<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foreword</td>
<td>3</td>
</tr>
<tr>
<td>Introduction</td>
<td>4</td>
</tr>
<tr>
<td>Strategic Objectives</td>
<td>5</td>
</tr>
<tr>
<td>Resources and Wales Gene Park Structure</td>
<td>6</td>
</tr>
<tr>
<td>Key Partners and Who's Who</td>
<td>7</td>
</tr>
<tr>
<td>Lay Summary</td>
<td>8</td>
</tr>
<tr>
<td>Work Packages:</td>
<td></td>
</tr>
<tr>
<td>1. Genome Editing and Transgenics</td>
<td>10</td>
</tr>
<tr>
<td>2. Genomic Facility</td>
<td>12</td>
</tr>
<tr>
<td>3. Education and Engagement</td>
<td>14</td>
</tr>
<tr>
<td>Case study: Enhancing the Welsh Knowledge Economy</td>
<td>18</td>
</tr>
<tr>
<td>Case study: Generating Models of Disease to Support Fundamental Research</td>
<td>19</td>
</tr>
<tr>
<td>Case study: Supporting The 100,000 Genomes Project in Wales</td>
<td>20</td>
</tr>
<tr>
<td>Achieving Impact</td>
<td>24</td>
</tr>
<tr>
<td>Key Achievements 2017-18</td>
<td>25</td>
</tr>
<tr>
<td>Highlights from 15 Successful Years of Wales Gene Park</td>
<td>26</td>
</tr>
<tr>
<td>Looking Forward</td>
<td>27</td>
</tr>
<tr>
<td>Conclusions</td>
<td>28</td>
</tr>
<tr>
<td>Contact Us</td>
<td>29</td>
</tr>
</tbody>
</table>
This annual report captures the value and impact of the broad portfolio of work undertaken by the Wales Gene Park team. It ranges from technical developments in the laboratory to supporting the development of public policy by Welsh Government, but the common purpose of these diverse activities is to ensure that the full benefits of genomics are realised in Wales.

When the Wales Gene Park was founded fifteen years ago we anticipated a future when patients might have their entire genomes sequenced as an integral part of their medical care. But at that time the costs were over £50M per genome and it was difficult to know what the time scale for such an advance might be. This year, through the 100,000 Genomes Project, NHS patients in Wales with suspected but undiagnosed rare diseases started to have their whole genomes sequenced at a cost of £1400 pounds each, including costs for data analysis and storage. The genomic transformation of healthcare is truly well underway. The pace of change brings challenges as well as opportunities. The Wales Gene Park is helping medical researchers in Wales to make the most of these opportunities and ensuring that the NHS workforce has the knowledge and skills to use the advances that are being made to benefit patients.

To get in touch or to find out more about us, please do visit our website at:
www.walesgenepark.cardiff.ac.uk

“Harnessing Genetics and Genomics to advance Research, Healthcare, Education and Innovation”
Introduction:

Wales Gene Park is an infrastructure support group funded by Welsh Government through Health and Care Research Wales. We support, promote and perform Medical Genetic and Genomic Research of the highest quality, and work to ensure its translation for the benefit of patients and society in Wales and beyond.

Wales Gene Park Mission:

- To promote and facilitate Welsh Medical Genetic and Genomic Research and its application to improve health and wealth in Wales
- To engage the public and health professionals to improve understanding of the opportunities and challenges arising through genetics and genomics

Wales Gene Park Aims:

To support the implementation of the Welsh Government’s Genomics for Precision Medicine Strategy by:

- Promoting and facilitating high quality genetic and genomic health research in Wales
- Ensuring seamless translation of advances in genetics and genomics to improve NHS services and commercialization
- Ensuring the informed involvement of patients, public and professionals in the development of genomic medicine in Wales
Strategic Objectives

To develop and provide **expertise and infrastructure** that will help Wales compete at the **forefront** of genetic and genomic research in its areas of **priority and strength**, in particular by supporting Health and Care Research Wales funded research activities and programmes.

To **support Welsh researchers** through provision of conventional and novel applications of Next Generation Sequencing, transgenic and genome editing technologies, focusing on areas of **research and clinical expertise** and **patient needs** in Wales.

To **drive the development** of genomic medicine in Wales, focusing particularly on **translational genetic research** in common and rare disorders in which Wales has **research strength**.

To provide **leadership** in rare genetic disease research by helping set priorities, **engaging** patients and families, promoting **research collaboration** using existing Welsh Government, NHS and Higher Education Institution mechanisms and by creating **stronger links** with industry.

To **help Wales develop capacity** to undertake genomic analysis on a significant scale and support the **linkage** of genomic information to clinical data and other relevant data sets.

