Wales Gene Park

Annual Report 2023-2024

CONTENTS

WELCOME

Welcome to the Wales Gene Park annual report which summarises activities during the period 1st April 2023- 31st March 2024.

This year marks the 21st anniversary of the founding of Wales Gene Park. Over the past two decades Wales Gene Park has supported research, innovation and healthcare in Wales through advances in genomic sequencing, developing novel laboratory methods and facilitating hundreds of cutting-edge research projects.

We are working hard to deliver key aspects of the Genomics Delivery Plan for Wales 2022-25. To achieve this, Wales Gene Park has a broad portfolio of activities that include an extensive programme of engagement with patients and the public, education of medical professionals, providing researchers access to advanced genomic technologies, and bespoke support with bioinformatic analysis.

Wales Gene Park is an integral part of Genomics Partnership Wales (GPW), and many of the team have now moved to the new Canolfan Iechyd Genomig Cymru (Wales Genomic Health Centre) in Coryton, Cardiff to co-locate with the NHS All Wales Medical Genomics Service and the Pathogen Genomics Unit of Public Health Wales.

FOREWORD

This annual report captures the value and impact of the broad portfolio of work undertaken by the Wales Gene Park team.

One role of Wales Gene Park is to make genomic technologies available to biomedical researchers in Wales. In the last 12 months the Wales Gene Park has generated sequencing data for 45 genomic projects, provided essential non-sequencing NGS support to 2 projects and bioinformatics support for 67 projects. It has also supported external research grants bringing in over £5.8M to Wales. Wales Gene Park provides bespoke support for critical areas of research - cancer, rare disease, immunology, and others – including many projects that could not be accommodated by larger commercial organisations.

Another key goal of Wales Gene Park is to engage with the public to promote understanding of the opportunities and challenges raised by genomics. We are working hard with public and patient representatives to develop secure and appropriate strategies for sharing routinely collected NHS genomic data to empower health research.

Genomics is a fast-moving field and Wales Gene Park continues to evolve and adapt. In the past year we have been sad to see the retirement of Dr Kevin Ashelford and Angela Burgess. Kevin joined the Wales Gene Park in 2011 and led in areas such as bioinformatics, data science and development of data sharing infrastructure. Angela Burgess worked in Wales Gene Park for over 20 years and led the Education and Engagement team. We are very grateful for their hard work and dedication to Wales Gene Park and wish them both all the very best in their retirement.

Dr Rhian Morgan, who worked alongside Angela for 9 years has taken on leadership of the Education and Engagement team and will continue to develop the team and their activities. We are also happy to welcome Caroline Ready, who has a background working in industry relations and has commenced as our Business and Operations Manager.

Dr Andrew Fry, Director, Wales Gene Park

A WORD FROM OUR PATIENT AND PUBLIC REPRESENTATIVES

Diagnosis of a rare disease for some may bring a sense of isolation and helplessness over outcomes. Getting involved with Genetic Alliance UK and Wales Gene Park with the opportunities to represent other patients and carers on RD Groups and learning from the experiences of both patients and professionals gives valuable insight and understanding. I have also gained lifelong support and friendships from others on this Rare Disease journey.

Getting involved with as many research opportunities as possible has helped me to keep updated and informed and I believe that this is fundamental to be able to best advocate for oneself or for a loved one with a Rare Disease.

I welcome the focus on the four key priorities identified in the Rare Disease Framework. These priorities are the major challenges highlighted by the rare disease community. There is much to be done in the areas of speedier diagnosis, increasing awareness of rare diseases amongst healthcare professionals, better co-ordination of care and improving access to specialist care treatment and drugs will be crucial to the commitment to improve the lives of Rare Disease individuals and that of families like mine, living with loved ones who have a Rare Disease.

Patients and their carers need to have access to a health professional who has knowledge of their condition, who can talk about the condition and be aware if something unusual is happening and to guide on best possible treatment options and support. There is a need for better mapping and signposting of existing services such as the TSC Specialist Clinics and to help find a clinician who has relevant special interests.

To enable best possible outcomes for all rare disease patients there is a need to make Education, Social and Healthcare pathways and signposting clearer. Holistic approaches for all Rare Disease Patients that focus on enhancing day-to-day experiences together with speedier access to emerging life-saving, life-enhancing treatments should be fundamental. Opportunities to take part in Research projects should be part of the care plan for all with a Rare Disease.

Marie James - Patient representative on Rare Disease Implementation Network (RDIN) and Parent

I am proud to guide and support Wales Gene Parks' efforts to ensure advances in research are centred around benefiting those affected by unmet healthcare needs. Wales Gene Park engages and involves patients and the public and puts them at the centre of genomics to benefit the people of Wales ensuring the voice of those affected is at the centre of decision making and policy developments. I will continue to work to support Wales Gene Park's mission to deliver last change through research, innovation and engagement

Alan Thomas - Patient Representative on Wales Gene Park Strategic Advisory Group

INTRODUCTION & STRATEGIC OBJECTIVES

Introduction

Wales Gene Park is funded by the Welsh Government through Health and Care Research Wales. Hosted by the Division of Cancer and Genetics (DCG), at Cardiff University School of Medicine.

We support, promote genetic and genomic research across Wales, thereby aiding the implementation of the Welsh Government's Genomics for Precision Medicine Strategy.

Mission

- To promote and facilitate Welsh medical genetic and genomic research and its application to healthcare in priority areas identified by the Welsh Government, in order 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.

Aims

Wales Gene Park works 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 the informed involvement of patients, public and professionals in the development of genomic medicine in Wales.

