Pierce held a number of positions at Amgen and was instrumental in the development of Amgen's neurobiology and tissue regeneration programs and experimental pathology department. Dr. Pierce holds numerous patents in various areas of drug delivery, tissue engineering, medical devices and gene therapy vectors. He has published more than 100 papers in scientific and medical journals and has given dozens of lectures and presentations all over the world. He has served two terms as the volunteer president of the National Hemophilia Foundation (NHF) in 1992 and in 2002. He initiated the NHF's first blood safety and gene therapy committees in the early 90's and has organized NHF's annual gene therapy workshops since 1996. Currently Glenn serves on NHF's Medical and Scientific Advisory Council and on the World Federation of Hemophilia's gene, cell, and novel technologies committee. He earned both his M.D. and a Ph.D. in

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Immunology and Experimental Pathology at Case Western Reserve University in Cleveland, Ohio and completed a pathology residency and hematology research fellowship at Washington University in St. Louis.

## **Mr Adam Jones**

Born April 26<sup>th</sup> 1972, I am the youngest of 5 children (2 brothers and 2 sisters).

I was diagnosed with severe haemophilia B (Christmas disease) when I was 6 months old.

I have 2 cousins, and a nephew who are also affected by severe haemophilia B.

I attended Sunderland University (1998 – 2001) to study Physiology, and have worked previously as a research technician in the fields of lung cancer and calcium activated chloride ion channels.

I currently work as a trainer for the NHS Expert Patients Programme, working with Strategic Health Authorities and Primary Care Trusts to develop, administer and deliver courses in self-management for people living with long-term health conditions.

I married my best friend, Emma, in 2003 and we now have a 7 month old son who is our pride and joy.

**Mrs Renée Watson**

British Society for Gene Therapy



Renee trained as a biochemist in her home town Canberra, Australia, before travelling through the US, Asia, Indonesia and Europe. She landed in the UK in 2000 and took up post with the team that established the National Patient Safety Agency. In 2001, Renee moved to Oxford to help set up the National Translational Cancer Research Network, where she is currently employed as Operations Manager. Renee has been integral in the establishment of the British Society for Gene Therapy, and was elected to the board in 2003 with responsibilities for public awareness and patient involvement. Renee's dedication to improving health care for patients helps her to deal with the UK weather and not miss home too much.

# **Abstracts and presentations**

Demystifying Gene Therapy

## **Opening Remarks**

**Professor Norman Nevin OBE**

Chair of GTAC

# **Demystifying gene therapy clinical trials**

**Dr Christian Ottensmeier**

**Cancer Research UK Senior Research Fellow**

**University of Southampton**

Gene therapy is a relatively young approach for the treatment of patients. It holds great attraction in disease such as haemophilia. These patients are ill because their body cannot make a particular substance, which is needed to make the blood clot. The missing or abnormal gene has been identified. Gene therapy aims to give back a correct version of the faulty gene by using delivery vehicles called vectors. If this is successful and the gene is delivered to the right cells it should be possible to correct the problem and cure the patient without causing the problems related to the currently available treatments.

The same approach may also help with other, often extremely rare illnesses in which genes are faulty. Although huge progress has been made in recent years, the best way of delivering these genes in a safe, effective and durable manner is still uncertain. Scientists all over the world are testing, whether gene therapy can indeed be used to safely help patients.

Distinct from gene therapy is genetic vaccination. Here also genes are given to the patient, but genetic vaccines are more similar to the well-known vaccines, which we all receive. The aim of genetic vaccines is to awaken and alert the immune system rather than replacing a missing gene and genetic vaccines do not need to persist. Genetic vaccines appear to be very safe and may offer new inexpensive alternatives for the prevention of infections like malaria, tuberculosis and hepatitis. Genetic vaccines are also being tested against cancer and a number of clinical trials are underway to find out whether we can harness the power of the immune system to fight cancer.

The presentation will show what a gene is, and how scientists try to correct faulty or missing genes. I will explain the concept of gene therapy and genetic vaccines. I will give an overview of what is necessary to get permission to bring these new approaches to patients and what the timelines for such a project are.

# **From molecule to market – developing a gene therapy drug**

**Dr John Ellis**

**Oncology Projects Leader**

**ML Laboratories Plc**

The possibility of delivering genes to cells to intervene in disease processes is highly exciting. However, the early optimism surrounding the potential of gene therapy has yet to be fulfilled in the approval of gene based drugs for widespread patient application. The drug development process requires exhaustive testing of new medicines to ensure that licensed drugs are as safe as possible and will benefit patients. My talk will highlight the steps involved in the development of new drugs relating specifically to gene therapy based products: and will illustrate why the process takes so long and why the various steps are required to ensure the quality of marketed medicines.