To enhance public and professional **awareness and understanding** of health-related genetic and genomic research and the **opportunities and challenges** this research brings.
The twenty two core staff (13.8 whole time equivalent) funded through Wales Gene Park are supported by senior academics, experts from the NHS in Wales, and managers and administrative staff from the host institution, Cardiff University.
Key Partners

Academic Partners
- Cardiff University
- Swansea University
- Bangor University
- Aberystwyth University
- Glyndwr University
- University of South Wales

NHS Partners
- Cardiff and Vale University Health Board
- All Wales Medical Genetics Service

Commercial Partners
- Agilent Technologies
- Apexion Pharmaceuticals
- AstraZeneca
- Bayer
- BioVitas Capital Ltd
- Calithera Biosciences
- Chromatrap
- Gaia Technologies
- Genentec
- GW Pharmaceuticals
- Merck KGaA
- Myriad Genetics
- Nanoether Discovery Science Ltd
- New England Biolabs
- Novartis Pharmaceuticals

Third Sector Funders and Partners
- Genetic Alliance UK
- Rare Disease UK
- Cancer Research UK
- Cancer Research Wales
- Bowel Cancer West
- Bowel Cancer Wales
- Leukemia & Lymphoma Research
- Techniquest
- The Neuro Foundation
- The Children’s Tumour Foundation
- The Wellcome Trust
- Tenovus Cancer Care
- Tuberous Sclerosis Association (UK)
- Tuberous Sclerosis Alliance (USA)
- SWAN UK

Who’s Who

Strategic Advisory Group
- Chair: Professor Colin Dayan,
  School of Medicine, Cardiff University
- Mr Ifan Evans, Deputy Director,
  Healthcare Innovation Welsh Government
- Professor Julian Hopkin,
  Experimental Medicine, Swansea University
- Dr Clive Morgan, Cardiff and Vale
  University Health Board
- Professor Malcolm Mason OBE,
  College of Biomedical and Life Sciences,
  Cardiff University
- Mr Alastair Kent OBE, Former
  Genetic Alliance and Rare Diseases UK
  Ambassador
- Dr Mick Hunter, CSO and Director of
  Development at Atopix and CEO at Orca
  Pharmaceuticals
- Rachel Butler MBE, Head of
  Laboratory at the NHS All Wales Medical
  Genetics Service Laboratory

Patient Representatives
- Mr Perry James
- Mr Alan Thomas

Executive Team
- Professor Julian Sampson, Director
- Dr Karen Reed, Operations Manager
- Ms Sherrie Witts, Finance Manager
- Professor Mark Rees, Impact Lead
- Dr Kevin Ashelford, Bioinformatics
  Lead
- Ms Sarah Edkins, Genomic
  Laboratory Lead
- Professor Ros John, Genome Editing
  Lead
- Dr Ming Shen, Transgenics Lead
- Mrs Angela Burgess, Education and
  Engagement Lead
- Mrs Emma Hughes, Genetic Alliance
  Policy and Engagement Manager
Overview:

Wales Gene Park is an *infrastructure support group* funded by Welsh Government through Health and Care Research Wales. We support research via three work packages and through the provision of technical support, researcher governance and patient recruitment activities associated with several genetics research studies registered on the Health and Care Research Wales Clinical Research Portfolio.

**Work Package 1**

*Genome Editing and Transgenics*

Making and using pre-clinical models of disease through genome editing and related methods

**Work Package 2**

*Genomic Facility*

Sequencing and analysing genomic information in collaboration with researchers

**Work Package 3**

*Education and Engagement*

Enhancing awareness and understanding of health-related genetic and genomic research for the public and health professionals
Supporting Policy

Working with patients with rare disease

The Wales Gene Park Education and Engagement team oversee the Welsh Rare Disease Patient Network, ensuring patients are informed of, and effectively represented in, development of appropriate Welsh Government health and social care policies.

The Genomics for Precision Medicine strategy was officially launched by Welsh Government in July 2017 setting out the plan for strengthening genomic medicine in Wales. Wales Gene Park contributed to the development and implementation of this strategy.

Pre-clinical trials

Wales Gene Park also undertakes pre-clinical trials for rare diseases in collaboration with several drug companies. This work uses genetically modified mouse models and human patient samples. Such trials have tested four new drug combinations for the treatment of kidney tumours, adding to the scientific knowledge and informing future clinical trials.

Clinical Research

Access to patient samples and clinical data is essential for clinical research. Wales Gene Park manages the study governance, patient recruitment and organising of study data for three UK Clinical Research Network (UKCRN) / Health and Care Research Wales Clinical Research Portfolio projects in rare disease research. Through banking samples from patients with cancer or rare diseases, we have supported four laboratory based research projects that aim to improve future NHS diagnostics.

Sequencing provision

Next Generation Sequencing (NGS) is a powerful cost-effective, time-efficient technique used to sequence genes and genomes. At Wales Gene Park we use sequencing machines within Cardiff University and the NHS All Wales Medical Genetics Services (AWMGS) to generate sequence data for researchers. We have supported 25 research projects, 28% were rare disease projects, 72% were for common diseases including cancer, arthritis, diabetes and Alzheimer's projects.

Raising awareness

Genetics and genomics are fast becoming part of our health care system. The Wales Gene Park Education and Engagement (E&E) team run many events to raise awareness and understanding of these advances. This year, through 95 events, they have reached:
- 1624 Health professionals,
- 1630 School and College students,
- 2513 members of the public, and patients with rare genetic diseases

“Harnessing Genetics and Genomics to advance Research, Healthcare, Education and Innovation”
Purpose:

Transgenics (making changes to the genetic material by introducing new DNA sequences) and genome editing (making direct changes to the genetic material) enable the generation of genetically modified mouse models (GEMM) of inherited disease and cancer. Wales Gene Park supports research by using these technologies for the production and use of pre-clinical models.

The outputs from this work package span mechanistic to pre-clinical therapeutic research. The models generated form the basis for many external research funding applications. This work also generates evidence that informs the development of clinical trials in patients.

