the WALES GENE PARK

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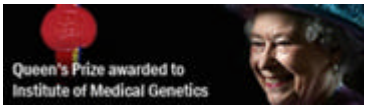

***End of Year Report* 2007-2008**

Summary

The Wales Gene Park aims to support and promote the creation, dissemination and application of genetic knowledge in Wales, particularly to improve health and to contribute to the development of a "knowledge economy". With continuing financial backing from the Wales Assembly Government via WORD the Wales Gene Park has established a broad portfolio of work ranging from support for basic and translational research in medical genetics to educational initiatives for health professionals, schools and the general public.

Vice Chancellor Dr David Grant and Professor Julian Sampson receiving the Queen's Anniversary Prize for Higher Education, on behalf of the Institute of Medical Genetics.

Wales is fortunate to have a depth and breadth of genetics expertise that is exceptionally strong for such a small country. In the current year this was recognised by the award of the Nobel Prize for Physiology or Medicine to Professor Sir Martin Evans of Cardiff University for the discovery of embryonic stem cells and the award of a Queen's Anniversary Prize for Higher Education to Cardiff University's Institute of Medical Genetics in recognition of the quality of its research and teaching.

During the current year over £3.6M of external funding for medical genetics research has been won for Wales and genetic researchers have contributed to many interdisciplinary projects (with clinical oncology, cardiology and others) that have brought much additional research funding into Wales. The facilities and expertise provided by the Wales Gene Park have been a critical factor in this success. Genetic discoveries made in Wales have been developed to provide new tests to improve the diagnosis of disease and to enable some of the first drug trials for previously untreatable inherited disorders. The Wales Gene Park's educational programmes continue to up-skill the NHS workforce so that these advances can be implemented to provide better care for patients and families across Wales. Through our outreach programme we have involved over 3000 school pupils in challenging educational events addressing topical issues such as genetics and mental health, designer babies and the Police National DNA Database.

Through their enthusiasm and hard work the Wales Gene Park team have contributed significantly to the continuing development of genetics as a unique strength for Wales. I hope that in this annual report I have succeeded in representing properly their achievements.

Julian Sampson, Chairman

The Work of the Wales Gene Park

The work of the Wales Gene Park is delivered through 9 current work packages. These address different aspects of the health priorities, educational needs and commercial opportunities identified in the Science Policy for Wales. The work of the Wales Gene Park builds upon existing areas of strength within Wales but retains flexibility to support newly emerging priorities.

Work Package 1: Management and Governance

The Wales Gene Park Executive Management Team (representing stakeholders from the NHS Wales, Techniquest, the Universities of Glamorgan, Swansea and Cardiff) meets three times each year to review progress on its work packages, address problems, consider feedback from the Advisory Group, note the outcomes of quarterly review meetings with the WORD Project management team and agree any changes to the work-plan.

The Chairman, Secretary and Strategic Director of the WGP meet quarterly with the WORD WGP project management team to map progress against milestones set out in the annual work plan, agree any variations to the work plan and discuss opportunities for future developments. At the quarterly meeting WGP undertakes financial reconciliation and identifies funding needs for developments.

The Wales Gene Park Advisory Group meets twice a year to ensure the governance and appropriate reporting structures for WGP within Cardiff University. In the current reporting period the advisory group 1) resolved an internal reporting structure for the governance of the WGP within the current Cardiff University committee structure. WGP will report via the School of Medicine to the Health Schools Strategy Board and from there via its chair, Professor Malcolm Jones to the University Board 2) advised on future plans for accommodation of the WGP within the School of Medicine at Cardiff University from August 2008 when the lease on WGP's current accommodation expires.

On 01.09.2007 Professor Mark Rees was appointed on a 0.25 FTE basis as Strategic Director of WGP with funding from the School of Medicine, Cardiff University. WORD made available additional funding to WGP to enable appointment of a project manager and this post is currently out to advertisement.

Work Packages 2 and 3: Wales Gene Park Technology Platforms

WGP supports two platforms that provide access to core genetic technologies for researchers in Wales - Genomics and Transgenics. The Genomics Facility also supports the delivery of DNA diagnostics through the NHS All Wales Medical Genetics Service via high throughput automated DNA handling. Where capacity permits a small number of projects from outside Wales are undertaken on a cost-recovery basis.

Much of the work undertaken by the facilities is reported under the relevant disease-area Work Packages but projects and metrics are summarised here:

> Genomics Facility

During the reporting period the facility has completed 12 projects for a range of genetics researchers with a particular focus on support for the COINTrans clinical trial to identify genetic markers for efficacy and safety in colorectal cancer chemotherapy (for further information on COINTrans see Work Package 9: Cancer Genetics)

Figure 1: The Wales Gene Park Genomics Facility supports research for Welsh HEIs and DNA Diagnostics for the NHS All Wales Medical Genetics Service. The facility handled 99,840 samples during the current reporting period

Colorectal Cancer Genetics:

1. Identifying SNPs from on-line databases and publications for 151 DNA repair genes (Cardiff University).

2. Sequence analysis of all known DNA repair genes in a Caucasian sample set to determine SNP frequencies (Cardiff University).

3. Assessment of LightScanner to identify novel SNPS (Cardiff University).

4. Genotyping MUTYH SNPs in 384 control DNA samples (Cardiff University).

5. Screening the Pol Lambda gene for SNPs in 114 DNA samples (Cardiff University).

6. Assessment of assay to amplify 4 exons of human TP53 from paraffin embedded tissue (Cardiff University).

Technology Development:

7. Investigation of cost effectiveness of two alternative genotyping techniques for the Lightscanner to expand the services offered by the facility.

Other projects:

8. DNA extraction and genotyping of the ACE I/D polymorphism in 24 saliva samples (UWIC).

9. DHPLC screening for mutations in the "2APRE" region of the TNF gene in 90 samples (Cardiff University).

10. Extraction of DNA from 20 synovial joint tissue samples and genotyping of SNPs in the PBEF1 gene (Cardiff University).

11. Mutation screening of WT1 gene for SNPs (Bristol University).

12. **OPA1** and **3** gene SNP discovery (School of Optometry, Cardiff University).

> Transgenic Facility

The transgenic facility has supported 34 projects during the year through provision of services for Pronuclear Microinjection (production of transgenic mice, 12 projects), Blastocyst Microinjection (production of knockout mice, 5 projects) and Rederivation (17 projects). All projects have been undertaken for researchers based at Cardiff University. The University has invested to expand the capacity of the facility through the appointment to two additional technical support posts.

In addition to its core laboratory work the facility has provided training courses on "Blastocyst Microinjection" and "Introductory Embryology Course" for researchers from UCD in Dublin and the Institute for Animal Health in Edinburgh.

