Issue 9
Winter 2026

ISSN 2755-7782

ADELPHI GENETICS FORUM

exploring heredity and society

ADELPHI REVIEW

www.adelphigenetics.org

CONTENTS

***Images**: Cover image of the Adelphi Vase: Helen Middleton-Price*
Adelphi Conference images: Rosemary Ekong

Published by:

Adelphi Genetics Forum, 19 Northfields Prospect, London, SW18 1PE www.adelphigenetics.org

Executive Secretary: Mrs Ruth Matthews
executiveoffice@adelphigenetics.org

Review Editor: Mr Robert Johnston

Charity No: 209258

Editorial

2025 was an eventful year in many ways for the Adelphi Genetics Forum. In October, we held our Annual Conference at the Royal Society. The theme was **Population Genomic Screening – Exploring its Complexities** and we were fortunate enough to have seven amazing speakers. The highlight was the Adelphi Lecture given by **Dr Margaret McCartney** from the University of St Andrews and, at the conclusion, she was presented with the new Adelphi Vase, as shown on our front cover. There is a full report in this issue and videos of the talks can be found on our website.

Planning for our 2026 conference is already well advanced and it will be held on 22 October. Another date for your diary is our biennial Teachers' Conference in Manchester on 26 June at NOWGEN. Details of both conferences can be found on pages 30-32.

The most notable event of 2025, however, was the retirement of our long-serving General Secretary **Betty Nixon**. Every fellow and member has come into contact with Betty at some point and will have found her to be welcoming, friendly and utterly efficient. Everyone wishes her a long and happy retirement and on page 26 there is touching tribute by past president, **Professor Veronica van Heyningen**. At the same time, we welcome our new Executive Secretary, **Ruth Matthews** and hope she enjoys her challenging new role.

In this issue, we also have articles by two trustees: **Dr Sarah Wynn** tells us about her 'Life in Genetics' and we have another thought-provoking book review by our treasurer, **Professor Andrew Read**.

Robert Johnston

The Adelphi Genetics Forum Annual Conference

Population Genomic Screening –
Exploring its Complexities

23 October 2025 at the Royal Society

The full programme for this conference is available on our web- site along with a link to videos of the lectures and accompanying slides. The organisers were **Professors Shirley Hodgson, Anneke Lucassen, Andrew Read, Gregory Radick, Veronica van Heyningen and Nicholas Wood, Drs Helen Middleton-Price and Rosemary Ekong and the General Secretary, Mrs Betty Nixon.** The Vice President, **Professor Dian Donnai** opened the conference and welcomed the various speakers and the attendees. She also thanked the other organisers for all their hard work.

The first session was chaired by **Dr Rosemary Ekong** who introduced **Professor Richard Houlston (Institute of Cancer Research)** whose talk was titled **"An Overview of Population Screening Programmes"** - giving examples from his own area of interest, namely cancers - set the scene for the rest of the programme. Since early diagnosis is reported to dramatically affect cancer survival, the research goal has been to devise early diagnostic tools followed by intervention to reduce morbidity and mortality.

He began by reviewing evidence for inherited cancer risk, describing some of the opportunities, he then focussed on difficulties of, and misunderstandings of the interpretations. The use of family linkage studies and positional cloning in the 1990s led to the discovery of a number of key cancer genes of large effect; BRCA1 as a risk gene for breast cancer and MLH1 and

MSH2 in colon cancer, fuelling the deterministic interpretation of these genes in causing cancer. Even for these key genes, penetrance was highly variable, but in families, initially using linkage studies, it was useful to identify the members of the family who were at risk to provide presymptomatic screening, and even prophylactic surgery or chemoprevention.

Genetic studies to identify cancer variants moved on from linkage analysis to Genome Wide Association Studies (GWAS). This in turn was followed by the advent of whole genome sequencing as this has become much cheaper, but interpretation is another story. Deciding which are functional variants is not even straightforward for protein coding regions but for gene regulatory regions which are likely to be involved in multifactorial disease, it is not yet possible.

He described how current governmental/NHS policy is moving towards extensive population screening, in particular whole genome sequencing at birth by 2030. The general and worthy philosophy of this endeavour is to pick up all deleterious and risk variants so that resources can be focussed on further screening of at-risk individuals, with a view to preventing or treating their illnesses efficiently. This was great advertising but the problems are many and include the following constraints:

Professor Richard Houlston

From whole genome sequence it is not simple to predict disease risk. There is so much variation in the genome and allele frequ-

encies can vary dramatically within and between populations. This means that predictions can be quite different in different ancestry groups. Determining which alleles are pathogenic is also extremely hard. Even though there are reporter assays, functional screens are very difficult or impossible. There are many variants of uncertain effect. If key functional/risk variations are identified, is there any effective intervention that can be offered? Where we do have interventions, have they been validated? Do they affect survival?

This led to the idea that the way forward, would be to sum these alleles to make a polygenic risk score (PRS). Houlston explained and discussed this now popular approach, for which there have been adverts in the private sector as well as moves in the NHS. The principle is to cut the extreme 'risk' end of the distribution and offer them further screening.

The problem lies in the balance of false positives and false negatives. There is inadequate discriminatory power. Increasing the detection rate increases the false positive rate, e.g. comparing outcome shows that most breast cancer cases do not occur in the high-risk score group. Combining poor PRS with other poor discriminatory testing methods likely affords no improvement, as for example is the case of PRS and PSA testing for prostate cancer. PRS on its own detects a large number of individuals with non-aggressive disease who do not need invasive testing. Including more variants also does not improve things significantly, since all the power is obtained from the lower SNP density testing. And finally, there are issues with reproducibility across studies.