Core Activities:

- Developing CRISPR (Clustered Regularly Interspersed Short Palindromic Repeats) genome editing technology to produce novel genetically modified models
- Embryonic Stem (ES) cell derivation from models of disease
- Consultation for researchers requiring support in ES cell and genome editing techniques
- Use of GM models for research into disease mechanisms and pre-clinical trials

Prof Ros John
Senior Research Fellow in Cancer Genetics and Wales Gene Park Lead for Genome Editing
**Progress:**

Prof Ros John oversees the strategic development of genome editing, while Mrs B Allen manages the day-to-day running of the genome editing facility. Two approaches are now used for the generation of new animal models of disease: 1) CRISPR modification of embryonic stem (ES) cells derived from pre-existing GM animals to introduce secondary/tertiary modifications 2) direct injection of CRISPR components into fertilised embryos.

Support for the former approach has been provided to **four research groups** working in the areas of cancer biology, epilepsy, neurodevelopment and neuropsychiatric illnesses, all based at Cardiff University. **Two proof of concept projects** are being developed using the latter approach, one in the area of cancer biology, the other in developmental programming. **Training** in embryology techniques has been provided to 5 research groups (4 based in Cardiff, 1 international), **tissues have been shared** with 4 research groups (2 based in Cardiff, 1 in Swansea and 1 international) and 3 **new transgenic lines** have been established in Cardiff using **in vitro** fertilisation (IVF) to support new avenues of research and grant applications.

Dr Ming Shen leads on pre-clinical trials for rare diseases and cancer using GEMMs for TSC-associated kidney tumours. In collaboration with several drug companies, Dr Shen’s research team undertake **preclinical trials** involving new drugs, **re-profiling of established drugs** and **testing new drug combinations** that offer the prospect of improved treatment options. They also investigate the role of genes in tumour development by conditionally deleting genes in the kidneys. In the past year, they have **tested four drug combinations** which has given rise to two publications. This year their research has demonstrated:

- sorafenib/everolimus combination is superior to everolimus alone for treatment of renal tumours
- rapamycin/atorvastatin combination does not provide additional benefits over rapamycin treatment alone (current standard of care)
- the dual PI3K/mTOR inhibitor GSK2126458 (a single drug that targets two cell signalling pathways) can inhibit tumour growth. Further studies are needed to investigate whether rapamycin / GSK2126458 combination could improve anti-tumour therapy

These findings add to scientific knowledge and **inform the design of clinical trials**.

The pre-clinical kidney tumour GEMMs are also being used to support a collaboration with researchers in Cardiff University School of Engineering. This project aims to develop a new platform for isolating exosomes from blood for cancer diagnosis. Exosomes are cell-derived vesicles that are present in many body fluids, and potentially can be used for diagnosis of disease.

**Outcome of work:**

- Support for 12 research groups for ES cell derivation and modification, embryo and sperm cryopreservation, IVF, pronuclear microinjection of CRISPR constructs and/or genome modification of ovarian epithelia
- Five Peer Reviewed publications, adding to scientific knowledge

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**“We support researchers in Wales and beyond”**
Work Package 2 : Genomic Facility

Purpose:
The Genomic Facility provides access to **competitive and flexible** Next Generation Sequencing (NGS) for researchers in Wales together with **expert bioinformatics support**. By providing these technologies, Wales Gene Park improves the quality and quantity of genomic research that is undertaken in Wales, and ensures that a greater proportion of externally awarded research funding is spent in Wales.

The Genomics Facility also **supports innovation** by contributing to collaborations with the Pharma and Biotech sectors.

“We provide competitively priced next generation sequencing for researchers at the forefront of medical genetics and genomics research”

Core Activities:
- NGS of **DNA and RNA**
- Bespoke **bioinformatic analysis** for novel sequencing applications
- **Pipeline analysis** of standard data outputs (genomes, exomes etc.)
- Computing, processing and data storage for genomic medicine research
- Contribution to healthcare professional education
Progress:

We support research projects involving genomic analyses through several routes; i) the provision of NGS, ii) the provision of bioinformatics analysis, iii) the provision of computing capacity and iv) the provision of secure, robust data storage.

This reporting period we have provided NGS for 25 research projects, 52% of which were with Health and Care Research Wales supported researchers. 28% of projects were in rare disease research, while 72% were for common diseases including cancer, arthritis, diabetes and Alzheimer’s. A collaborative project with researchers at Wales Kidney Research Unit established the protocols required for the provision of small RNA-seq analysis.

A further 14 research projects have been supported through bioinformatics provision alone (using outsourced NGS data). Of the 39 new bioinformatics projects instigated this year, two explicitly involved training and consultancy provision, six involved established bioinformatic techniques and 13 involved bespoke novel bioinformatic techniques. 18 required quality control, data packaging, storage and distribution to researchers with no analysis. Computing capacity and secure, robust data storage has been provided for over 20 further researchers.

Wales Gene Park leads the All Wales NGS network, through which we have established collaborative projects with researchers in Bangor and Swansea Universities, and we have provided a NGS service for Aberystwyth University. Wales Gene Park now successfully uses a very high throughput Illumina instrument housed within the Division of Psychological Medicine and Clinical Neurosciences, Cardiff University. This has released pressure on NHS instruments and provided a 20% reduction in sequencing costs for our collaborators.