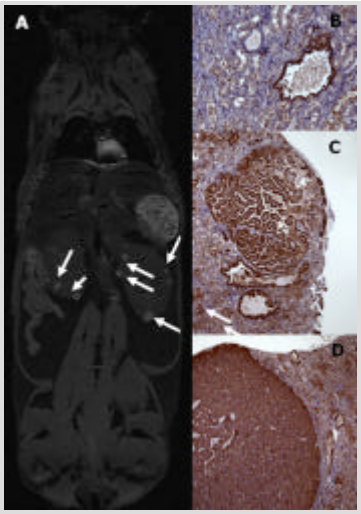

Figure 2: A mouse model of kidney tumour development

(A) is an MRI scan of a transgenic mouse showing many small kidney tumours (arrows). The tumours can be identified and measured readily when just a fraction of a millimeter across enabling researchers to monitor responses to experimental treatments (Courtesy of Dr M Hong Shen, Institute of Medical Genetics, Cardiff University).
(B), (C) and (D) show progressive stages in the development of kidney cancer in a transgenic mouse (Courtesy of Cleo Bonnet, Institute of Medical Genetics, Cardiff University).
The mouse model makes it possible to study the very early stages of tumour development and to test novel treatments. The findings are paving the way for improved diagnosis and treatment in patients with inherited predisposition to kidney tumours.

Work Package 4: Education and Public Engagement

Year on year growth has continued in the size and scope of the WGP's activities in education and public engagement (Figure 3 and Table 1). This work package is delivered across three areas – education for health and biomedical science professionals, schools and the public.

Table 1: Attendance Figures for Educational Events:
April 2007 - March 2008

	Month	Event	Health Professionals	Schools	Public
2007	April	Boy Genius		980	
	May	Living with Genetic Conditions		32	
		Science Café, Bangor			7
		Science Café, Swansea			38
	June	Mammalian Genetics Meeting	108		
		Democs in Schools		27	
	July	Democs in Schools (x10)		247	
		Democs for Public			13
		Meet the Mighty Gene Machine		159	
	August				
	September	Democs for Public			29
		Democs for Schools & Colleges		11	
		Meet the Mighty Gene Machine		178	
	October	Democs for Public			83
		Democs for Schools & Colleges		23	
	November	Public Discussion Event			64
		Democs for Public			51
		Democs for Students		11	
		Orphan Drugs & Rare Diseases	64		
		Cardiovascular Genetics	119		
		VHL Masterclass	38		
	December	Schools' Events		226	
		DNA Photocopying Workshops		320	
2008	January	Dabbling with DNA (KS4)		105	
		Democs			57
		Careers Event, Caerleon Comprehensive		62	
		Discuss DNA (Cardiff)		216	
		The Mighty Gene Machine		39	
	February	Dabbling with DNA (KS4)		51	
		Democs			54
		6th Form Talks - Merthyr Tydfil		105	
		The Mighty Gene Machine		93	
	March	DNA Photocopying Workshops		219	
		6th Form Talks		170	
		Democs			56
		Discuss DNA		193	
		The Mighty Gene Machine		289	
		TOTALS	329	3756	452

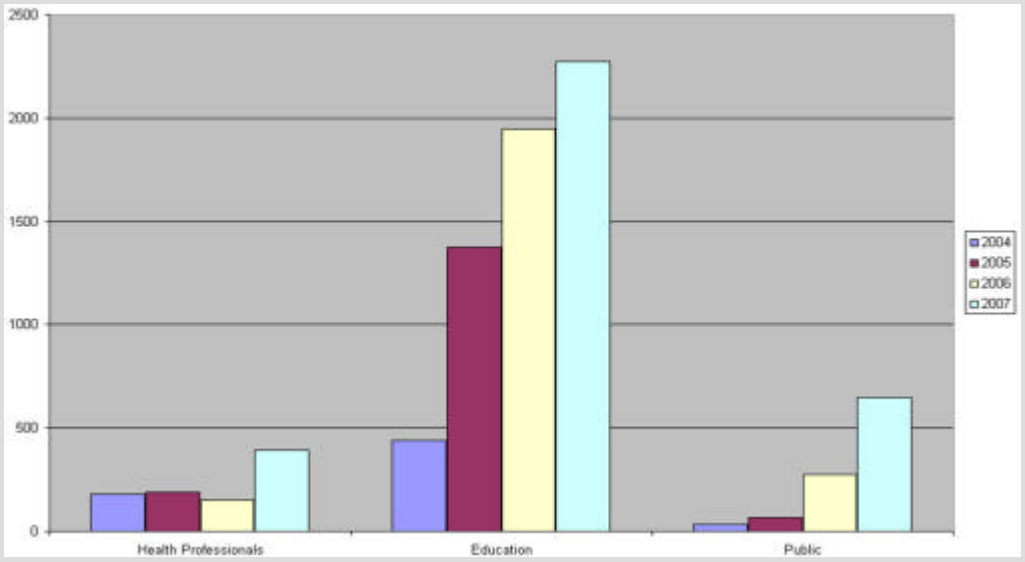

Figure 3: Year-on-year growth in participant numbers in the Wales Gene Park's educational programmes

> Educational Programme for Health and Biomedical Professionals:

Each year the WGP runs a number of courses and conferences focusing on selected areas of clinical and biomedical genetics. Faculty for these events includes experts from within Wales together with UK and international invited experts. This approach enables dissemination of expertise, provides a forum for networking and showcases areas of expertise in Wales to the wider biomedical community.

- **Mammalian Genetics, Development & Disease Workshop**
  29th June 2007
  Cardiff

  108 delegates

  The event included keynote talks from invited speakers and junior researcher presentations with two prizes awarded for the best presentations. These went to Brenda Meinhard, Cardiff University and Anthony Dalloso, Bristol University.

  Sponsorship was received from The Genetics Society, The Company of Biologists and GRI.

- **Orphan Drugs and Rare Diseases**
  8th November 2007
  Welsh Assembly building, Cardiff Bay

  64 delegates

  This policy engagement event addressed critical issues in the funding of treatments for patients with rare diseases, focusing on Enzyme Replacement

Therapies to highlight the policy dilemmas presented by orphan drug treatments. The programme of presentations and discussions included consideration of scientific, health economic, industry, ethical, patient and clinical perspectives. A workshop during the event focused on "Weighting Ethical Principles for Commissioning Decisions".

This was supported by an unrestricted educational grant from Genzyme Therapeutics Ltd. and CESAGen (ESRC Centre for Social and Economic Aspects of Genomics), Cardiff University.