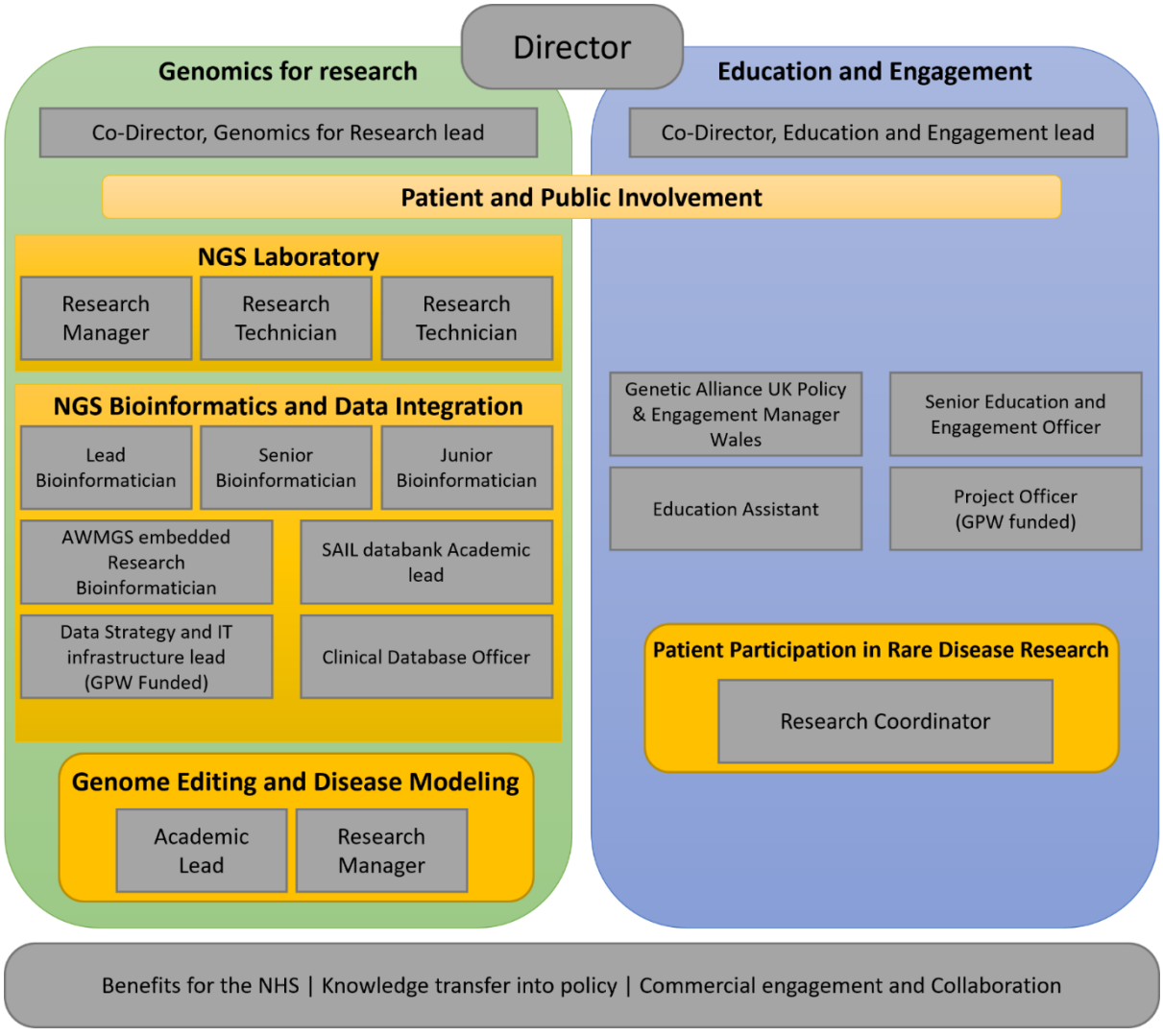
Strategic Objectives

The Wales Gene Park objectives are to provide and develop expertise and infrastructure that will help Wales compete at the forefront of genetic and genomic research in its areas of priority and strength, particularly by supporting Health and Care Research Wales funded research activities and programmes. We will do this through providing support for Welsh researchers working collaboratively to help drive the development of Genomic Medicine in Wales. In doing so Wales Gene Park works to provide leadership in rare genetic disease research to help Wales to develop capacity in genomics, to undertake genomic analysis on a significant scale and support the linkage of genomic information to clinical data and other relevant data sets. These activities are underpinned by the objective of raising awareness and understanding, to enhance public and professional awareness and understanding of health-related genetic and genomic research and the opportunities and challenges this research brings.

RESOURCES AND WGP STRUCTURE

The Wales Gene Park annual budget employs a team of staff who are supported by senior academics, experts from the National Health Service (NHS) in Wales, managers and administrative staff from the host institution, Cardiff University.

Wales Gene Park Structure 1st April 2023- 31st March 2024.



More information about the team is available on the Wales Gene Park website:

https://www.walesgenepark.cardiff.ac.uk/our-teams/

KEY PARTNERS AND COLLABORATORS

Academic Partners

- Aberystwyth University
- Bangor University
- Cardiff University
- Cardiff Metropolitan University
- Glyndwr University
- Swansea University
- University of South Wales

NHS Partners

- Cardiff and Vale University Health Board
- Genomics Partnership Wales
- All Wales Medical Genomics Service

Commercial Partners

- Agilent Technologies
- Cellesce Ltd.®
- GW Pharmaceuticals Plc
- Illumina
- Illumine Theatre
- New England BioLabs, (UK) Ltd
- Oxford Nanopore
- PTC Therapeutics
- Roche
- Theatr Genedlaethol

Third Sector Funders and Partners

- Bowel Cancer West
- Bowel Cancer Wales
- Cancer Research UK
- Cancer Research Wales
- Genetic Alliance UK
- Pathological Society (GB & Ireland)
- Rare Disease UK
- SWAN UK
- Techniquest
- Tenovus Cancer Care
- The Wellcome Trust
- Tuberous Sclerosis Alliance (USA)
- Tuberous Sclerosis Association (UK)

Executive Management Team

- Dr Andrew Fry, Director
- Mrs Caroline Ready, Operations Manager/Co-director (commenced November 2023)
- Mrs Angela Burgess, Education and Engagement Lead/Co-director
- Mrs Sherrie Witts, Finance Manager
- Dr Hywel Williams, Impact Lead/Co-director
- Dr Kevin Ashelford, Data strategy and IT infrastructure Lead
- Professor Nick Allen, Genome Editing Lead
- Professor Kerina Jones and Dr Owen Pickrell – Data linkage Lead

- Mrs Emma Hughes, Policy and Engagement Manager (Wales) Genetic Alliance UK, PPI Lead
- Professor Andy Tee, Commercial Interaction Lead

Patient Representatives

- Mr Alan Thomas
- Mr Nathan Davies

Strategic Advisory Group (SAG)

- Chair: Professor Colin Dayan, School of Medicine, Cardiff University
- Mrs Emma Hughes, Third Sector Representative and WGP PPI Lead
- Dr Rob Orford, CSO Health, Welsh Government
- Dr Dee Ripley, Deputy Chief Scientific Adviser for Health Welsh Government
- Chris Newbrook, Head of Health Sciences Branch, Welsh Government
- Dr Claire Morgan, Programme Director for the MSc Genomic Medicine, Swansea University
- Dr Ramsey McFarlane, Bangor University
- Professor Richard Adams, Director of Cancer Trials, Cardiff University
- Dr Mick Hunter, Entrepreneur in Residence Evotec, COO Viatem Ltd, and CEO Orca Pharmaceuticals Ltd
- Joanne Ferris, Operations Manager, the Association of the British Pharmaceutical Industry
- Clive Morgan, Managing Director, All Wales Medical Genomics Service, Cardiff and Vale University Health Board
- Sian Morgan, Head of NHS All Wales Medical Genomics Service Laboratory
- Michaela John, Head of Programme, Genomics Partnership Wales
- Dr Mark Bale, Head of Science Partnerships, Genomics England
- Dr Francis Sansbury, Health and Care Research Wales Specialist Lead for Genomics and Rare Diseases

LAY SUMMARY

Wales Gene Park is funded by Welsh Government through Health and Care Research Wales to support research into genomics (the study of an organism's genome – its genetic material – and how that information is applied). During the 2023-2024 reporting period, we supported research via two areas:

Area 1 – Genomics for Research

- Sequencing (determining the order of a DNA fragment) and analysing genomic information to support researchers.
- Making and using pre-clinical models of disease through genome editing (inserting, deleting, modifying or replacing DNA in the genome of a living organism) and other methods.
- Developing IT infrastructure that enables research using genomic data.
- Developing a Trusted Research Environment (TRE), which has catalysed researchers in Wales to think differently, work more collaboratively, and put data at the heart of patient-centred cancer research over the coming years.

Area 2 – Education and Engagement

- Enhancing awareness and understanding of health-related genetic and genomic research for the public and health professionals.
- Involving those with lived experience in research prioritisation, development and delivery.
- Facilitating opportunities for patient and public involvement in genomic research.

Summary of Activities

Sequencing Provision

Next Generation Sequencing (NGS) is a powerful, cost-effective, time-efficient way to sequence genes and genomes. Wales Gene Park use short read sequencing machines based within Cardiff University and the All Wales Medical Genomics Services (AWMGS) NHS facility to generate sequence data for researchers. Long-read sequencing using Oxford Nanopore Technology for patient samples is currently under development to broaden our provision of NGS services to our colleagues. We have enabled sequencing access for 45 projects, including areas such as cancer research, immunology and rare diseases.

Establishing the IT Infrastructure for Genomic Research

We work with academic (Universities), healthcare (the NHS) and industrial partners to improve the computational and data storage resources essential for genomics research. We continue to provide dedicated IT infrastructure to support genomic research through the Sêr Cymru IT infrastructure and the planned infrastructure at WGP's new home at Cardiff Edge.

Bioinformatic Analysis

Bioinformatics is the way complex biological data is interpreted, such as genomic sequence data, using computers. At Wales Gene Park, our team of bioinformaticians have supported 67 research projects this year and provided access to computing capacity to researchers and postgraduate students.

Genomic Data Integration into the SAIL Databank

The challenges identified by this study informed the next stage of the project and led to the installation of a pipeline to process genetic data on a separate server within a secure research platform (SeRP). The intention is that during this processing any identifiable personal information would be removed and the annotated files would be suitable for upload into the SAIL Databank following the standard procedure. The separate pipeline also allows for the annotation software to be updated so that the genetic datasets (Variant Call Format [VCF] files) can be reannotated with the latest datasets.

Developing Models of Disease
At Wales Gene Park we use cutting-edge methods (such as using specialised stem cells, CRISPR genome editing, and a range of cell and 'mini-organ' technologies) to generate new human genetic models of disease to undertake pre-clinical studies.

We have supported projects that have looked at conditions including Alzheimer's disease, Huntington's disease, Glioma, and Motor Neuron Disease.

Rare Disease Research
The Inherited Tumour Syndrome Research (ITSR) group work on several different rare disease studies. Professor Julian Sampson is the Chief Investigator for the *Genes and the Kidney in Tuberous Sclerosis* study (funded by WGP and the Tuberous Sclerosis Association) which aims to determine the natural history of renal disease in patients with the TSC2/PKD1 contiguous gene deletion and compare this with patients with mutations in TSC2 or TSC1 alone. The study has recruited 288 patients and is due to close in December 2024.