Outcome of work:

- NGS provision via collaborative partnerships for 25 research projects from 19 different research groups
- Bioinformatics team have instigated 39 research projects from 23 different research groups
- 17 researchers supported through the provision of computing capacity
- In collaboration with the Human Gene Mutation Database (HGMD) we have developed a new machine learning algorithm to better automate curation of databases relied on for genetic diagnosis

Working with the NHS

The Welsh Government’s Genomics for Precision Medicine Strategy outlines the required development of IT infrastructure needed to support the work of NHS diagnostic services in Wales. Wales Gene Park continues to support the All Wales Medical Genetics Service’s plan for genomic data storage by:

- facilitating AWMGS’ partnership with Supercomputing Wales at Cardiff University
- providing advice on IT design
- helping to solve the information governance challenges of building NHS IT within a University datacentre.
- Providing back-up data storage for clinical research

‘With access to WGP compute we can analyse data 5-times more quickly’

- Dr Robert Andrews, Lead Bioinformatician Systems Immunity Research Institute, Cardiff University.
Work Package 3 : Education and Engagement

Purpose:
Wales Gene Park carries out a wide portfolio of activities in professional and public education and engagement. We ensure opportunities for engagement and involvement of patients and families in research, service development and health and social care policy.

Wales Gene Park’s education activities draw on expertise in the Welsh Higher Education Institutions and NHS, and on the wider UK and international genomics community.

“Enhancing awareness and understanding of genetics and genomics in Wales by engaging with health and science professionals, schools, colleges, and the public”

Core Activities:
- **Education and engagement events** via public and schools programmes.
- **Recruitment** to Health and Care Research Wales and NIHR genetics clinical research studies.
- **Approved continuing professional development** (CPD) in genetics and genomics for those working in healthcare and allied professions.
- Public input to Welsh Government policy in genetics and genomics.

Outcome of work:
Wales Gene Park Education and Engagement team organised 95 different events between April 2017 and March 2018 in which 5785 people participated. Many more visited the Wales Gene Park interactive stand at external events.

- Health Professionals - 20 events & 1624 attendees
- Schools/Colleges - 18 events & 1630 attendees
- Public/Patients - 41 events & 2531 attendees
- Interactive stand at 16 external events

Angela Burgess
*Education and Engagement Manager*
Progress:

Genetics and genomics are increasingly becoming part of our health care system bringing advantages of quicker and more accurate diagnosis and more individualised treatments. However, the technology also raises numerous practical and ethical questions, such as:

· Who will have access to my genetic information?
· How will they use it?
· Who will own it?
· Will it be secure?
· What will it say about my future health?

These are issues on which everyone’s opinion needs to be heard. Wales Gene Park delivers an active programme of education and engagement events involving health professionals, schools, colleges, patients and the public.

Public and Patients

A variety of events were held for public and patient groups, including:

- Annual Conferences on Genetics & Genomics for the 3rd Generation (3G)
  Held in North and South Wales, these events were attended by over 190 people.
- Community Group talks
  26 events took place following requests from groups such as University of the 3rd Age (U3A), Rotary, Women’s Institute and Library Groups.
- Annual Welsh Rare Disease Day Reception at The Senedd
  This annual reception attracted an audience of over 100 people. This year the Cabinet Secretary for Health and Social Services, Vaughan Gething AM, launched the 100,000 Genomes Project in Wales at this event.
- Film screening
  The film GATTACA that raises issues in genetics and genomics was shown to an audience at the Savoy Theatre in Monmouth. The screening was followed by a discussion on how the latest advance in genomics have brought this science fiction film closer to science fact.
- Patient specific events
  The Annual Rare Disease Patient Network Meeting and several family days for those affected by rare diseases received positive feedback.

“The President of our club… recommends the Presidents of other Rotary Clubs in Cardiff invite the speaker to give a similar talk to their members”

- Feedback from community group talk
Work Package 3 : Education and Engagement

Health Professionals
20 events were held for health care professions over the year. Highlights include:

- **Spotlight on Rare Diseases at the University of South Wales**
  After the success of the Living with Genetic Conditions sessions at the University of South Wales, we were invited to organise a half-day session on Rare Diseases for nursing undergraduates. **Over 311 nursing students** attended. The feedback was positive and more genomics sessions have been requested.

- **Start of Genomics Roadshow**
  In July 2017, the Welsh Government launched its Genomics for Precision Medicine Strategy. Wales Gene Park has been tasked with rolling out an engagement programme to raise awareness of the strategy amongst health professionals in Wales. Although due to start in April 2018, several events were organised ahead of schedule, including presentations at Nevill Hall and The Princess of Wales and Hospitals’ Grand Round sessions and an information stand at the Aneurin Bevan University Health Board Healthcare & Support Workers conference.

- **Living with Genetic Conditions**
  These popular sessions were held for undergraduate nursing students at University of South Wales, Swansea University, Cardiff University and for Allied Health Professional students at Cardiff Metropolitan University.

- **Neurofibromatosis 1 (NF) meeting in Kerala**
  This meeting was organised in collaboration with Professor Meena Upadhyaya OBE. Over 26 world-renowned specialists travelled to Kerala, India, to present their latest findings at this one-off conference. As a result of the meeting an NF clinic has been established in the area and international collaborations were set up.