Challenges of Clinical Cardiovascular Genetics
22nd & 23rd November 2007
Millennium Centre, Cardiff Bay

119 delegates from UK and Europe.

This event brought together clinical and laboratory experts from across the UK who are involved in the development of new services for inherited cardiac diseases.
The event launched WGP supported projects in inherited disorders of cardiac rhythm and cardiac muscle, and familial hypercholesterolaemia.

VHL Disease: A Multidisciplinary Masterclass
27th November 2007
Millennium Centre, Cardiff Bay

38 delegates.

This workshop brought together a UK-wide multidisciplinary expert panel to focus on best management for this complex inherited cancer predisposition syndrome.

> Genetics for the Nursing Professions

(Lead Professor M Kirk, University of Glamorgan)

The *Telling Stories* project provides an online resource of narratives relating to patients and families with genetic disorders. The site www.geneticseducation.nhs.uk/tellingstories was launched at the Millennium Stadium in June 2007. The resource is part of a coordinated UK initiative to increase genetics skills in the NHS workforce in response to the UK Government white paper "Our inheritance our Future". The project is a collaboration between Universities of Glamorgan and Plymouth, the Wales Gene Park and the Genetics Interest Group. The project has been widely disseminated through professional meetings and publications (Appendix 2).

> Schools Events

- **Living with Genetic Conditions**

Bishop Gore High School, Swansea 4th May 2007 and Pembrokeshire College, Haverfordwest 3rd December 2007

139 participants

Health professionals and members of families affected by genetic disease addressed the difficulties and hopes posed by genetic conditions.

- **Discussion sessions on the National DNA Database**

The Wales Gene Park has developed a game called "Discuss DNA – The National DNA Database", inspired by the format of a discussion game by Democs©. "Discuss DNA" allows small groups of people to explore and discuss the social and ethical issues surrounding the National DNA Database.

Initially, Discuss DNA was trialed in secondary schools in South-East Wales with 281 KS4 and KS5 students:

27th June	St Cyres School, Penarth
28th June	Bridgend College
2nd July	Ysgol Pencoed School, Pencoed
5th July	Brynteg Comprehensive, Bridgend
9th July	Brynteg Comprehensive, Bridgend
10th July	Howells School, Cardiff
26th September	Howells School, Cardiff
10th October	Newport School of Education

"Discuss DNA" was then translated into Welsh, redesigned by Techniquest's graphic designer and professionally printed. The event is now being delivered as an ongoing project in schools across Wales. To date, these include:

Eirias High School, Conwy (2 visits)
Howells School, Denbigh
Darland High School, Rossett, near Wrexham (2 visits)
Ysgol Ardudwy, Harlech
Ysgol David Hughes, Menai Bridge
Ysgol Syr Hugh Owen, Caernarfon
Newbridge Comprehensive, Gwent

- **Events for Sixth Form Students**

December 2007	Whitchurch High School, Cardiff. Ruth Glew, Genetics counselor at the Institute of Medical Genetics, spoke about inheritance and family history of disease, Dr Joan Haran, CESAGen, spoke about stem cells and the media and Paul Bryant, Assistant Forensic Intelligence Officer with South Wales Police, spoke on the use of DNA in crime detection. 119 students attended.
February 2008	Researchers from the University of Glamorgan discussed issues surrounding 'Designer Babies' to 100 students in Afan Taf High School, Merthyr Tydfil.
March 2008	A half day conference was hosted at Hereford Sixth Form College for smaller schools across Mid Wales. The speakers were: Dr Alastair Sloan, Cardiff University, on stem cell research; Robert Pratt, West Mercia Police, on the National DNA Database and crimes which have been solved using DNA evidence; and Dr Robert Herbert, University of Worcester, on the science behind DNA forensics.

- **Teachers' Genetics Network**

The Teachers' Genetics Network has grown steadily since it was started 4 years ago. Every term a newsletter is issued by the WGP to the members of the network. It discusses past educational projects and future events. It also provides a list of teaching resources on genetics topics.

> Public Events:

Discussion sessions on contemporary genetics issues:

- **Discuss DNA**

"Discuss DNA" has been used with adult groups since September 2007. It is proving to be very popular with this audience. In addition, discussion sessions using Democs© on Preimplantation Genetic Diagnosis, GM Foods and Stem Cells have been piloted with various adult groups in the South Wales community.

July 2007	Women's Institute, Llandaff
Sept 2007	Techniquest@NEWI
	Cardiff St Davids, Rotary Club
	Biosciences, Cardiff University
October 2007	PROBUS, Barry
	Techniquest, Cardiff
	Cardiff University, Postgraduate Social Society
	Women's Institute, Whitchurch and Llandaff
November 2007	Women on Wednesday, Dinas Powys
	Lifelong Learning, Cardiff University
	Women's Institute, St Fagans
January 2008	Barry Men's Forum
February 2008	PROBUS, Barry 2
	UWIC, Cardiff
March 2008	Ladies' Circle, Rhiwbina
	Rotary Club, Dinas Powys

- **National DNA Database**

15th November 2007

A public discussion on the National DNA Database was held in Cardiff on 15th November 2007. Paul Bryant from South Wales Police spoke about DNA forensics and the benefits of the National DNA Database, and Professor Steve Bain from Swansea University, and who is a Member of the Human Genetics Commission, Lead of the Identity Testing Group, Member of the National DNA Database Strategy Board and Member of the NDNAD Ethics Non-departmental Advisory Group, discussed the social and ethical issues surrounding the National DNA Database.
The event was attended by 64 people and the talks were followed by a lively discussion.

- **DNA & Forensics**

12th December 2007

Gartholwg Lifelong Learning Centre

Claire Morse from the Forensic Science Service talked about the history and application of forensic techniques.
The event was attended by 52 people.