Professor Jeremy Cheadle is the Chief Investigator for our *Genetic Mechanisms in Polyposis of the Bowel* study (funded by Ser Cymru and WGP) which aims to discover novel genetic mechanisms underlying polyposis of the bowel and the development of tumours in this group of disorders. This study has underpinned the identification of a genetic change that reduces the activity of a known tumour suppressor gene, causing the polyposis phenotype seen in a 4-generation family. This genetic change was not identified from the standard clinical diagnostic services because it does not occur in the main body of the gene. However, this highlights the potential usefulness of expanding the diagnostic screen, particularly for patients with suspected polyposis when a classical genetic change has not been identified. This study has reached its recruitment target of 375 patients and is now in follow-up.

Dr Laura Thomas is Chief Investigator for two of our studies. The *Molecular Genetic Analysis of Duodenal Polyposis in the Inherited Colorectal Adenoma and Cancer Predisposition Syndromes* study (funded by a number of organisations including WGP, Health and Care Research Wales, WCRC, Accelerate, Bowel Cancer West and Swansea University) is investigating if patients with familial adenomatous polyposis (FAP) and MUTYH associated polyposis (MAP) are also at risk of developing premalignant and malignant tumours in the duodenum as well as the colorectum. This study investigates the genetic factors, inherited and somatic, associated with growth and progression of duodenal adenomas to cancer in MAP and has recruited 72 patients.

Dr Thomas' other study is *Exploring Genetic Causes of Duodenal Polyposis Using Healthy Volunteers* (funded by Accelerate, Swansea University and WGP) which uses 3D organoid models to explore the genetic causes of duodenal polyposis by comparing affected patients with healthy volunteers. A comparison of healthy volunteers with 3D duodenal organoids established from patients with FAP and MAP (established as part of the *Molecular Genetic Analysis of Duodenal Polyposis in the Inherited Colorectal Adenoma and Cancer Predisposition Syndromes* study) can help to determine how polyps are arising in patients with these conditions and we have recruited 13 patients from Cwm Taf Morgannwg University Health Board.

Our researchers (including a Research Coordinator funded through WGP) are also working on the first multi-centre European prospective study of duodenal disease in MAP that aims to provide evidence as to whether surveillance recommendations developed for patients with FAP are also appropriate for patients with MAP. It aims to collect long-term data on the endoscopic findings and provide follow-up information to aid understanding of the natural history of duodenal disease in MAP, taking into account that some patients may require therapeutic procedures including removal of polyps where there is advanced duodenal disease. It will also prospectively collect data on the occurrence of colorectal cancer

and extra-intestinal cancers. This study has recruited 716 patients with MAP and will continue for 20 years in total.

Education and Engagement

The Education and Engagement team have delivered a large programme of events and activities to raise awareness and increase understanding of the advances of genomics in Wales. Current audiences include health care professionals, patients and families, schools and colleges, and the public. We also prioritise involvement of the public and patients, using our networks to ensure their views are communicated clearly and effectively to Welsh Government.

There are a huge range of activities which enable the team to raise awareness of genomics including, community talks, public lectures, genomics cafes and conferences.

Enabling patient involvement in research
Wales Gene Park continues to facilitate opportunities for patient and public involvement in genomic research. Opportunities are circulated to our rare disease patient network, the Genomics Partnership Wales Patient and Public Sounding Board and through Genetic Alliance UK's Member Newsletter which is circulated to our 230 member organisations on a bi-weekly basis. Alongside our social media platforms, including our website and X (Twitter). Attendees at events such as the Genomics Cafes are also made aware of opportunities for involvement.

Examples of how we have involved people in projects focussed on genetics and genomics:

- Cardiff Science Festival- opportunity to engage with the public through interactive stands and workshops
- Genomics After Dark in Techniquest Cardiff and Wrexham's Science Discovery Centre 'Xplore!'.
- Joining the recently established RDIN Leadership Group and supporting members in different areas of the Plan, including recruiting a PPI representative to support the Cwm Taf Bevan Exemplar Rare Disease clinic.
- Delivering community group talks, public lectures and healthcare conferences.
- Festival of Genomics 2024- raising the profile of Wales through our presence alongside partners at the London based event.

CORE METRICS

Reporting period 1st April 2023 – 31st March 2024

Health and Care Research Wales infrastructure award to the group

Direct funding awarded

£820K

Grants won during reporting period

Grants won	Led by group	Group collaborating
Number	**4**	**7**
Value	**£363K**	**£5.8M**
Funding to Wales	**£363K**	**£5.8M**
Funding to group	**£363K**	**£0**

Number of publications

Number of public engagement events

Number of public involvement opportunities

WORK PACKAGE 1
Genomics for Research

Core Activities

- NGS for a range of applications using DNA and RNA
- Development of new NGS technologies
- 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
- Pathway development for the integration of genomic data into Secure Anonymised Information Linkage (SAIL) databank (Swansea)
- Contribution to healthcare professional education
- Derivation and growing human iPSCs (Induced Pluripotent Stem Cells)
- Utilising CRISPR (Clustered Regularly Interspersed Short Palindromic Repeats) genome editing technology to generate new models of disease for research
- Consultation for researchers requiring support in cell and genome editing techniques

Purpose and Progress

Wales Gene Park supports and promotes the application of genomic technologies via a range of activities delivered through:

- An NGS laboratory (45 projects supported in the last year)
- Bioinformatics provision (67 projects this year)
- Data science/integration expertise
- Genome editing and disease modelling.

Development work and innovation is supported through collaborations with academia, NHS, AWMGS, Pharma and Biotech sectors.

The provision of access for flexible NGS for research, together with expert bioinformatics support underpinned by dedicated high-performance computer infrastructure for genomic analysis, ensures the quality and quantity of genomic research undertaken in Wales and sees a greater proportion of externally awarded research funding is spent in Wales.

Wales Gene Park Genomics Facility Activity

Sequencing provision

NGS is a powerful, cost-effective, time-efficient technique used to sequence genes and genomes. At Wales Gene Park, the genomics facility lab team of 3 individuals use sequencing machines within Cardiff University and the AWMGS to generate sequence data for researchers.

This approach allows a cost-effective strategy, optimising capacity utilisation to maximise the use of the sequencing machines. We have enabled sequencing access for 45 projects researching areas of cancer biology, rare disease research, arthritis, kidney disease, immunological conditions, neurodegeneration, and Alzheimer's projects.

Establishing the IT infrastructure for genomic research

We work with academic, healthcare and industrial partners to improve the computational and data storage resources essential for modern genomics research. We continue to provide dedicated IT infrastructure to support genomic research through the Sêr Cymru IT infrastructure and the planned infrastructure at WGP's new home at Cardiff Edge.

Bioinformatic analysis

Bioinformatics is the science of analysing complex biological data, such as genomic sequence data, using computers. At Wales Gene Park, our team of two bioinformaticians have supported 67 research projects this year and provided access to computing capacity to researchers and postgraduate students.

Genomic data integration into the SAIL Databank

We have previously described how files holding genetic variant information for individuals who donated samples to the Swansea Neurology Biobank were uploaded and annotated within SAIL. The annotation process identifies rare and potentially damaging variants, and we were able to investigate the presence of such variants in groups of individuals with different epilepsy outcomes. This was possible by linking the annotated variant dataset to routinely collected data from GP and hospital records and with the information derived from clinic letters. The results of this work were presented at the International League Against Epilepsy (ILAE) European Epilepsy Congress in July 2022 and at the ILAE meeting in Cardiff in October 2022. They have also been submitted for publication in a peer-reviewed journal.

The challenges identified by this study informed the next stage of the project and led to the installation of a pipeline to process genetic data on a separate server within a secure research platform (SeRP). The intention is that during this processing any identifiable personal information would be removed and the annotated files would be suitable for upload into the SAIL Databank following the standard procedure. The separate pipeline also allows for the annotation software to be updated so that the genetic datasets (Variant Call Format [VCF] files) can be reannotated with the latest datasets.

Since 2023, PhD student Rob Maddison has been funded by Health and Care Research Wales to explore mobilising routine genetic tests for data linkage in SAIL. 16,181 cystic fibrosis (CF) gene test records have been annotated and uploaded to enable investigations into the health impact of being a CF carrier. This work has identified the data formatting challenges keeping routinely acquired genetic data and metadata from research platforms and will inform recommendations for future data integration. Analysis in collaboration with clinical scientists at the All-Wales Medical Genomics Service (AWMGS) has produced updated frequencies of CF-causing variants in Wales for use in clinical risk assessment.

Data Integration Team

In the last year, the Data Integration Team has catalysed researchers in Wales to think differently, work more collaboratively, and put data at the heart of patient-centred genomic research.

By combining the data we already have (with data linkage and better data reuse) with advanced analytic approaches we will accelerate patient outcomes to provide novel scientific insight and reduce the costs of research. The teams various project collaborations will deliver across all the key checkpoints necessary to use data integration to improve health outcomes.