- **Two new meetings on genetics and mental health in Cardiff:**
  - The Psychiatry of Huntington’s Disease in collaboration with Dr Duncan McLauchlan, Division of Psychological Medicine and Clinical Neurosciences, Cardiff University
  - Clinical Genetics & Psychiatry with Professor Jeremy Hall, Neurosciences & Mental Health Research Institute, Cardiff University


“it was brilliant. One of my year 13s just came to see me and said, “That’s it, I know now I’ve deffo applied for the right course - I loved listening to Dr H”. That makes my day, I’m so pleased you could come”
- Teacher Feedback from Schools’ Genetics Roadshow

Schools and Colleges
Through the Schools’ Genetics Roadshow, 18 events were held across Wales with students from over 30 schools and colleges attending.
Additionally, Continuing Professional Development meetings for post-16 biology teachers were held in North and South Wales. These events updated teachers on the latest advances in genetics & genomics. At each location a focus group was held to find out what topics the teachers wanted covered and to make our schools’ events more relevant.
Work Package 3: Education and Engagement

Policy

- **Genomics for Precision Medicine Strategy**
  Several Wales Gene Park staff contributed to the Welsh Government’s Genomics Taskforce and play essential roles in the working groups set up to implement the Strategy. The Education and Engagement Team have initiated a Genomics Roadshow to raise awareness of the strategy across Wales, starting with health professionals.

- **Welsh Rare Disease Implementation Group**
  The Genetic Alliance UK Policy & Engagement Manager for Wales represents the third sector on the Welsh Implementation Group responsible for delivery of the Implementation Plan for Rare Diseases. We provided a number of case studies, showcasing the impact of aspects of the plan, for the groups annual report.

- **Cross Party Group for Rare Genetic & Undiagnosed Conditions**
  In 2017, we began work to establish a Cross Party Group in the National Assembly for Wales which will represent the interests of those affected by rare, genetic and undiagnosed conditions. Genetic Alliance UK identified a number of Assembly Members to participate.

Research

- **Rare Disease Research Portal**
  Wales Gene Park started work to develop a research portal which enables those affected by rare diseases to have improved access to research opportunities available to them. To ensure the portal design meets the needs of the intended end-users, we hosted a consultation workshop during the Annual Rare Disease Patient Network meeting, thereby involving patients, families, researchers and health professionals in the development and design of the portal. As part of its development, the portal will be tested by potential users to ensure that it has the right functionality and appropriate content for those who will be navigating it.

- **SiGNAL Research Project**
  We acted as a third sector representative on the SiGNAL Project which received funding from the Health and Care Research Wales Research for Patient and Public Benefit fund. The project piloted the use of diagnostic clinical exome sequencing (CES) in the NHS in Wales.

- **Research project governance**
  Wales Gene Park manages the study governance, patient recruitment and curation of study data for three UK Clinical Research Network (UKCRN) / Health and Care Research Wales Portfolio projects in rare disease research. Through banking samples from patients with cancer or rare diseases, we have supported four laboratory based research projects that aim to improve future NHS diagnostics.

- **Opportunities for patients and families to become involved in research**
  A number of different opportunities were offered for patients and families to become involved in research projects. These include participation on advisory groups or to provide input on project design or development. One researcher received over 300 responses to a project entitled ‘What do genetics patients most value from their healthcare services, and how can we measure the outcomes?’
CASE STUDY: Enhancing the Welsh Knowledge Economy

Wales Gene Park is helping strengthen Welsh Research and Development (R&D) capabilities in genetics and genomics, fulfilling a key strategic objective in line with Welsh Government policy. Through the provision of our academic and technical expertise, Welsh researchers can more successfully develop their research programmes, including those in collaboration with the commercial sector, in priority healthcare areas such as cancer treatments.

An exemplar collaboration is with Dr Andrew Tee, Reader in the Division of Cancer and Genetics at Cardiff University. Wales Gene Park provides Next-Generation Sequencing, bioinformatics analysis, compute and data storage for RNA sequencing for Dr Tee’s work. This includes research collaborations with both pharmaceutical companies and international higher education institutions.

Dr Tee’s research aims to provide better understanding of the molecular mechanisms that drive tumour growth in several familial tumour syndromes. He anticipates that his findings could drive the development of new approaches to treating these tumours, with the possibility that these approaches could be also applied to more common cancers in the future.

Dr Tee’s key collaborations include:

- Professor Elizabeth Henske at Harvard University Medical School and colleagues at GW Pharmaceuticals (a global leader in developing cannabinoid-based medicines) on pre-clinical research using model systems to test the efficacy of cannabinoids.
- Professor Mark Kelley of Indiana University’s School of Medicine and founder of the clinical stage biotech company, Apexian Pharmaceuticals, to analyse panels of STAT3 and Ape1/Ref1 inhibitors in genetic models of cancer.
- Professor Maurice Van Steensel of the Institute of Medical Biology, A*STAR, Singapore, to ascertain the driving mechanism behind Birt-Hogg/Dubé syndrome, a genetic disorder that predisposes patients to renal cancers.

“With Wales Gene Park’s support, and in collaboration with our partners, we are starting to understand the vulnerabilities of tumour cells in patients with inherited tumour syndromes. This is allowing us to develop better strategies for treatment in the future.”

- Dr Andrew Tee

Dr Andrew Tee
Reader in the Division of Cancer and Genetics at Cardiff University
CASE STUDY: Generating Models of Disease to Support Fundamental Research

Wales Gene Park is supporting the work of Wales’ up-and-coming scientific researchers by providing resources and expertise which facilitates their research at this crucial early stage. By nurturing Wales’ brightest and best scientific minds, Wales Gene Park is helping create the next generation of scientists.