- **Science Café Wales**

Science Café Wales allows people in Wales to find out more about new, exciting and topical areas of science in an informal and entertaining manner. A short talk by an invited speaker is followed by an interactive discussion session. Two talks on genetics were organised with the Science Cafés in Bangor and Swansea:

3rd May 2007, Bangor

Wildlife conservation and wildlife forensics
Dr Rob Ogden, Wildlife DNA Services

30th May 2007, Swansea

The challenges for conserving endangered species in the tropics
Professor Mike Bruford, Cardiff University

Figure 4: WGP Debate on Stem Cells – the experts go public

- **Genetic Diversity Display**

The exhibition has been displayed at the following venues:

2007	
Rhondda Heritage Park, Trehafod	to 16 April
The Old Library, Cardiff City Centre	16 April – 24 May
Gartholwg Lifelong Learning Centre, Church Village	24 May – 31 June
Margam Park, Port Talbot	1 July – 20 August
Afan Forest Par Visitor Centre, Port Talbot	20 August – October
Barry Library, Barry, Vale of Glamorgan	28 October – December
2008	
UWIC, Western Avenue, Cardiff	6 January – 11 March
Aberdare Library, Aberdare	12 March – 15 April
Monmouthshire County Hall, Cwmbran	Current

- **The WGP has contributed to a number of Wales and UK science education events:**

Science Alliance Cymru inaugural meeting	6 June 2007
Science Alliance Cymru Meeting, Cardiff	5 September 2007
Launch of the "Forensic Use of Bioinformation: Ethical Issues" report from the Nuffield Council of Bioethics, London	20 September 2007
Launch of 'Darwin 200' at Natural History Museum, London	9 October 2007
Science Alliance Cymru meeting, University of Glamorgan	5 March 2008

Work Package 5: Societal Issues and the Patient Voice

> Genetics and Mental Health

Boy Genius Theatre Project

This participative theatre in education project for young people addressed genetics issues in mental health and was funded by a grant to Wales Gene Park from the Wellcome Trust. It was completed in July 2007.

Boy Genius explored contemporary developments in human genetics related to mental health through interactive theatre. It encouraged an appreciation of alternative views about this complex area of science and the associated social and ethical issues through participation in the story of a young man's experience of mental illness. Boy Genius was a collaboration between the Wales Gene Park, the Genetic Interest Group and Gwent Theatre Company. It was developed for school and college students aged 14 - 18 studying science, humanities and art subjects as the issues upon which it focused were relevant to cross-curricular citizenship requirements. There were 28 performances across South Wales involving 983 participants from 15 schools.


Figure 5: School pupils get to grips with issues of genetics and mental health in "Boy Genius"

- **Venues:**

Melville Theatre, Abergavenny
The National Botanic Gardens, Camarthen
Bedwas Workman's Hall
Theatr Powys, Llandrindod Wells
Cardiff University (including one Cardiff University audience)
Sherman Theatre (one public performance and one invited audience)

- **Participating Schools:**

Abersychan Comprehensive School
Tregib School, Ffairfach, Llandeilo
Newbridge Comprehensive School, Caerphilly
Bedwas High, Caerphilly
Llandrindod High School, Llandrindod Wells
Llanfyllin High School, Llanfyllin
Llanidloes High School, Llanfyllin
West Monmouth School, Pontypool
Nantyglo Comprehensive
Chepstow Comprehensive
King Henry VIII Comprehensive, Monmouth
Crickhowell High School
Ysgol Gyfun Plasmawr, Y Tyllgoed, Cardiff
Cantonian High School, Cardiff
St. Telio's High School, Llanedeyn, Cardiff

The final report of the project (summarized in Appendix 3) was widely distributed and is publicly available through the Wales Gene Park website. Presentations about the project have been made to the British Society of Human Genetics Conference, York (Sept. 2007), the ESRC Genomics Network Conference, London (Oct. 2007) and The Centre for Society & Genomics & ESRC Genomics Network Conference, Amsterdam (April 2008).

Funding is being sought to build upon this project through an application for a Wellcome Trust Medical Humanities Strategic Award (submitted April 2008) which will involve a programme of research and public engagement around the theme of *Psychiatry, Genetics, and Society.*

Social Science Focus on Psychiatric Genetics

WGP is collaborating with CESAgen (ESRC Centre for Economic & Social Aspects of Genomics) to develop a focus on Genomics and Psychiatry. Building upon the work of the WGP Genetics and Society Officer, WGP and CESAgen have jointly funded a new post-doctoral researcher (A. Bartlett) to strengthen the group studying issues surrounding identification of "susceptibility genes" for major psychiatric conditions, the geneticization of identity, and behavioural genetics. An application has been made to the Wellcome Trust Medical Humanities Strategic Awards (April 2008) for funding of a programme of research and public engagement activities around the theme of *Psychiatry, Genetics, and Society.* Funding sought: ~£1.14m (decision expected July/August 2008).

> Familial Hypercholesterolaemia (FH) – securing patient and family involvement

To raise awareness and achieve a commissioned diagnostic service for Familial Hypercholesterolaemia across Wales, the FH Family Forum has been established by WGP to provide affected families with direct involvement in the process. Several meetings around South Wales were organised, a Steering Group established and membership of the British Heart Foundation's Heart Support Network was secured. A website has been created, managed by the Wales Gene Park's FH database coordinator: www.fhwales.co.uk

In March 2008, a reception at the Assembly was held to further raise awareness among Assembly Members. Over 100 family members and 20 politicians attended. 32 of 45 AMs have subsequently supported the Statement of Opinion regarding a diagnostic service for FH: www.assemblywales.org/bus-home/bus-guide-docs-pub/bus-business-documents/bus-business-documents-state-opinion.htm?act=dis&id=78215&ds=3/2008

> Patient Needs and Neuromuscular Services in Wales

On 6th February 2008 an awareness day at the National Assembly was organised in conjunction with the Muscular Dystrophy Campaign, Action Duchenne, Charcot-Marie-Tooth-UK, Duchenne Family Support Group, Myotonic Dystrophy Support Group & the Myasthenia Gravis Association. 70 family members and 27 Assembly Members attended the event. A full report as presented to the Welsh Assembly Government is at www.muscular-dystrophy.org/campaigns/building_on_foundations/building_on_1.html

Through its Genetics Interest Group Officer WGP has also submitted evidence to several consultations and inquiries by the Welsh Assembly Government and the National Assembly for Wales in relation to neurogenetics services: (report at www.assemblywales.org/bus-home/bus-committees/bus-committees-third-assem/bus-committees-third-hwlg-home/bus-committees-third-hwlg-agendas.htm?act=dis&id=66942&ds=12/2007)

Figure 6: On February 6th 2008 patients and families affected by inherited neuromuscular disorders joined medical specialists to present the case for specialist services to the Wales Assembly Government.

> National DNA Database on Trial: Avoiding the Usual Suspects

The Wales Gene Park is building upon its public engagement work on the National DNA Database in an innovative and highly challenging project led by Dr Rachel Iredale, who has recently won funding from the Wellcome Trust for the project. The project, undertaken in conjunction with The Wales Gene Park, Techniquest and Abertawe Bro Morgannwg University NHS Trust, will focus on young people from South East Wales aged 16-19 who have been convicted of a criminal offence and whose details are already on the National DNA database. In a reversal of roles they put the National DNA Database itself on trial.
The charge is: 'That the National DNA Database is an unacceptable infringement of civil liberties'. All the roles at this Trial (jurors, witnesses, prosecution and defence) will be undertaken by the young offenders. The Trial will take place in November 2008 in order to coincide with Inside Justice week. The project is timely as it coincides with a public consultation recently launched by the Human Genetics Commission who will be reporting on the forensic use of DNA and genetic information to government later this year. The Human Genetics Commission has estimated that 25% of the male population and 7% of the female population will soon be on the National DNA database. It is planned that the participants will go to HGC in London to present their verdict. Dr Iredale says that the project will enable these young people to think about the National DNA Database in ways they may not have previously done. They will acquire an understanding during the course of the project about genetic issues that make personal sense to them and which are located within their own particular environments.