Activity Highlights

Unlocking NHS genomic data

The team have aligned the desire of **NHS All Wales Medical Genomics Service** to make routine data for research with the aspiration of **Wales Cancer Biobank** to become a databank. This delivers for parts of the Genomics Delivery Plan for Wales and the AWMGS data linkage roadmap. We team have been working to establish pipelines of access to routinely generated, diagnostic genomic data and hope for this to fully implemented and available to researchers via WCB's broad consent model later in 2024.

Creating multimodal data models

Rethinking the way data is stored and analysed in a more patient-centric way, the Data Integration Team have led on the creation of a fully funded PhD studentship involving the **Cardiff Interdisciplinary Precision Oncology Hub**, **Centre for Trials Research**, **School of Computer Science** and **Cardiff Experimental Cancer Medicine Centre** to establish a Digital Twin model for linked multi-modal data.

Routine data for trials

The quicDNA trial is a Welsh cancer trial unique to the UK that will integrate liquid biopsy data into the lung cancer diagnostic pathway. Working with **NHS Digital Health and Care Wales**, the **Cardiff Centre for Trials Research** and the **NHS All Wales Medical Genomics Service** the team have been finding ways of using Secure Data Environments to create a trial control arm from routine NHS data.

Advanced analytics

Interlinked multi-modal datasets are perfect for the application of advanced analytics approaches. Our Digital Twin model (collaboration with **IPOCH**, **CTR**, **ECMC**, **Computer Science**) , is using Acute Myeloid Leukaemia trials data from the Centre for Trials Research, to establish AI and machine learning techniques to predict patient specific outcomes.

A continuing collaboration with **Swansea Medical School** is looking at the use of machine learning for biomarker discovery from Next Generation Sequencing datasets in prostate cancer.

Influencing stakeholders

The team have been invited to present their work the **Welsh Government Cross Party working group for Digital Rights and Democracy**, have worked with **Cancer Research UK** developing their Data Strategy and given talks to the **Public Genomics Cafés** on data ethics and Artificial Intelligence applied to healthcare. Governance expertise within the team helping develop the **Heath Data Research UK** legal toolkit.

Community development and outreach

The use of routine data and data reuse within research is becoming a key focus for many organisations. The Data Integration Team have taken the initiative to bring many organisations together with events such as a *"A roundtable to: accelerate our collective journey towards patient-centred multi-modal data science"* and a *"Workshop on Information Governance within healthcare research".*

These events were extremely successful attracting an audience of 80 people, representing the interests of both senior academics and earlier career researchers plus NHS clinical academics and Leaders.

Further consolidation of this community approach is a key goal into 2024/2025.

Developing Models of Disease

Advances in genomics are having unprecedented impact on our understanding of the genetic basis of disease, from the identification of mutations responsible for rare genetic disorders to understanding the complex interactions of multiple (polygenic) genes that increase a person's risk of developing common disorders such as dementia or some cancers. Pathways to therapy require us to understand gene functions, firstly in models of disease. At Wales Gene Park we use cutting edge induced pluripotent stem cells (iPSC), CRISPR genome editing, cell differentiation and organoid technologies to generate new human genetic models of disease to undertake pre-clinical research.

We have supported 9 research groups, supporting 14 new grant proposals ranging from PhD studentships and early career fellowships to UK Research and Innovation (UKRI) and charity funded project grants and drug discovery initiatives. Projects have addressed Alzheimer's disease, Huntington's disease, Glioma, and Motor Neuron Disease.

Rare Disease Research

The Inherited Tumour Syndrome Research (ITSR) group work on several different rare disease studies. Professor Julian Sampson is the Chief Investigator for the *Genes and the Kidney in Tuberous Sclerosis* study (funded by WGP and the Tuberous Sclerosis Association) which aims to determine the natural history of renal disease in patients with the TSC2/PKD1 contiguous gene deletion and compare this with patients with mutations in TSC2 or TSC1 alone. The study has recruited 288 patients and is due to close in December 2024.

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Publications and presentations:

- Kearney A, Butlin L, Coffey T, et al. *The overlap between randomised evaluations of recruitment and retention interventions: An updated review of recruitment (Online Resource for Recruitment*

in Clinical triAls) and retention (Online Resource for Retention in Clinical triAls) literature. Clinical Trials. 2024;0(0). doi:10.1177/17407745241238444

- Channing J. Paller et al., *Pan-Cancer Interrogation of MUTYH Variants Reveals Biallelic Inactivation and Defective Base Excision Repair Across a Spectrum of Solid Tumors*. JCO Precis Oncol 8, e2300251(2024).
- Meuser, Elena et al. *(2024). PIGA Mutations and Glycosylphosphatidylinositol Anchor Dysregulation in Polyposis-Associated Duodenal Tumorigenesis. Molecular cancer research : MCR. 22. 10.1158/1541-7786.MCR-23-0810.*
- PhD student Amy Houseman is presenting at the INSIGHT conference in June, 2024.

WORK PACKAGE 2

Education & Engagement

Purpose

Wales Gene Park carries out a wide portfolio of activities in professional and public education and engagement. The programme provides 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.

Core Activities

- Education and engagement events and activities via public and schools' programmes
- Support through events, initiatives, and campaigns, for those affected by Rare Diseases
- Management of networks for each of WGP's four key stakeholder groups (patients, schools, the public and professionals)
- 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, including rare diseases.

Progress

Public

A varied and wide-ranging programme of engagement activities were held for public groups which included:

Genetics & Genomics for the 3rd Generation (3G) Public Conferences

Now in its 8th consecutive year, the annual 3G conference took place virtually in December. The event is aimed at the over 50 age group, but open to any members of the public with an interest in DNA, genetics, genomics and related topics. Attendees joined via Zoom to enjoy talks including *V for Vaccination: from Cowpox to Covid*, *Nutrigenomics of Coffee*, *Let's Talk About Bowel Cancer*, *Using the Arts to Raise Awareness of Rare Diseases,* and *History, declines and genetic contact in the northern and southern white rhinoceros.*

- *Thank you for an excellent day. I enjoyed all the talks - so interesting!* 3G Attendee
- *One of the most absorbing presentations I've ever heard on the subject of rare diseases. Thank you so much!* 3G Attendee

Genomics Cafés

Public Genomics Cafés form part of the Genomics Partnership Wales engagement programme that WGP designs and delivers. Free and open to all, the cafes include short, informal talks about genomics relating to health and medicine with guest slots from health professionals, researchers, third sector groups and those affected by genetic and rare conditions, who share personal experiences. Since April 2023, seven cafes have taken place for the general public, attended by more than 320 people. Examples of talks included *Can your IL-6R gene influence your exercise choices?, The plan for genomics in Wales for the next three years; Measuring DNA Damage in Circulating Blood in Oesophageal Cancer; Data linkage to investigate the health impacts of carrier status for cystic fibrosis; Providing genomic testing for cancer patients: the whys, the how's & the next steps; From silence to sound: Finding my voice as a Rare Disease patient.*

- *Brilliant sessions thank you for organising - really informative and beneficial*. Public Genomics Café attendee
- *Thank you for a phenomenal presentation, so insightful.* Public Genomics Café attendee

"Wales Gene Park public cafés have been valuable in revealing the fascinating research and significant developments in therapies relating to genomics. The recent case of the young girl who had her hearing restored through groundbreaking infusion treatment is just one example". Genomics Café attendee.

Following the positive response to the Public Cafés, separate Young People's Genomics Cafés were initiated. Aimed at those aged 16 to 25, they are held three times a year on a termly basis, and in the last 12 months were attended by over 90 people. Topics included *Careers in Cancer Research: My journey so far, Where would we be without research,* and *We are WHEN we eat.*

- *Thank you! Can't wait for the next session* 🤓 Young People's Café attendee
- *Time flies when you're having fun and science is fun!* Young People's Café attendee

In addition, the first hybrid café was held this year in Chapter Arts Centre Cardiff, with attendees able to attend in person or online via zoom to experience live talks, and the first Christmas Café was held in December, with members of Genomics Partnership Wales' Sounding Board presenting an engaging Christmas Quiz. A blend of online and in-person cafes will return over the coming months.

Genomics After Dark @ Techniquest

As part of an ongoing programme of communication and engagement with the public around genetics/genomics, the 2nd *Genomics After Dark* outreach event was organised and delivered by Wales Gene Park's Education and Engagement Team in conjunction with Genomics Partnership Wales. Held at the Techniquest Science Discovery Centre in Cardiff, the event was aimed at an adult audience (particularly the hard-to-reach 18 to 50 age demographic) and free to attend. Over 200 members of the public attended. It comprised a range of engaging, hands-on activities which included:

- Laboratory-based DNA extraction workshops
- Public talks focusing on ethics in clinical genetics/genomics, and Genomics in the Media
- A wide range of interactive stands from organisations across sectors such as healthcare, research, public health, higher education and the arts
- Virtual Reality games

A *Genomics After Dark* was also held in Wrexham's Science Discovery Centre 'Xplore!', where members of the public enjoyed activities including hands-on stands on the subject of genomics, scientific exhibits and VR games.