“I love seeing these cells under the microscope – it’s the start of life. It’s incredible and so beautiful. My research could not have happened without the valuable input from Wales Gene Park.”

- Jessica Griffiths

Jessica Griffiths, a final-year PhD student in the School of Biosciences at Cardiff University, is one of the beneficiaries from Wales Gene Park’s assistance. Ms Griffiths’ research focuses on analysing PCDH19, a gene involved in a rare disorder that causes epilepsy and cognitive decline in young girls, known as Early Infantile Epileptic Encephalopathy-9 (EIEE9). Using mouse Embryonic Stem (ES) cells generated in collaboration with Wales Gene Park’s Genome Editing Research Manager, Bridget Allen, Ms Griffiths is investigating the role of the Pcdh19 gene in cortical cell synapse formation, which is intended to decipher the mechanism behind the disorder. This could result in further pharmacological research and help identify possible therapeutic targets for EIEE9 in the future.

Synapses are the critical structures through which nerve cells communicate. These structures therefore have important roles in diseases such as epilepsy. It is possible to use ES cells, which have the potential to specialise into different cell types in culture, to study factors, including genetic factors, that influence the formation and function of synapses. By manipulating culture conditions, Ms Griffiths is able to make ES cells develop into nerve cells allowing her to study the formation of synapses in real time.

The use of ES cells generated within Wales Gene Park has been essential for Ms Griffiths’ doctoral studies.

Ms Griffiths praises the crucial technical assistance she has received from the Wales Gene Park as fundamental to her current studies and future career development. She intends to submit her doctoral thesis for examination this year, and hopes to go on to research at postdoctoral level.
CASE STUDY: Supporting The 100,000 Genomes Project in Wales

Genomics plays a rapidly expanding role in diagnostics. It brings the possibility of earlier, quicker and more accurate diagnoses in many settings, including for a multiplicity of rare inherited diseases that have traditionally been difficult to diagnose and which together affect as many as 150,000 people in Wales.

The 100,000 Genomes Project was initiated in Wales this year, through a collaboration between the NHS in Wales and Genomics England Ltd. supported with funding from the Medical Research Council awarded to Cardiff University. The project has enabled access to diagnostic whole genome sequencing for NHS patients in Wales who have suspected but currently undiagnosed rare disorders. It has also catalysed development of the virtual Wales Genomic Medicine Centre (GMC) to handle the results of whole genome sequencing for NHS patients through partnership of the All Wales Medical Genetics Service, academics in Welsh Higher Education Institutions and the Wales Gene Park.

The project is helping to transform the NHS in Wales to a service that can handle and utilize genomic information in everyday healthcare. The Welsh Government is investing heavily in new equipment, IT infrastructure and clinical and laboratory staff to ensure that the NHS in Wales can make these changes and bring the associated benefits of quicker and more accurate diagnosis and better personalised treatments to patients across Wales. It published its strategy on Genomics for Precision Medicine in July 2017 and this sets out how the changes are being made.

The GMC and 100,000 Genomes Project in Wales, are helping us realise the Welsh Government’s objectives as described in its Genomics for Precision Medicine Strategy and its Rare Diseases Implementation Plan.

Dr Iris Egner
100,000 Genomes Project Manager
CASE STUDY: Supporting The 100,000 Genomes Project in Wales

Wales Gene Park is providing support for the GMC and the 100,000 Genomes Project next year by:

- Supporting NHS/AWMGS to develop an IT and bioinformatics infrastructure for genomics
- Helping develop mechanisms for researchers in Wales to access genomic data with appropriate consent and governance
- Working with the Wales GMC team and the Secure Anonymised Information Linkage (SAIL) databank (hosted at Swansea University), to scope the potential for databank sharing procedures using this Data Safe Haven
- Providing consultancy support for the continuing development of the Wales GMC to benefit patients in the NHS across Wales

Wales Gene Park is also leading public and professional education and engagement activity for the Wales GMC and 100,000 Genomes Project in Wales. It is raising awareness and understanding of the project and of wider genomic medicine in Wales through talks, workshops and promotional material for the general public, healthcare professionals, service-users, and Rare Disease stakeholders. Wales Gene Park is collaborating with Swansea University in public engagement for the Genetic Data Integration (GeDI) project. This project seeks to integrate genetic data safely into the SAIL national database for research that will provide new insights into health conditions with a genetic component.

“Through collaboration with our partners, we are making Wales a centre of excellence for genomics research and data sharing, to the benefit of the NHS, researchers, and most of all Welsh patients with Rare Diseases.”

- Dr Iris Egner, 100,000 Genomes Project Manager
CASE STUDY: Supporting The 100,000 Genomes Project in Wales

IMPACT ON PATIENTS

For the first time, Welsh NHS patients affected by rare but undiagnosed conditions have the opportunity to have their entire genome sequenced and analysed, with the hope that they will be diagnosed. Each patient on the 100,000 Genomes Project has already undergone extensive investigation with no definitive diagnosis being found prior to referral into the programme. The project offers the prospect of potential diagnosis and possibly subsequent treatment options.

Ffion’s story

Ffion’s family were referred by her NHS Genetics Consultant to the project. All agreed to give blood samples for their genomes to be sequenced in order to compare Ffions genome with that of her parents, which increases the likelihood of finding the cause of her condition.