# **Research ethical issues in gene therapy**

**Dr Tuija Takala and Dr Lisa Bortolotti**

**Centre for Social Ethics and Policy, University of  
Manchester**

# **The process of informed consent in gene therapy research**

**Mrs Debbie Beirne**

**Senior Research Nurse**

**Cancer Research UK Clinical Centre, Leeds**

**GTAC lay member**

Translating developments in science and medicine into potentially viable therapies necessitates that novel approaches or agents be tested in human patients. Key to achieving this process is to gain the voluntary consent and cooperation of patients to participate in clinical trials. The process of 'obtaining informed consent' encompasses many aspects of ethical trial conduct, the most important of which is the protection of patients. This is particularly relevant in newer areas of early phase medical research such as gene therapy where the outcome or result of the procedures are uncertain, potential side effects less well known than in conventional therapies, and for the most part, at least currently, personal benefit to the individual is doubtful.

Therefore the aim of this presentation will be to describe the process of informed consent, what it constitutes and what gene therapy research means to and for patients.

# **Haemophilia and Gene Therapy**

**Mr Adam Jones**

## **Severe haemophilia B patient**

Haemophilia is a genetic x-linked recessive characteristic that affects roughly one in one hundred and fifty thousand live births. It is a disorder of the clotting process where one of the clotting factors (most commonly factor VIII or factor IX) is under produced by the liver.

Haemophilia is exhibited to varying degrees in different individuals. In mild haemophilia clotting factor levels are around approximately 10 – 40% of normal levels. In moderate haemophilia clotting factor levels are around approximately 1 – 10% of normal levels. In severe haemophilia clotting factor levels are less than 1% of normal levels.

As haemophilia is a genetic disorder the condition will persist for the entire duration of the individuals life. Currently, there is no cure.

Gene therapy presents an interesting and exciting prospect for people living with genetic disorders. Unlike some disorders (e.g. S.C.I.D.) for which gene therapy presents the only real prospect for an improved quantity and quality of life, the level of care and treatment for haemophilia is currently excellent in the developed world. The lifespan of haemophiliacs has increased dramatically and improved care and prophylaxis ensures fewer bleeding episodes and reduced joint damage along with social inclusion in sports and socio-economic and educational outcomes. Thus, to engage in gene therapy trials would mean the abandonment – if only temporary – of this level of treatment, which could very well have a major impact upon that individual's quality of life. Therefore careful consideration is required on the part of the haemophiliac as to whether to engage in trials or not.

Questions still remain around the use of gene therapy. These questions include:

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1. The relative safety of gene therapy as compared to the recombinant clotting factor currently in use.
2. The efficacy of the product in relation to current treatments.
3. Cost, again in relation to current treatments and outcomes.
4. Time from trials to treatments.
5. Time from treatment becoming available to it becoming accepted as a mainstream treatment.

This said, there are many potential benefits to gene therapy, such as:

1. Inhibitors become a non-issue.
2. Greater inclusion in extra curricular and outdoor activities and sports.
3. Improved educational, psycho-social and socio-economic outcomes.
4. Improved self-efficacy for patients and their families.
5. No need to worry about future generations.

Even though current treatments for haemophilia are of an excellent nature, we should never forget the price we have paid to get here. Human Immunodeficiency Virus (HIV), Hepatitis C (HCV) and the recent admission that there is a theoretical risk of contracting Variant Creutzfeldt Jacobs Disease (vCJD) through blood and blood products have had a major impact upon the haemophilia community. This memory should be a motivating force for continued improvements in treatments and care.

The present situation is encouraging, as generations of haemophiliacs are growing up fitter, healthier and more positive about the future. There is greater inclusion in sporting activities, social activities and improved educational achievements.

The future is exciting. All indications are that gene therapy is on the way and its impact will be huge. The only question remaining is "how far away is that moment"?

# **Hemophilia gene transfer: solution to global treatment gaps**

**Dr Glenn Pierce**

**World Federation of Hemophilia**



**GTAC is grateful to the Katharine Dormandy Trust for sponsoring this presentation.**

**Awareness and involvement: BSGT, patients  
and the public**

**Mrs Renée Watson**

**British Society for Gene Therapy**