- *Lots of enthusiastic staff and support!* Genomics After Dark attendee
- *Engagement, lectures, interaction, covers a lot of bases – fun!* Genomics After Dark attendee
- *This has been great!* Genomics After Dark attendee

Community Group Talks

Thirty-nine DNA and genetics/genomics-related talks were given to community-based organisations including The Rotary Club, Women's Institute groups, Probus Clubs, The University of the Third Age, retirement fellowships, library groups and social clubs throughout Wales. Topics included Personalised Medicine, Journey to the past: Tracing your genetic roots using DNA, Genetics and Genomics in Everyday Life, DNA Fingerprinting, Pharmacogenomics, Epigenetics, Genomics in the Media.

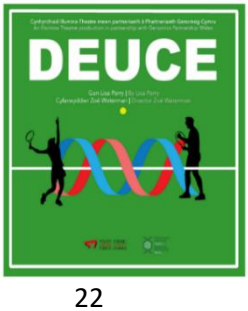
Public Lectures

Wales Gene Park's public lectures are aimed at engaging with a lay audience about genetics and genomics-related subjects. Attendees are varied and range from Sixth Form students through to retired members of the public. An example from this year was a collaboration with Cardiff University's School of Medicine Science in Health public lecture series, with an excellent lecture by Dr Neil Stephens, University of Birmingham *Let's talk cultured meat: reflections on the socio-politics of growing meat in vats*.

Launch of Deuce: a new bilingual audio drama from Illumine Theatre and Genomics Partnership Wales

Produced by Illumine Theatre in partnership with Genomics Partnership Wales and in conjunction with Wales Gene Park, *Deuce* is a podcast drama written by Cardiff-based playwright Lisa Parry and directed by Zoë Waterman, which explores the inherited condition hypertrophic cardiomyopathy (HCM). Translated by Branwen Davies, there is a Welsh and English version available to stream for free, to ensure a wide range of listeners can experience this powerful and thought-provoking production. The 30-minute podcast tells the story of Alys, a teenage tennis player who collapses during the final of the Girls' Junior Championship at Wimbledon.

The world as Alys knows it is then turned upside down when doctors diagnose her with HCM; a condition where the muscular wall of the heart becomes thickened and pumping blood around the body becomes more difficult. Not only does Alys understand that her diagnosis could spell the end of her own career,



she realises that this inherited condition, caused by a fault in her genome, could have also been the cause of her father's so-far unexplained death.

Lisa's script, informed by the experience of experts in genetics and genomics, cardiologists and those living with hypertrophic cardiomyopathy, explores the life-changing impact of diagnosis on relationships, ambitions and mental health. *DEUCE* was launched in summer 2023 and is free to access via platforms including Spotify and Apple Podcasts.

Public Genetics Network

Wales Gene Park also continued to engage with members of the public through its *Public Genetics Network* and associated biannual newsletter which provides news, information and details of events and opportunities.

Cardiff Science Festival

For the first time this year, Wales Gene Park took part in Cardiff Science Festival at an event held by Cardiff University called 'Be a Scientist'. Over 500 members of the public attended during February half term and enjoyed the range of interactive stands and workshops, including WGP's Discovering DNA stand.

Schools and Colleges

During the last 12 months, WGP has delivered a busy and varied programme of engagement for post-16 School and Colleges which included:

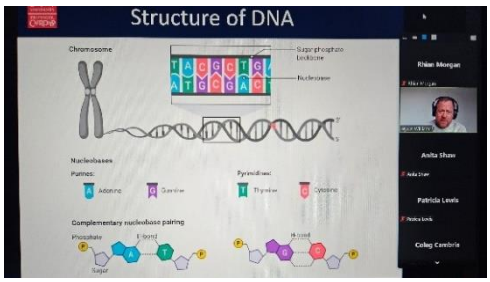
- Genetics/genomics-focused careers stands and talks at school and colleges (examples include Cowbridge High School, Cardiff and Vale College, Archbishop McGrath High School Bridgend, Teachers' & Careers Advisors Fair)
- Bespoke genetics/genomics education sessions at schools, as well as an *Ethical Dilemmas* session with the All-Wales Medical Genomics Service as part of Cardiff University Sutton Trust Summer School, and a Cardiff University Widening Participation Summer School
- Engagement via Wales Gene Park's ***Teachers' Genetics Network*** and associated termly newsletters.
- Interactive information stands at events, highlights of which included the *Life Sciences Challenge* and *Science in Health* Sixth Form event at Cardiff University's School of Medicine

Students at Cowbridge have benefited from presentations from the Gene Park engagement team which showed the diverse career opportunities available in this little understood aspect of healthcare. And the intriguing exhibits on their stand proved very popular with the many students that visited it during lunch! **Careers Teacher**

Sixth Form Conference

WGP was delighted to hold its Sixth Form Genetics & Genomics Conference in November – the first time since the Covid pandemic. The conference took place online and provided a great opportunity for year 12 & 13 students to hear about the latest advances in genetics & genomics from expert speakers, including: *An Introduction to Genomics, V for Vaccination: from Cowpox to Covid, Dreams and Nightmares of the Genetic Age* and *Genetic Influences on Young People's Mental Health.* The conference was attended by 970 students & teachers throughout Wales.

- *One of my year 12 students has even spent his free this afternoon hunting down information about stem cells now, and he was inspired...that's exactly perfect. Thanks for organising.* Teacher, Sixth Form Conference



Health Professionals and Researchers

Throughout the year a range of activities were facilitated for health professionals, healthcare students, and researchers working in the field of genetics and genomics, which included:

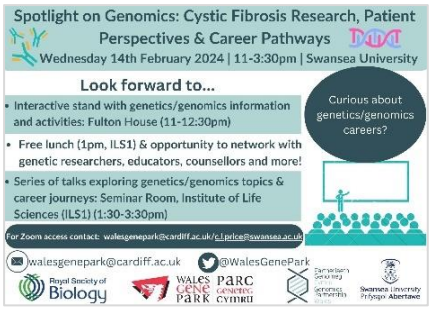
Education sessions

A series of genetics/genomics-related sessions were delivered to support the education of professionals such as health professionals, healthcare students, and researchers. These included:

- GP Training sessions
- *Living with Genetic Conditions* sessions and patient experience talks - which include personal narratives from individuals affected by genetic, rare or undiagnosed conditions – delivered for the All-Wales Medical Genomics Laboratory Service and at HEIs throughout Wales (attended by nursing, midwifery and Allied Health Professional students). Sessions included lived experience of conditions including covered ataxia, Lynch syndrome, tuberous sclerosis, cystic fibrosis, Fragile-X syndrome, cancer, and SWAN (Syndromes Without a Name)

Swansea University: Spotlight on Genomics Careers Event

In collaboration with Swansea University and the Royal Society of Biology, Wales Gene Park held a hybrid Genomics Careers event for undergraduate and postgraduate students, which included an interactive information stand and drop-in talks. This was a great opportunity for students to hear about a range of different genomics-related careers, and from a cystic fibrosis patient to place these careers in context.



Festival of Genomics

Wales Gene Park was part of a collaborative Genomics Partnership Wales (GPW) presence at the Festival of Genomics 2024 in London, along with colleagues from GPW, All Wales Medical Genomics Service, and Public Health Wales' Pathogen Genomics Unit. Over two days, partners engaged and networked with

hundreds of stakeholders, and delivered talks in areas including the QuicDNA study, the All-Wales Psychiatric Genomics Service, and pathogen genomics.

Specialty Certificate Examinations (SCE) Revision course

The annual Clinical Genetics Revision Course, hosted by the All-Wales Medical Genomics Service, was held for doctors training and specialising in this area of medicine.