Ffion’s family are keen for her to receive a precise diagnosis for her medical conditions. “It’s difficult without a label,” said mum Hannah, “but having a diagnosis should help both us and her school to make the necessary adjustments so that she can achieve her potential.”

“We want Ffion to know and understand her condition” said grandad Bryan.

“Having access to genomic testing at home in Wales and available on the NHS has made the process much easier and less time-consuming.”

- Paula, Grandmother of Ffion

Around 80% of Rare Diseases are genetic
CASE STUDY: Supporting The 100,000 Genomes Project in Wales

IMPACT ON PATIENTS

The 100,000 Genomes Project in Wales is at an early stage. Extensive information is being provided to prospective participants and patients are being recruited. The patients’ blood samples are sent to the Sanger Centre in Cambridge for Genomics England Ltd. to analyse. The results are sent back to the 100,000 Genomes Project team and their NHS partners in Wales.

Oscar’s story

Two year old Oscar has been undergoing genetic testing since before he was born, but with negative results to date. Parents Ria and Owain have previously sent genetic samples to as far away as Spain in the hope of achieving a diagnosis. They are pleased that there is now an opportunity for Welsh patients with rare diseases to receive parity of diagnostics testing with the rest of the UK.

“When you have a diagnosis, you can gauge how Oscar could be affected in later life and prepare for this,” said mum Ria, “for now, we are just taking things as they come.”

Dad Owain sees the potential for the future of genomics-focused healthcare as, “patients will definitely benefit from conditions being identified at an early stage, which could help prevent them from becoming more problematic later on.”

As many as **150,000 people in Wales** suffer from a Rare Disease - that’s **1 in 17** of the entire population

There are over **6,000 different Rare Diseases**

For further details on the 100,000 Genomes Project, contact the team on **029 21 847 083** or **029 21 841 712** or by email at **100k.Genomeproject@wales.nhs.uk**
As an infrastructure support group, Wales Gene Park strives to achieve the greatest possible reach and significance for the impact of its work by:

- Providing researchers in Wales from HEIs, NHS and commercial sectors with access to Next Generation Sequencing, bioinformatics and genome editing.
- Working with researchers to increase the quality and quantity of genomic research in Wales to grow the significance and reach of associated impact.
- Improving understanding in the NHS workforce and amongst patients and the wider public of the opportunities and challenges presented by genomic medicine.
- Working with NHS genetic and genomic services and clinical researchers to ensure efficient knowledge transfer from research to diagnostic provision for better and faster genetic and genomic tests.
- Facilitating the development of well-informed and effective policies for genomic medicine by Welsh Government and other organisations
  - Participation in working groups, taskforces and the provision of expert advice
  - Helping patients, their families and carers, and the wider public to have their views represented.

Wales Gene Park Impact Lead, Professor Mark Rees (Swansea University and Wales Gene Park Executive Team) is supported by the Operations Manager, Dr Karen Reed, who liaises with the wider Health and Care Research Wales infrastructure to identify areas for joint working to achieve the greatest reach and significance for research.
Key Achievements 2017-18

The Genomic Facility undertook NGS (next generation sequencing) for **25 research projects** from **19 different research groups**

**Grant income secured**
17 successful grant applications have been supported directly, **worth £3,947,130** and providing 10 whole time equivalent positions in Wales

**Wales Gene Park provided dedicated compute and robust, secure data storage for genomic medicine research**

**Our Education and Engagement programme reached over 5,700 people**

**The 100,000 Genomes Project in Wales**
The project team has been established and patient recruitment is underway

**The Wales Gene Park interactive stand has been exhibited at several meetings throughout the year, and won the “most engaging stand” at the Involving People meeting for the third consecutive year**

**The Genomic Facility increased the breadth for support and provision of NGS for common disease genomics, and through the ALL WALES NGS NETWORK provided NGS for projects across Wales.**

The bioinformatics team in collaboration with Human Gene Mutation database have developed a novel **MACHINE LEARNING ALGORITHM** to improve databases that support diagnostic, research and commercial applications

"**WGP bioinformatics are instrumental to our Data Clinic, enabling scientists to analyse their own data**"
Dr Robert Andrews, Lead Bioinformatician Systems Immunity Research Institute, Cardiff, commenting on support provided to help run data clinics and training opportunities that have reached over 500 researchers in the reporting period.

We have expanded the **WGP Patient Network** (now **138 members**) and the **Public Network** (now **543 members**) to facilitate public engagement and involvement in genetic and genomic research.

WGP represented the public and patient voice within **two** Welsh Government Strategy documents:
The Welsh Implementation Plan for Rare Diseases Genomics for Precision Medicine strategy

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Highlights from 15 Successful Years of Wales Gene Park

2002
Wales Gene Park was established with support from the Welsh Assembly Government, the Department of Trade and Industry (DTI) and the Knowledge Exploitation Fund.

2005
For the first time, the Education and Engagement team reached over 1000 participants at their events.

2006
Diagnostics for mutations within the Neurofibromatosis Type 1 (NF1) gene were developed and transferred to the NHS.

2008
The phase 2 TESSTAL trial demonstrated the efficacy and safety of Sirolimus treatment for kidney tumours in patients with Tuberous Sclerosis or Sporadic Lymphangioleiomyomatosis (LAM). This trial paved the way for phase III trials and the routine use of mTOR inhibitors in the clinical management of these diseases.