Work Package 6: Sir Peter Harper Clinical Research Fellowship in Medical Genetics

The Fellowship provides part funding for training in clinical genetic research at higher degree level with the strategic aim of developing sustainability and leadership for academic clinical genetics in Wales. The current Fellow is Dr D Mark Davies whose work focuses on a translational early phase clinical trial (TESSTAL) of the mTOR inhibitor Sirolimus for treatment of renal tumours in patients with the inherited disorder tuberous sclerosis and the related sporadic disorder LAM. The trial exploits new genetic knowledge gained through the work of the Institute of Medical Genetics on the TSC1 and TSC2 tumour suppressor genes. The trial is still underway but promising interim results published in January 2008 in the New England Journal of Medicine (Davies DM et al. NEJM 2008 Jan, 358(2): 200-203) have already generated significant interest in the research community and from pharma companies with which the WGP is now planning larger scale follow-on studies.

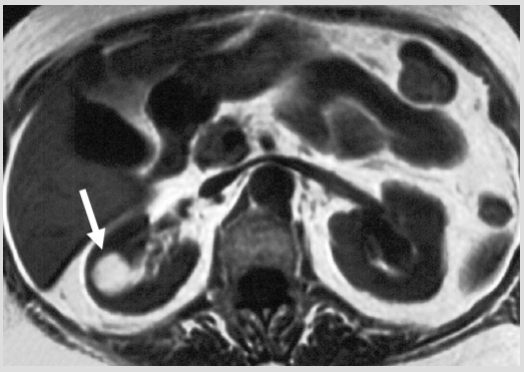

Figure 7: MRI scan showing a renal tumour (angiomyolipoma, arrowed) in a patient with tuberous sclerosis. The experimental treatment with Sirolimus has led to tumour shrinkage in all patients in the phase II TESSTAL clinical trial.

- **Platform presentations on the TESSTAL trial during the reporting period:**

University Hospital, Zurich	13th April 2007
LAM Conference, Cincinnati	17th April 2007
Tuberous Sclerosis International Research Conference, Rome	26th May 2007
British Society for Human Genetics, York	17th September 2007
Wyeth Clinical Research Meeting, London	15th November 2007
Clinical Genetics Society, Liverpool	12th March 2008

Work Package 7: Cardiovascular Genetics

> The Familial Hypercholesterolaemia (FH) Cascade Testing Project

(K Haralambos, WGP FH Project Co-ordinator)

FH is a genetic disorder that leads to high blood cholesterol and early onset coronary heart disease. Treatment with statins can restore life expectancy to normal. 1 in 500 of the population (approx 6000 individuals in Wales), are affected but the great majority are not currently diagnosed or treated.

The FH Cascade Testing Project aims to develop, pilot and evaluate a coordinated service for those with FH and their families. So far the project (initiated in June 2007) has identified individuals from ~250 separate families with FH. In 130 of these families cascade testing of family members has been started.

An FH forum for patients and families affected by FH has been established in South Wales. Through the Forum affected families have a say in how NHS Services are developed.

Several different databases have been evaluated to allow efficient follow-up of FH families. A collaboration has been established with the Dutch FH Service (the leading international service for the disorder) to utilize its well established IT systems. A website has been developed to support the FH project (www.fhwales.co.uk).

A proposal has been submitted to the Welsh Assembly Government linked to the National Service Framework for Cardiac Diseases for a family cascade-testing programme for FH in Wales based upon the pilot study experience.

At H.E.A.R.T UK 21st Annual Medical & Scientific Meeting, 27th to 29th June 2007, Edinburgh two presentations were given by members of the FH team (see Appendix 2).

> Developing Clinical Research and Services in Cardiac Genetics

A Cardiovascular Research Network (CvRN) is being established led by two new Chair appointments, Professor Julian Halcox and Professor Mark Rees. Following a scoping exercise across Cardiac Services in Wales and the Cardiff University School of Medicine's Cardiovascular Interdisciplinary Research Group an 'emerging strength' application to support the Network is being prepared to put to WORD in summer 2008. The Network will guide research in two main research areas, vascular and myocardial disorders with cross-cutting themes including genetics and cell biology, advanced imaging, clinical trials coordination, informatics & public health, plus cardiac modelling and nanomedicine. The genetics arm of the Research Network is being integrated with parallel service developments through the Wales Cardiovascular Genetics Interest

Group, led by Dr Dhavindra Kumar, Consultant Clinical Geneticist with the All Wales Medical Genetics Service. The Wales Gene Park has committed to support the genetic arm of the Network through the appointment of a dedicated research post that the Network plans to implement in September 2008.

Work Package 8: Neuro-Psychiatric Genetics

> Genetic Progress and New Challenges in Psychiatric Disorders

The discovery of genetic variants that predispose to bipolar disorder (severe episodic depression) and schizophrenia has been achieved in a major study by the Neuropsychiatric Genetics Group at Cardiff University (projects lead by Professors Cradock, Owen and O'Donovan, **Nature** 447, 661-678, 7 June 2007 and further papers in press). These researchers have exploited an approach known as genome-wide association, GWA, which has become technically feasible only in the last couple of years, to identify genetic factors involved in common complex diseases. Part of the group led by Professor Julie Williams is currently undertaking the largest GWA of Alzheimer's disease to date involving over 19,000 people and 8 billion genotypes. The Wales Gene Park supported a researcher to enable application of very high throughput Sequenom Mass Spectrometery for characterisation of the gene variants identified. The MRC Co-Operative Group in Neuropsychiatric Genetics at Cardiff University (lead by Professors Owen, Craddock Williams, Thapar and O'Donovan) is an exceptionally strong research team with programmes of research including schizophrenia, bipolar disorder, Alzheimer's disease, attention deficit hyperactivity disorder (ADHD) and dyslexia. The identification of genetic variants associated with common psychiatric disorders is presenting major challenges for psychiatric research and for its application in the clinical setting. The Wales Gene Park has established a jointly funded programme of work with CESAgen (the ESRC-funded Centre for Economic and Social Aspects of Genomics based between Cardiff and Lancaster Universities) to examine the emergence, acceptance and implementation of genetic technologies in the field of psychiatry.