- *The course is great at covering a huge amount of material in just 2 days, and really helps focus revision.* SCE course attendee

Genomics Exhibition Stand

Wales Gene Park, also representing Genomics Partnership Wales, exhibited at numerous scientific and healthcare conferences, meetings and careers-focused events throughout the year, providing information and hands-on activities. Examples include:

- Health and Care Research Wales Annual Conference
- The Bevan Commission Annual Conference
- NHS Confederation Conference
- Wales Health Science Conference
- Royal College of Midwifery St David's Day Conference
- Minority Ethnic Communities Health Fair
- Cardiff Metropolitan University Careers Fayres

Ministerial launch of new Canolfan Iechyd Genomig Cymru/Wales Genomic Health Centre

Canolfan Iechyd Genomig Cymru (CIGC) in North Cardiff was officially opened during a visit from The then Cabinet secretary for Health and Social Services, Eluned Morgan on 7th December, to serve as a cornerstone of Wales' precision health ambition. Funded by Welsh Government, the state-of-the-art facility co-locates some of Wales' leading experts in the field of genomics: Genomics Partnership Wales, the All-Wales Medical Genomics Service (AWMGS), Pathogen Genomics Unit and Public Health Genomics Programme, and Wales Gene Park.

With the NHS at its heart, this collaborative environment combining industry and academia has been co-produced by staff across all Partners, patients and members of the public. The new space will be home to world-class clinical and research laboratories and purpose-built clinical spaces, bringing patients right alongside the research which will continue to expand their treatment options and improve care outcomes.

I am delighted to officially open The Canolfan Iechyd Genomig Cymru and see first-hand how the NHS and academia are working together to revolutionise genomics and how we treat illnesses in the future. It is fantastic Welsh Government has been able to fund this state-of-the-art facility and shows our commitments to advancing healthcare through genomics and precision medicine.

We have already seen success with ground-breaking initiatives in this field and I hope this new facility will help build on this work and create more opportunities for genomics to transform healthcare, improve patient outcomes, and contribute to the prosperity of the people of Wales. The Canolfan Iechyd Genomig Cymru is more than a facility; it is a hub of knowledge, innovation, and hope for the future of healthcare in Wales. **Eluned Morgan MS, Cabinet Secretary for Health and Social Care**

20 years of WGP Education & Engagement Celebratory Event

In spring 2024, WGP marked over 20 years of delivering genetics/genomics Education and Engagement with a celebratory event at the new Canolfan Iechyd Genomig Cymru. This was also an opportunity to wish Angela Burgess a happy retirement after 20 years leading WGP's E & E programme. Key stakeholders and partners old and new (including patients, public, health professionals and researchers) came together to network, reflect on achievements and look towards future plans.

Professionals' Genetics & Genomics Network

Wales Gene Park continued to engage with professionals with an interest in genetics and genomics through its biannual *Professionals' Genetic Network* and associated newsletters, providing news, information, and details of opportunities for education, research, PPI and more.

Patients & Families

The programme of activities to support and empower those affected by genetic, rare, and undiagnosed conditions included:

Events

Genomics & Newborn Screening Drop-in Sessions at Welsh Parliament

Genetic Alliance UK took part in two drop-in sessions focused on genomics and newborn screening in 2023. A member of the GPW Patient and Public Sounding Board attended the genomics session to speak with Senedd members about new developments and the need to keep abreast of changing pace. We had cross party engagement from a third of Senedd Members during these sessions. We also presented at a roundtable event focused on rare bone conditions that was held at the Welsh Parliament and engaged with Members to raise awareness of the UK Rare Diseases Framework.

SWAN Family Day 2023

As part of Undiagnosed Children's Day 2023, SWAN UK Cymru with support from Wales Gene Park held an information and networking fun day for families with over 30 people in attendance and a variety of information, signposting and activities available to engage families and give them an opportunity for peer-to-peer support.

The SWAN UK Cymru Sounding Board which consists of 6 SWAN UK members in Wales have been instrumental in providing feedback to the SWAN clinic in Wales and evaluating patient reported outcome measures (PROMs) and patient reported experience measures (PREMs) that have been developed for patients attending the clinic. These are now being used in practice to determine how beneficial the clinics have been for families in attendance.

Rare Disease Patient Network Annual Meeting 2023

Wales Gene Park held its ninth annual Rare Disease Patient Network meeting in November. The aim was to bring members of the Rare Disease Patient Network together as well as guest speakers and others with an interest in rare, genetic and undiagnosed conditions. The event featured talks including:

- Rare Minds Matter – mental health and rare conditions
- The UK's first SWAN Clinic and establishing the Global Rare Disease Nurse Network
- How to get involved in raising awareness of rare diseases by taking part in activities for Rare Disease Day 2024

During the afternoon session, attendees were invited to take part in an online workshop focused on providing feedback on the update to the Welsh Rare Disease Action Plan led by the Coordinator of the Rare Disease Implementation Network, Rhiannon Edwards.

- *I just wanted to say that I thought the morning session was excellent and really helpful. I'll definitely draw several of the initiatives to other' attention* Attendee of RD Patient Network meeting

Rare Disease Day 2024 – highlights

- Wales Gene Park supported the NHS Wales Rare Disease Implementation Group and All Wales Medical Genomics Service staff to create a 'rare' garden - the first in a series of events to mark Rare Disease Day. On Sunday 11th February, the family of Violet Taylor, who passed away in 2023 at just 11 months old from a rare neurogenetic disorder, planted the first of 700 bulbs to launch a special garden at the Canolfan Iechyd Genomig Cymru (Wales Genomic Health

Centre) in Cardiff. These outdoor spaces are designed to bring communities and families together, providing a place for reflection and enabling people with lived experience of rare disease to gather and share their stories. It is hoped the gardens will become a focal point for those beginning their journey with rare disease, as well as those already living with one.

- Wales Gene Park hosted a Young People's Genomics Cafe - one of the speakers, Tyler Mclleland spoke about his experiences of having a rare condition and being a paralympic athlete who plays Boccia and Wheelchair Football.
- A member of the GPW Patient and Public Sounding Board, Mel Williams shared a case study about her experience of the rare condition HPP and how it affects her and her family.
- Genetic Alliance UK in collaboration with Wales Gene Park organised two events to highlight the day - an in person parliamentary reception in Cardiff Bay and a joint virtual event in collaboration with the other 3 nations of the UK (see information below).

Rare Disease Day 2024 - Parliamentary Reception

On 20 February, over 80 stakeholders from across the rare disease community came together for the first Rare Disease Day reception of 2024 at the Norwegian Church, Cardiff Bay. There was a great atmosphere as friends and colleagues came together to celebrate achievements from the year and hear about plans for the latest refresh of the Welsh Rare Disease Action Plan published in January. Prof Iolo Doull, Chair of the Rare Disease Implementation Network (RDIN) presented on key areas of progress within the four priority areas of the Welsh plan.

We heard inspirational talks from Lucy Vers and Sophie Pierce. Lucy spoke about her 6-year-old son Elliott who was diagnosed with Duchenne Muscular Dystrophy. Lucy has been advocating for more clinical trials for rare conditions to take place in Wales. Sophie has Cystic Fibrosis (CF) and spoke about not letting her condition define her. Wales Gene Park and charity Rare Minds had stands at the event and it was a great opportunity for networking and making new connections. One attendee commented: *So lovely to meet ... Our stories are different but so many similarities connecting over our beautiful, rare girls.*

You can view photos from the evening by following this link: Wales 2024 Rare Disease Day | Flickr

Rare Disease Day is an annual international event aimed at raising awareness and highlighting the needs of people with rare conditions. It provided an opportunity for the rare community to come together to raise awareness of the common issues affecting those living with rare conditions.

Rare Disease Day Joint Nation Virtual Event

Alongside the in-person event, over 70 people attended an online joint-nation event. Over the past few years, our networks have valued bringing the whole UK community together online, making new connections and reaching people who may not usually join our Rare Disease Day events. Representatives across the four UK Nations shared the progress being made around implementation of

their Rare Disease Action Plans, and there were also personal accounts from people from each nation who live with rare conditions.

From Wales, Rhys Holmes, shared his experience of living with Superficial Siderosis. Prof Iolo Doull, Chair of Rare Disease Implementation Group (RDIG) now Network gave an update on Wales and its implementation of the Rare Disease Action Plan. Rhys was also interviewed as part of the Genetic Alliance UK report, 'Stats Behind the Stories' that was published for Rare Disease Day - available here: Stats-behind-the-stories-Genetic-Alliance-UK-2024.pdf (geneticalliance.org.uk)

Policy

Welsh Disease Action Plan
Members of the Welsh Rare Disease Patient Network alongside the GPW Sounding Board have provided feedback on the draft iteration of the Welsh update to their Rare Disease Action Plan ahead of its publication. We continue with our role as PPI representative on RDIN working closely to explore opportunities to collaborate. We have joined the recently established RDIN Leadership Group and supported members in different areas of the Plan; for example, recruiting a PPI representative to support the Cwm Taf Bevan Exemplar Rare Disease clinic.