2010
Initiation of Next Generation Sequencing through Wales Gene Park for researchers in Wales.

2011
Acquisition of a High performance computing cluster and data storage within the Advanced Research Computing at Cardiff (ARCCA) facility, enabled a step change in data management and processing of genomic data for researchers.

2014
A special service for familial hypercholesterolaemia (FH) which, if untreated, predisposes people to heart attacks at an early age, was developed and transferred to the NHS across Wales.

2017
100,000 Genome Project in Wales was established allowing NHS Patients in Wales with suspected, but currently undiagnosed, rare genetic disease to gain access to diagnostic Whole Genome Sequencing.

2017
The Welsh Government’s Genomics for Precision Medicine was launched.

2004
Molecular testing for MUTYH-Associated Polyposis was developed and transferred to the NHS services.

2004
Citizens’ Jury on Designer Babies. A group of 16-19 year olds debated and agreed their views on what choices couples should be able to make in using genetics for family planning. The decisions were reported to the HFEA (Human Fertilisation and Embryology Authority).

2008
The “Police DNA Database on Trial project. Young people used a formal court setting and legal procedures to question the ethics of the National DNA Database. The views captured during this project were reported to the Human Genetics Commission and the Welsh Government for consideration in policy development.
Mainstreaming Genomic medicine in the NHS

The vision for Wales, set out by the Welsh Government in the Genomics for Precision Medicine strategy, sees the development and standardisation of personalized medicine throughout healthcare. Wales Gene Park will work with The All Wales Medical Genetics Service, The Wales Genomic Medicine Centre and Welsh Government to help realise this vision.

We will:
- Coordinate the implementation of NHS workforce training associated with the Genomics for Precision Medicine Strategy
- Contribute to the IT infrastructure development and associated strategy for networking capability required for storing and processing genomic and precision medicine data

Supporting commercialization from research

Pre-clinical research being undertaking in collaboration with commercial partners will continue.

We will increase our collaboration with commercial partners and prioritise the commercialisation of genomic research.

We anticipate seeing the rewards for Wales of previous Wales Gene Park support for commercializable research such Prof Duncan Baird’s work on changes in the telomeres - the ends of chromosomes - in cancer. This work underpins TeloNostix - a spin-out company from Cardiff University.

Facilitating big data analysis utilizing genomic data

Working with the experts in e-health research at the SAIL (Secure Anonymised Information Linkage) databank at Swansea University, and the Genetic Data Integration (GeDI) project team, we will:
- Develop methods for interfacing genomic data with clinical and other e-health related data for research innovation and service development
- Consult with patients and the public to support the development of an open, transparent and publically agreed approach to the sharing of genomic data for service development and research

Utilising new technologies for genomic research

- The Wales Gene Park Genomic facility will continue to extend the repertoire of services available, while taking advantage of methodologies that reduce costs, as and when they become available.
- NGS provision for small RNA work has been established. The utilisation of NGS using single-cell samples will expand in line with demand, and NGS from RNA and/or DNA extracted from formalin-fixed-paraffin-embedded samples will be established.
- The Wales Gene Park genome editing work will focus on developing our expertise in the use of human models of disease using induced pluripotent cells (hiPS cells).

“A public and patient portal to be hosted on the Wales Gene Park website is to be developed to help patients find opportunities to become involved in research”

The GeDI project – an opportunity to participate in research

For more information contact the project lead Dr Kerina Jones (k.h.jones@swansea.ac.uk), or the project researcher Dr Helen Daniels (h.daniels@swansea.ac.uk)
Genetics and Genomics are becoming ever more important for health research and health care. Wales Gene Park is an essential partner helping Welsh Government, Higher Education Institutions, the NHS and industrial partners to make advances and to develop and deliver better quality health and care services in Wales.

Our commitment to support the delivery of the Welsh Government’s Genomics for Precision Medicine strategy, and the Implementation Plan for Rare Disease, will continue to inform our priorities and working practices. We are proud of the integral role laid out for Wales Gene Park in the delivery of these strategies.

We are supporting researchers by expanding our portfolio of technologies to include cutting-edge techniques using human IPS cells. The continued development of models of disease, underpinning exploratory research in the pre-clinical setting, is essential to support the fundamental stages of the translational pipeline. The provision of competitively priced, bespoke NGS and bioinformatics for researchers across Wales, is being further developed to enable single cell and fixed tissue applications.

The Education and Engagement team have delivered a large programme of events for a range of audiences. Current priorities include roadshows for health care professionals, raising awareness of the Genomics for Precision Medicine Strategy. We also prioritise involvement of the public and patients, using our networks to ensure their views are communicated clearly and effectively to Welsh Government.

**Acknowledgements**

Many senior academics, university management and NHS staff continue to support Wales Gene Park, giving their time, energy and enthusiasm. We thank them for their invaluable help.

We further thank Mr Perry James and Mr Alan Thomas, our patient representatives, for their continued excellent support and advice.
If you would like to work with us, or require further information, help or advice, please contact Wales Gene Park’s Operations Manager, Dr Karen Reed at:

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ReedKR@Cardiff.ac.uk

Wales Gene Park, Institute of Medical Genetics, Cardiff University, Heath Park, Cardiff, CF14 4XN

To find out more about our current projects and areas of expertise, please visit:

www.walesgenepark.cardiff.ac.uk/

Follow us on social media at:

@walesgenepark

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