> Epilepsy Genetics Research

The work of the Wales Epilepsy Research Network (WERN) includes a focus on epilepsy genetics involving the collection of large epilepsy families and the formation of an epilepsy population eBioBank. 265 samples have been collected into the biobank in a pilot exercise. WERN genetics research led by Professor M Rees (also Strategic Director, WGP) is linking with WGP to undertake mapping and genotyping studies that will utilize the WERN sample resource. External grants have been obtained from MRC and The Royal Society.

Work Package 9: Cancer Genetics

> Colorectal Cancer

A. Translational Clinical Trials in Colorectal Cancer

At present patients with metastatic colorectal cancer are treated with drugs that improve survival and quality of life for some, but lead to side effects but little or no improvement in survival for others. Analysis of the genetic makeup of the patient and their tumour offers the possibility of individualizing treatments so that efficacy is optimized while side effects are minimized. WGP is participating in two trials that aim to improve treatment for this group of patients.

- **COINTrans**

  The WGP genomic facility is undertaking bioinformatic and genomic analyses for the CRUK-funded COIN Translational project. This project is identifying the inherited and tumour-specific determinants of response to and side effects from several agents used in the treatment of metastatic colorectal cancer. Approximately 400 nonsynonymous SNPs with minor allele frequencies >5% have been identified in either DNA repair genes or genes involved in the metabolic pathways of 5FU, oxaliplatin and cetuximab. 2,444 patients have been recruited into COIN and their DNA has been extracted for analysis of the SNPS to determine which might predict response to, and side effects from, chemotherapy.

- **FOCUS 3 Trial**

  This trial is a collaboration between the Section of Clinical Oncology and the Institute of Medical Genetics in Cardiff at Cardiff University, and collaborators from Leeds. It is testing the feasibility of using genetic testing of colorectal cancers to select and individualise anti-cancer therapy using the agents irinotecan, oxaliplatin, cetuximab and bevacizumab.

B. Mouse Models of Colorectal and Other Cancers

This programme of research (PI Clarke) utilizes the WGP transgenic facility to enable its analysis of tumorigenesis in the gastrointestinal tract and the identification of novel therapeutic targets. Significant findings reported in the current year include the identification of Lkb-1 as a modulator of prostate tumorigenesis and identification of Prox-1 as a modulator of colon tumorigenesis (see Appendices). The team have used WGP support to generate new transgenic mouse lines to underpin a collaboration with CCMB (Bangalore, India) and also to support collaborations requiring the shipment of transgenic lines from the USA, Holland and Germany.

> mTOR signalling and Urological Tumours

The Wales Gene Park has supported the development of a translational pipeline of research that builds upon previous successes at Cardiff University in identifying TSC1 and TSC2 as key regulators of the mTOR signalling pathway. The pathway is a therapeutic target in important disorders that are highlighted as priority areas in “A Science Policy for Wales” including diabetes, cardiovascular disease, obesity and cancer. The Tumour Genetics Group at Cardiff University’s Institute of Medical Genetics has developed expertise in mTOR signalling (Tee), mouse models to explore mTOR-related tumour pathology (Cheadle) and pre-clinical trials (Shen) and early phase clinical trials of mTOR inhibitors in patients with inherited tumour syndromes (Sampson

and Davies). Over £1M has been secured in recent external funding from AICR, TS Association, TS Alliance and CRUK. The programme of research is utilising the WGP Genomic and Transgenic facilities and WGP is supporting directly the pre-clinical therapeutic project to ensure translation of the basic research.

- **Platform Presentations, mTOR Basic Science:**

"Hypoxia inducible factor 1alpha is regulated by the mammalian target of rapamycin	April 2007
(mTOR) via an mTOR-signalling motif." LAM Foundation conference, Cincinnati, Ohio, USA	June 2007
"Mammalian Target of Rapamycin (mTOR) and Human Disease." Institute of Cancer	September 2007
Research, Chester Beatty Laboratories, London	November 2007

See also work-package 6 for platform presentations relating to the clinical part of the research programme.

Commercialisation

WGP invested in the commercial development of the Human Genome Mutation Database (HGMD), maintained at the Institute of Medical Genetics. HGMD has achieved a £750,000 deal with BioBase GMBH, a German biological database company.

> Licensing of Testing for Mutations in the MYH Gene

Cardiff University licensed patented MUTYH gene testing to Myriad Genetics, Inc., Utah, USA through the WGP. This agreement provided the University with an upfront payment and has also provided a subsequent royalty income.

Myriad now market and perform MYH gene testing across the USA following the incorporation of the MYH test into their COLARIS *AP*® product. COLARIS *AP*® is a predictive medicine product for risk of hereditary colorectal polyps and cancer. COLARIS *AP*® detects mutations in the *APC* and *MYH* genes, which cause adenomatous polyposis syndromes, including familial adenomatous polyposis (FAP), attenuated FAP (AFAP), and *MYH*-associated polyposis (MAP). The number of MYH tests has increased steadily quarter on quarter, providing a revenue stream to the University.

Date	Number of Tests	Cumulative Income
March 2004-April 2005	622	£14268.19
April 2005-March 2006	858	£19163.97
April 2006–March 2007	1247	£27666.25
April 2007-March 2008	1669	£33421.47

Health Services Research

> Department of Health – Health Services Research and Genetics Programme

Deaf individuals' understanding and perception of genetics and their needs from a genetic counselling service

(Lead – Dr. Anna Middleton, Cardiff University)

Deaf adults are often interested to know why they are deaf and whether this can be passed on to their children – issues routinely addressed within genetic counselling. However, very few deaf adults utilise this service. There may be many complex reasons behind this – e.g. lack of information, assumptions about inheritance, mistaken beliefs of a link between present-day genetics services and eugenic practices of the past in relation to deafness or fears about being told not to have children. This project aims to gather the views of deaf people with respect to their beliefs about inheritance, flow of information through families and communication of genetic risk. The study will also assess what attitudinal barriers may possibly be preventing access to genetic counselling. The project is informing the design of a genetic counselling service that is applicable, relevant and sensitive for deaf people and their families.

Cancer Genetics Psychosocial Research

(Lead – Dr. Kate Brain, Cardiff University)

The Cancer Genetics service for Wales (CGSW) is an innovative service for people across Wales who are concerned about a family history of cancer. Funding from Tenovus, the Wellcome Trust, Breast Cancer Campaign and Cancer Research UK (amongst others) has allowed Wales to lead the rest of the UK in developing ways of helping people with family histories of cancer. The broad aim of the team's research is to evaluate the psychosocial impact of genetic assessment and to develop models of service delivery that best meet patients' information and support needs.