We have supported two bids to LifeArc for rare disease funding; one led by Cardiff University and RDIN to develop a virtual health hub for rare diseases and another led by Swansea University which was successful in its bid for funding for a rare disease research node focussed on lipidomics and metabolomics. The Node was officially launched by the Health Minister. We have supported the PPIE aspects of the Node through opportunities to present at our Genomics café initiative.

The Welsh SWAN Clinic
WGP and Genetic Alliance UK continue to collaborate with stakeholders to secure ongoing funding for the UK's first Syndromes Without a Name (SWAN) clinic in Wales, which has been piloted for the last few years. WGP has been coordinating input from the SWAN Cymru Council and meets monthly with the team to ensure there is engagement between the clinic and SWAN community. We have developed a case study focused on care coordination to support the case for future funding. As part of this collaboration, Genetic Alliance UK was invited to have a stand at the Welsh Paediatric Society annual conference.

Collaborating with Congenital Anomaly and Rare Disease Information Service (CARIS)
We have continued working with the Welsh Registry to support development of their self-registration service for adults with rare diseases. We plan to support projects by clinical researchers analysing the CARIS data and to support collaborations with patient groups going forward.

Genomics Partnership Wales - Patient & Public Involvement (PPI) Sounding Board
WGP supported Genomics Partnership Wales to develop strong foundations for patient and public involvement and co-production, with a three-tiered approach established to ensure a broad range of opportunities for patients and the public to help strengthen the quality of genomics output.

WGP has continued to assist the Genomics Sounding Board, made up of 30 people with diverse experiences of rare, genetic conditions and cancer testing or diagnosis. Working together, they have developed guiding principles that will serve as the foundation for future delivery; a commitment to communicate clearly with patients and involving them in prioritising deliverables to ensure maximum benefit; to provide high quality inclusive and accessible services with appropriate levels of support; timely diagnoses, appropriate treatment and best care for patients and their families.

Wales Gene Park - PPI

Throughout the 2023-2024 reporting period, WGP has continued to engage with the Board as well as its wider Rare Disease Patient Network to offer opportunities to get involved in projects.

43 involvement opportunities were shared and 210 people took these up. Examples of how we have involved people in projects focussed on genetics and genomics:

- Patient & Public Sounding Board – regular consultation with our Board of PPI members to provide feedback on the best way to involve people/ communicate about genomics and asking them to influence ways of doing this
- Recruitment opportunity to be a lay member of the Genetic Counselling Registration Board
- PPI representative recruited to advise on clinical research project for rare disease clinic
- Bid development for proposals to LifeArc for rare disease research funding

ACHIEVING IMPACT

Impact in genetic and genomic research is of paramount importance as it holds the key to improving healthcare outcomes and transforming the lives of individuals and communities throughout Wales.

Wales Gene Park's mission is to support impact-driven research from across Wales to bridge the gap between scientific discoveries and their real-world applications.

The activities of Wales Gene Park are firmly grounded in collaborative work spanning various healthcare specialties.

Wales Gene Park continues to work with 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.

The following case studies highlight the breadth of workstreams located within Wales Gene Park and the remarkable impact.

CASE STUDY 1

Interdisciplinary Precision Oncology Hub PhD Studentship: *[collaboration with CTR, AML Group, COMSI and IPOCH]*

The Cardiff University Hub in Interdisciplinary Precision Oncology (IPOCH) offers opportunities for post-graduate research students (PGR) to join the cancer research community as part of a joint flagship programme between the schools of Engineering, Computer Science and Medicine. The Data Integration team developed and successfully recruited to a PhD Studentship in September 2023, funded by the EPSRC for three years. This project will perform secondary analysis of a multimodal dataset combining genomic data with clinical trial data to establish the concept of "Cancer patients' Digital Twins to investigate disease fragmentation and its impact on drug response in AML trials".

Genomic data available from a series of Acute Myeloid Leukaemia (AML) trials provides panel sequence data for around 2500 patients along with their treatment data, with survival data available for around half of these samples. This gives a unique opportunity to i) use machine learning approaches to identity disease fragmentation and patient response to specific drugs; ii) look for genetic explanations for differences in drug response common to different treatment pathways; and iii) develop models that use genomic data to predict drug response within standard AML treatment pathways providing routes to tailor interventions for maximum impact.

Peter Giles has provided oversight on the process of data acquisition and ethical approval in order enable access to the multi-model AML data needed for the machine learning of this digital twin model project.

This research concept brings together cross-disciplinary expertise and the establishment of new pipelines and streams of activity for the CTR, a successful and well-established clinical trials unit. Through the TRE team's innovation, our partners are now facilitating new analysis techniques and application of new technologies, with the potential to significantly increase the value and utility of "old" pre-existing data for future research.

CASE STUDY 2

Using Secure Data Environments to reduce the cost of clinical trials *[collaboration with the CTR, AWMGS and DHCW]*

The Data Integration team have been working to utilise the existing NHS Wales Pilot Secure Data Environment (SDE) Service to obtain data and undertake analysis for the control arm of the quicDNA trial. The quicDNA trial is a Welsh cancer trial unique to the UK that will integrate liquid biopsy data into the lung cancer diagnostic pathway. The DHCW SDE is run by members of their Advanced Analytics group using a UK SeRP tenancy provided by Swansea University as part of the SAIL Databank.

The NHS SDE is designed to make use of routinely collected data held by DHCW in the Welsh Demographics Service (WDS), National Lung Cancer Audit (NLCA) and Office of National Statistics datasets allowing for analysis to be performed by researchers in the Centre for Trials using datasets pre-filtered for trial participants from the anonymised cohort. This project demonstrates how some analyses required by the research community are only possible within the NHS SDE and provides a pathway to more cost-efficient trials by making certain data modalities more readily available to researchers, and thus reducing recruitment costs.

We will continue to work with colleagues in the CTR and DHCW throughout the remainder of the funding period to develop their future research proposals utilising DHCW as this new data provider to complement their research asset in this way.

CASE STUDY 3

Collaboration at the heart of Wales Gene Park for 20 years

Wales Gene Park (WGP) has been established for over 20 years; one of its core aims is to bring stakeholders from academia and the NHS together with patients and the public to facilitate collaboration, drive improvements and involve those who could benefit from advances in genomic medicine.

In addition to engagement with its well-established core stakeholder groups, WGP has led initiatives to inform genomic education and embed patient and public voice at the centre of decision making. Examples of key stakeholder collaborations include:

Genomics Partnership Wales – co-production and engagement is the core of the Genomics Delivery Plan for Wales (December 2022). WGP's Education and Engagement team has been a key collaborator delivering the education and engagement arm of the Plan on behalf of the partnership, working closely with the All-Wales Medical Genomics Service and the Pathogen Genomics Unit at Public Health Wales.

This has involved upskilling NHS staff; coordinating a hospital roadshow to inform them about mainstreaming genomics and supporting events within primary care and other specialties by exhibiting at conferences, events and incorporating the lived experience into teaching sessions. Most recently this has extended to work with Health Education Improvement Wales (HEIW) to deliver the genomics workforce plan. WGP has also led on engagement with the public which has included delivering an inaugural *Genomics Showcase* for Wales, regular Genomics Cafés for the public and young people, as well as organising and delivering other opportunities to learn about genomics such as talks and lectures, bilingual audio dramas (Tremolo and Deuce in partnership with Illumine Theatre), 'After Dark' events in the science discovery centres *Techniquest* and *Xplore*, and attending festivals.

Higher Education Institutions – WGP's remit covers the whole of Wales which has enabled us to build relationships with colleagues in the other Welsh HEI's and to support their teaching. We have organised speakers with lived experience to take part in teaching sessions throughout Wales and have collaborated to deliver bespoke 'spotlight' sessions with a programme focused on genomics and related careers, and rare diseases, with both Swansea University and the University of South Wales.

Genetic Alliance UK and the third sector – Since its inception, WGP has built a strong relationship with third sector partners. Having a role embedded between Wales Gene Park and the charity Genetic Alliance UK has meant WGP has strong links with their network of 230 patient organisations to inform and support its work and engagement/involvement activities.
Our stakeholder groups and key networks continually engage with us to ensure our programme is adapting and improving to keep up to date with the constant changing pace of developments within the genomics ecosystem. We are grateful for their feedback and interactions to ensure our education and engagement programme is delivering effectively to benefit the population of Wales.

> The WGP Education and Engagement team's invaluable close collaboration with Genetic Alliance UK brings our network of organisations supporting people living with genetic, rare and undiagnosed conditions closer to clinicians, researchers and policymakers in Wales. This unique connection fosters productive dialogue that improves awareness of the needs of our community, educates our community and ultimately drives better policy development
>
> **Nick Meade, Director of Policy, Genetic Alliance UK**

CASE STUDY 4

Spatial transcriptomics

Wales Gene Park is collaborating with colleagues from Swansea University on a Health and Care Research Wales grant to perform research into prostate cancer using spatial transcriptomics.

Spatial transcriptomics is a cutting-edge technology that offers researchers the opportunity to measure gene expression levels from discreet regions of a tissue sample. The technology gives unprecedented insights into disease related biological pathways that can be translated into the clinic to improve diagnosis, which in return will assist the clinical management of the patient.

Wales Gene Park is the unique provider of this service to academia in Wales, and is leading the early project design and development.

Our laboratory team are providing expert training in how to perform the protocols, including the laboratory sample preparation steps and running of the samples on the specialised equipment. Following the laboratory work our bioinformatician team offer vital support to analyse the data to ensure it is high quality. This includes comprehensive quality control checks before processing the spatial data to produce novel biological insights. Our experience so far ranges from projects focused on brain tumours, prostate cancer and leukaemia.

The spatial transcriptomic technology we provide a service for is the only spatial biology platform that non- destructively profiles expression of RNA and protein from distinct tissue compartments and cell populations with an automated and scalable workflow that integrates with standard histology staining.

This allows researchers to obtain spatial genomics data quickly and can discover biomarkers predictive of therapeutic response, understand disease progression and reveal molecular subtypes for diseases.

The collaborative spatial transcriptomics project will be ongoing throughout 2025, and the samples and anticipated outputs will be recorded and shape the way forward for this innovative area of work. This in turn will assist colleagues with grant applications, training and statistical analysis of the data, demonstrating Wales Gene Park laboratory and bioinformatics team ability to support and deliver the future of spatial transcriptomics.

LOOKING FORWARD

Supporting genomic research in Wales into the future

Wales Gene Park continues to build on our commitments to support delivery of Welsh Government's strategies, including the Genomics Delivery Plan for Wales 2022-25, and the Implementation Plan for Rare Diseases.

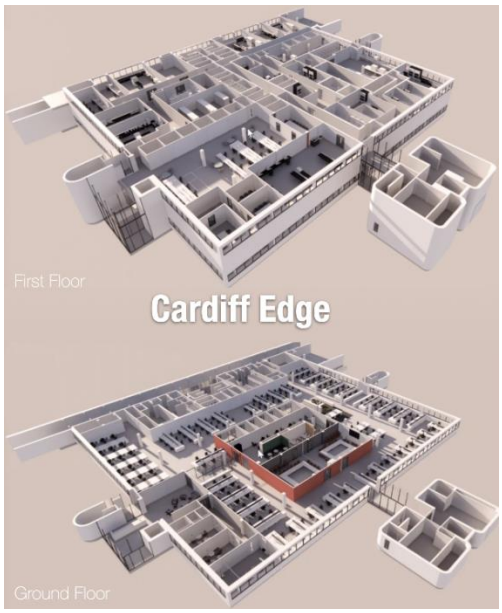
We will provide the technologies required by Welsh researchers:

- Partnership working to ensure the provision of cutting edge genomic and bioinformatic analysis techniques to support the needs of health researchers in Wales, including research undertaken in partnership with the NHS and with the commercial sector. These techniques will include long-read DNA and RNA sequencing, methylomic analysis and spatial transcriptomics.
- Human iPSC derivation and genome editing to support researchers needs through the provision of appropriate pre-clinical models of disease to understand the causes of disease and to develop and test potential treatments.
- Working with experts in e-health research at the SAIL databank at Swansea University to establish methods for integration of NHS genomic data with clinical and other e-health related data for research, innovation and service development.
- Consult with patients and the public to develop an open, transparent and publicly agreed approach to the sharing of genomic data for service development and research.
- Delivery of an extensive portfolio of events and activities to promote health professional and public education and engagement, and to facilitate the informed involvement and participation of patients and public in setting research priorities in health and social care and in research planning, funding, dissemination and translation.
- Service and policy development work, working with Genomics Partnership Wales, the new Welsh Parliament Cross Party Group for rare, genetic and undiagnosed conditions and other partners to influence and develop policy areas which improve the lives of patients and their families.

A time of change for WGP

Wales Gene Park has evolved since its initial founding in 2003 developing a strong reputation for its Education and Engagement activities and as a major provider of high throughput sequencing and genomic analysis in Wales.

Wales Gene Park will continue to move staff alongside the NHS All Wales Medical Genomics Service and the Public Health Pathogen Genomics Unit to Canolfan Iechyd Genomig Cymru (Wales Genomic Health Centre) in Coryton, Cardiff.



Being based at CIGC will assist maximising the benefits of working alongside partners and collaborators, with a focus on research and innovation. This work will harness the potential of genomics to improve the health, wellbeing and prosperity of Wales.

Further development of existing partnerships between clinical services, academia, industry and patients and the public are essential to realise the benefits of genomics for precision medicine in Wales.

A key priority over the next 2 years will be demonstrated through securing funding and defining our vision and financial sustainability.

ACKNOWLEDGEMENTS

Wales Gene Park could not operate without the continued support from many others. Notably, many senior academics at Cardiff University, the university management teams, Genomics Partnership Wales colleagues and NHS staff, all of whom give their time, energy, and enthusiasm to support Wales Gene Park. We thank them all for their invaluable help.

We further thank all members of the Strategic Advisory Group chaired by Prof Colin Dayan, and our patient representatives, Mr Alan Thomas, Mr Nathan Davies and Ms Marie James for their continued and excellent support and advice.

We are grateful for the budget provided by our funders which include the Welsh Government through Health and Care Research Wales and Genomics Partnership Wales; and Roche.

CONCLUSION

Genomics is among the most exciting arenas of 21st century healthcare and will give opportunities to better understand illness and improve patient outcomes.

Wales Gene Park continues to work with 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.

We are an integral part of the partnership at Canolfan Iechyd Genomig Cymru (Wales Genomic Health Centre) in Coryton, Cardiff and several staff have co-located with the NHS All Wales Medical Genomics Service and the Pathogen Genomics Unit of Public Health Wales at the CIGC. This move has placed Wales Gene Park at the centre of an exciting new Genomic Centre, supporting researchers in accessing samples and data, and translating cutting-edge genomic techniques into new diagnostic tests.

Wales Gene Park is committed to supporting the Welsh Government's Genomics Delivery Plan for Wales, Implementation Plan for Rare Disease, and Genomics Research Plan for Wales which is in

development, and we are exceptionally proud of the important role that Wales Gene Park has in the delivery of these strategies.

GLOSSARY

A

AML Acute Myeloid Leukaemia Group

AWMGS All Wales Medical Genomics Services

C

CARIS Congenital Anomaly and Rare Disease Information Service

CIGC Canolfan Iechyd Genomig Cymru (Wales Genomic Health Centre)

COMSI Computer Sciences Department (Cardiff University)

COVID-19 Coronavirus Disease

CPD Continuing Professional Development

CRISPR Clustered Regularly Interspersed Short Palindromic Repeats

CTR Centre for Trials Research

D

DCG Division of Cancer and Genetics

DHCW Digital Health and Care Wales

E

eFAD Early-onset Familial Alzheimer's Disease

EPSRC Engineering and Physical Sciences Research Council

F

FAP Familial Adenomatous Polyposis

G

GPW Genomics Partnership Wales

H

HCM Hypertrophic Cardiomyopathy

I

ILAE International League Against Epilepsy

IPOCH Interdisciplinary Precision Oncology (Cardiff University Hub)

iPSCs Induced Pluripotent Stem Cells

ITSR Inherited Tumour Syndrome Research

M

MAP MUTYH-Associated Polyposis

MRC Medical Research Council

N

NGS Next Generation Sequencing

NHS National Health Service

NLCA National Lung Cancer Audit

P

PenGU Public Health Wales Pathogens Genomics Unit

PPI Patient and Public Involvement

PROM Patient Reported Outcome Measures

PREM Patient Reported Experience Measures

R

RD Rare Disease Groups

RDIG Rare Disease Implementation Group

RNA Ribonucleic Acid

S

SAG Strategic Advisory Group

SAIL Secure Anonymised Information Linkage

SCE Specialty Certificate Examinations

SDE NHS Wales Pilot Secure Data Environment Service

SeRP Secure Research Platform

STEM Science Technology Engineering & Maths

SWAN Syndromes Without a Name

T

TRE Trusted Research Environment

TSC Tuberous Sclerosis Complex

U

UHB University Health Board

UK United Kingdom

UKRI United Kingdom Research and Innovation

USA United States of America

V

VCF Variant Call Format

W

WCB Wales Cancer Bank

WCRC Wales Cancer Research Centre

WGP Wales Gene Park

WDS Welsh Demographics Service