Appendices

1. (a) Selected Grants funding Genetic Research in Wales.

Title	Start	End	Applicant	Sponsor	Award
A Research Development Officer for the Wales Epilepsy Research Thematic Network	2007	2009	Prof M. Rees	Wales Office of Research and Development	£119,500
Psychosis investigation	01/12/2007	30/11/2009	Prof NJ Craddock	Mental Health Research Network Cymru	£5,000
Na+/Cl- Transporter Defects in Human Neurological Disorders.	2007	2010	Prof. M. Rees	Medical Research Council (MRC)	£639,156
PhD Studentship in the Phenotype/genotype studies in neurological syndromes co-morbid with epilepsy and neuronal migration disorders.	2007	2010	Prof. M. Rees	Wales Office of Research and Development	£59,810
Pattern of Neurodegeneration for an ovine transgenic Huntington's disease model.	2007	2011	Prof. M. Rees	Freemasons of New Zealand	NZ$450,000
Unrecognised bipolar spectrum disorders in primary care patients with depression	01/04/2008	01/04/2009	Dr DJ Smith, Dr SA Simpson, Dr K Hood, Prof NJ Craddock	National Assembly for Wales (WORDHSC)	£10,000
A Clinical Fellow for the Wales Epilepsy research Network	2008	2010	Prof. M. Rees	Industrial Partner: UCB-Pharma	£114,500
Further support for the Wales Epilepsy Research Network	2008	2010	Prof. M. Rees	WORD Extention of Thematic Network Status	£141,800
Unmet needs of families in Wales affected by sudden arrhythmic death syndrome	01/06/2008	01/06/2009	Dr K Brain, Dr R Iredale, Prof AJ Clarke	Sudden Adult Death Trust	£15,000
Defining the role of Wnt signalling in mammary stem cells	01/07/2008	30/06/2011	Prof T Dale, Prof AR Clarke	Breast Cancer Campaign	£198,643
Validating methylation sensing proteins as therapeutic targets	01/07/2008	30/06/2013	Prof AR Clarke, Prof M Ehrmann	Cancer Research UK	£349,239
Validating methylation sensing proteins as therapeutic targets	01/07/2008	30/06/2013	Prof AR Clarke, Prof M Ehrmann	Cancer Research UK	£700
A study to determine the feasibility of molecular selection of therapy in patients with metastatic colorectal cancer	01/09/2008	31/08/2010	Prof TS Maughan, Dr A Nelson, Dr R A Adams, Prof GT Williams, Dr B Jasani, Prof J Sampson	Medical Research Council	£425,892
Fronto-temporal connectivity and memory: Pattern of breakdown in ageing and diseases of old age	03/11/2008	02/11/2012	Prof AE Rosser, Prof K S Graham, Dr M O'Sullivan, Prof D K Jones	Medical Research Council	£526,141
Molecular genetics in schizophrenia	01/12/2008	30/11/2011	Prof M Owen, Dr V Moskvina, Prof PA Holmans, Prof M O'Donovan, Prof NJ Craddock	Medical Research Council	£1,686,836

(b) Financial Statement

Work Package 1	
Staff Costs	£3,762.25
Non-Staff Costs	£12,052.08
Travel and Subsistence	£1,907.10
Web Site	£46.98
Consumables	£1,259.15
Office Accommodation Costs	£8,791.87
Sundries	£46.98

Work Packages 2 & 3	
Staff Costs	£ 139,586.47
Non-staff Costs	£84,200.92
Equipment Maintenance Contracts	£46,600.12
Core Technology running costs	£8,097.72
Transgenic animal house costs	£28,374.30
Sundries	£762.04
Conferences	£366.74

Work Package 4	
Staff Costs	£78,217.39
Techniquest joint project costs	£8000.00

Work Package 5	
Staff Costs	£71,439.07
Non-Staff Costs	£3,281.03
Travel and Subsistence	£2,630.78
Miscellaneous	£242.46
Hospitality	£123.40
Conferences	£284.39

Work Package 6	
Staff Costs	£43,750.00
Non-Staff Costs	None

Work Package 7	
Staff Costs	£29,849.37
Non-Staff Costs	£2,287.62
Travel	£723.68
Conferences	£476.26
Training	£364.00
Equipment	£723.68

Work Package 8	
Staff Costs	None
Non-Staff Costs	None

Work Package 9	
Staff Costs	£43,691.53
Non-Staff Costs	None

1. Selected Publications

Basic and Clinical Research

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Tonkin E, Kirk M, McDonald K. Practice nurses and the business of genetics: referrals to genetics services from primary care and the role of the practice nurse. *Oral presentation,* ***RCN International Nursing Research Conference*** (Delivered in Liverpool, April 08)

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Tonkin E, Kirk M. Working with the nursing professions to support genetics education for health: the role of the NHS National Genetics Education and Development Centre. Genomics and Society: ***Today's Answers, Tomorrow's Questions,*** *London* (Oct. 07)

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2. Feedback and evaluation on "Boy Genius" project

BOY GENIUS represents an innovative approach to the exploration of contemporary developments in human genetics related to mental health within an interactive theatre environment. The activity encouraged an appreciation of different views about this complex area of science and associated social and ethical issues through participation in the story of a young man's experience of mental illness. A collaboration between the Wales Gene Park, the Genetic Interest Group and Gwent Theatre Company, Boy Genius was performed for school and college students, aged 14 - 18, from science, humanities and art subjects as the concepts and skill elements related to cross-curricular citizenship requirements.

Number of performances: 28
Number of participants: 983

Venues: 6
Melville Theatre, Abergavenny
The National Botanic Gardens, Camarthen
Bedwas Workman's Hall
Theatr Powys, Llandrindod Wells
Cardiff University (including one Cardiff University audience)
Sherman Theatre (one public performance and one invited audience)

Participating Schools: 15
Abersychan Comprehensive School
Tregib School, Ffairfach, Llandeilo
Newbridge Comprehensive School, Caerphilly
Bedwas High, Caerphilly
Llandrindod High School, Llandrindod Wells
Llanfyllin High School, Llanfyllin
Llanidloes High School, Llanfyllin
West Monmouth School, Pontypool
Nantyglo Comprehensive
Chepstow Comprehensive
King Henry VIII Comprehensive, Monmouth
Crickhowell High School
Ysgol Gyfun Plasmawr, Y Tyllgoed, Cardiff
Cantonian High School, Cardiff
St. Telio's High School, Llanedeyn, Cardiff

Evaluation

We addressed the evaluation of the project in the following ways:

1. The effectiveness of this participative learning experience as a method for stimulating and informing an exploration of complex issues
2. The overall effectiveness of the activity to encourage an appreciation and awareness of different views about genetics and mental health and associated social and ethical issues
3. As a collaborative process in developing and delivering the project

The full evaluation report provided a critical assessment of the successes of the project and of lessons learnt, to inform the practice of the project partners in the development of future projects, and will be of practical use to others developing projects that seek to engage people with issues relating to biomedical science and/or involve collaborative

partnerships between academics and those working in the arts. This summary report highlights the main points of the evaluation report.

Methods of collecting evaluation information

Evidence was collected from two main groups: the participants (students and their teachers) and the production team (co-applicants and others working on the production / delivery of the project) and was captured in various forms.

Production team	Participants
Regular project meetings, final de-brief meeting	'Question leaves' & 'mind maps' produced by participants during the activity
Individual diaries	Teachers' feedback from the INSET day
Advisory group meetings & communications	Teacher feedback forms completed immediately after the activity
Actors de-brief meeting	Student feedback forms completed immediately after the activity
Interviews with cast & director	Follow-up discussion with teachers five months after the activity

1. The effectiveness of this participative learning experience as a method for stimulating and informing an exploration of complex issues

Feedback from participants and the team have overwhelmingly expressed positive reactions to being part of Boy Genius. The learning gained from this activity was fresh, exciting and liberating to young people who currently work within a pressured timetable and from an exam-specific curriculum. Boy Genius presented a complex topic through an original methodology and this has proved to be accessible, appealing and rewarding to the young people who were its audience.

The writer/director made the following observation in a diary entry after a performance mid-tour:
"Every aspect of the intended 'learning areas' were passionately and articulately addressed by the participants... The team had to draw it to a close, but the questions kept on coming; and connections kept on being made. It was so gratifying to see that these 16 year olds had taken on the whole 'drama' aspect of the project; working totally in-role without concern or any sign of self-consciousness."

Comments from students:

"I enjoyed participating in the play as the "peer mediator", especially towards the end of the play when we got to discuss with the actors while still in character."

"I enjoyed the emotional journey the play gives you."

"I enjoyed taking part and sharing my opinion."

"I was surprised by how we could influence the ways the characters interacted."

Comments from teachers in follow up questionnaires and focus groups:

"Exam questions ask for the student's opinions about certain topics. Boy Genius was good in that it allowed them to express theirs. Students don't get the chance to share their opinions much."

"It was great for the pupils to experience a totally new dramatic form, interacting with actors."

"Pupils were very motivated –they responded in a really positive manner to the whole scenario. I wish you would develop this idea to show more pupils this production."

Asked about suggestions for future projects for this age group, teachers responded:

"Anything in a similar vein. It is hard to get kids out of school but this was a really worthwhile activity – probably the best one we've been involved with."

"Similar projects would be ideal as they enjoyed it so much"

"Similar interaction pieces. It was nice to have a non-clichéd production that enabled children to discuss a mature topic."

2. The overall effectiveness of the activity to encourage an appreciation and awareness of different views about genetics and mental health and associated social and ethical issues.

Boy Genius was not about telling young people the good, bad and ugly stories about genetics research related to mental health. Neither was it about sensationalising this area of research. Rather, Boy Genius introduced and presented different facets of this complex topic in a manner that whetted their appetite to find out more. It moved the subject away from an isolated situation within a research laboratory or a complicated research paper into a tangible and realistic story that they could relate to themselves, their families, friends and the future.

"As carers ourselves, it was good to see the topic of mental health out in the open, hopefully promoting empathy and understanding from other young people. This can only be good for reducing stigma and prejudice in later life."
[Member of Project Advisory Group Member of Hafal, Wales' leading charity for people with severe mental illness and their carers]

The education officer within the team had discussions with teachers following their visit to Boy Genius, he reported:
"*I was regularly told [by teachers] that participants were informed of things that they weren't aware of and that they were surprised about some of the historical information, on eugenics in particular."*

Comments from teachers in follow up questionnaires and focus groups:

"Things from the play came up [in class] whilst teaching. This was four months after seeing the performance."

"Pupils were very interested and enthusiastic about the topic and are continuing to explore it through practical and written work in class. A terrific day which was compelling and highly stimulating. Many thanks! Also the resource pack is superb and can be used to focus the students very effectively."

"Good content on the genetics topic and excellent links to e.g. history and topical issues. Excellent performance and treatment by staff. Thank you."

Comments from students:

"I enjoyed the whole play. The story was different, entertaining and twisted a lot."

"The complexity was amazing! So many questions running through my head!"

"I enjoyed the history part linking things from history with genetics"

Participants' surveys asked them what the day itself had made them think about. These responses to the question: "What did the activity make you think about afterwards?" demonstrate how the issues raised by the drama were picked up on by the participants:

"Society's outlook on the normal and the ill"

"Whether it is right to change people or to leave them as they are"

"The importance of history – how past events still affect people"

"How clinical and uncaring society can be and how we can prevent it from becoming like that"

"How many unanswered questions there are about genetics and that not all of them are 'black and white' – there are lots of sides to the argument"

3. The development of the activity as a collaborative process.

The development of this project was the first experience the Wales Gene Park (WGP) and Genetic Interest Group (GIG) team had of collaborating with a theatre company, and also the first time Gwent Theatre (GT) had collaborated on a project focusing on issues relating to biomedical science. It was also the writer's first experience of work relating to scientific issues. As such, part of the challenge of developing this project was that it required the production team to work in new ways, in unfamiliar territory and so became a learning experience for all involved.

Boy Genius was an ambitious project in its concept, form and its delivery. Although the partners had not worked together previously, it was each individual organisation's expertise in their area and their openness and commitment to working in new ways together that ensured the collaboration produced a successful venture in engaging young people in a discussion about bioscience through art.


theWALES
GENE
PARK
PARC
GENETEG
CYMRU


CARDIFF
UNIVERSITY
PRIFYSGOL
CAERDYDD


cesagen
ESRC Centre for Economic and
Social Aspects of Genomics


Grŵp
Buddiannau
Geneteg
Genetic
Interest
Group


geneteg feddygol
GWASANAETH I GYMRU
medical genetics
SERVICE FOR WALES


TECHNIQUEST


UNIVERSITY OF GLAMORGAN
PRIFYSGOL MORGANNWG


PRIFYSGOL CYMRU ABERTAWE
UNIVERSITY OF WALES SWANSEA


Llywodraeth Cynulliad Cymru
Welsh Assembly Government