Following a break for coffee, **Professor Gregory Radick** chaired the second morning session and the first speaker was **Professor Diane B Paul (University of Massachusetts) who spoke on "An Historical Perspective on the Realities of Newborn**

Screening". She began by describing the first success story of such screening, the testing for Phenylketonuria (PKU). Much of the early research on this rare condition (1 in 15,000 live births) was carried out in the UK and it was found that giving these babies a diet severely restricted in phenylalanine would prevent the severe brain damage from developing. The first special formula was produced in 1953. Initially, urine screening was used but once Robert Guthrie developed his heel prick test on blood samples in 1961, the uptake increased rapidly in the UK, but was slower in the US. Unlike the urine test which was unreliable for the first 6 weeks after birth, the blood test is carried out within 3 days, well before the PKU can impact brain development.

By the end of that decade, the test was used on all newborns in the UK and thoughts were given to which other conditions could be targeted in the same way. The next success story was testing for congenital hypothyroidism to avoid the irreversible neurological problems which will otherwise result. The turning point was the use of Tandem Mass Spectrometry to identify hundreds of abnormal metabolites in the infant's blood.

However, the main problem with this is whether the identified problem can actually be treated. At the same time, critics argue that a positive result initiates 'diagnostic cascades' involving other family members leading to large numbers of 'patients in waiting'. In the US, 29 conditions are screened in this way and 10 in the UK. The next big step is Whole Genome Sequencing which the government is planning to introduce for all newborns by 2030.

Professor Diane B Paul

However, Professor Paul went on to show that some of these successes are not as clear cut as was first believed. Although PKU testing is undoubtedly valuable, the dietary treatment is arduous for both patient and family and almost no-one adheres to it after the early years of life. Food plays such an important part in so many social interactions and, in the end, many adults with PKU suffer some degree of long-term impairment. Similar issues are likely to arise with future screening programmes with many false positives expected. PKU screening was a success but should not be regarded as a model for all future programmes. PKU turned out to be genetically more complicated than the single autosomal recessive condition it was initially thought to be, with more than 3,400 variants already identified.

The next speaker was **Professor Felicity Boardman (University of Warwick)** who described **"Ethical Considerations in Screening Programmes"**. She highlighted how topical newborn screening is global, with initiatives such as the Generation Study in England which will sequence 100,000 newborn genomes and screen for over 200 rare genetic conditions. This evolution offers new opportunities for early intervention but also a myriad of ethical considerations.

Professor Boardman drew on data from families involved in several studies. She began by speaking about the benefits of newborn screening in the words of parents and families, showing the life-changing impact early diagnosis can have. The clinical benefits are clearest in conditions where presymptomatic treatment alters outcomes. In spinal muscular atrophy, for example, parents describe profound differences in quality of life when treatment is initiated early. When early treatment is not possible, some parents reported feeling they had "failed" their children, illustrating the moral injury experienced by both families and clinicians who know a child's prognosis could have been different. Another key benefit is reducing long and difficult

diagnostic odysseys that leave families feeling dismissed and isolated. Earlier diagnosis enables timelier referral and support a-nd may reduce conflict within families, where parents sometimes blame one another for not “doing enough.”

Professor Felicity Boardman

She then addressed the possible harms. Consent is a challenge for all screening programmes. She shared the example of Lucy, who, despite going through newborn screening three times, said, “I still don’t know what the bloodspot sort of looks at.” Sleep deprivation and the cultural normalisation of screening can make informed consent difficult. As genomic screening expands to more conditions, issues of privacy, long-term data storage, and one-off proxy consent become more complex. Questions also arise about who the “patient” is, since genetic data is relevant to wider family members. Cascade testing can be beneficial but may create feelings of “genetic responsibility”. Ethical issues cluster around which conditions should be reported and what counts as “treatable.” Some parents favour a broader definition of actionability, while others fear it risks “making a well child sick.” Indeterminate results, such as CF-SPID in cystic fibrosis, further complicate matters. Some families find uncertainty useful (“a foot in the door”), while others feel “in no man’s land”. Late-onset conditions and carrier status also complicate what information should be returned.

In conclusion, genomic newborn screening offers transformative health benefits but must be balanced against harms, uncertain-ties, and inequalities. Professor Boardman left us with a central question: **What do we, as a society, want newborn screening to do for us?**

The final speaker of the morning session was **Professor David Hunter (University of Oxford)** whose talk was titled **"The Clinical Utility of Common Genetic Variation"**. Professor Hunter focussed on the use of common variants to enhance risk estimation for individual patients, rather than their use to guide large-scale population screening. He defined "common" as meaning a variant with a minor allele frequency of at least 1%, meaning that at least 2% of individuals in that population would carry one or more copies of the variant.

In the late 1990s, as the Human Genome Project moved towards its conclusion, there was a widespread expectation that this would lead to rapid advances in precision personalised medicine. The expectation was summarised in the well-known diagram showing the relation between the population frequency of a disease-associated variant and the magnitude of its effect on the risk.

Hunter focussed on the intermediate category of variants that were 'common' by his definition and had a significant, though not definitive, effect on disease risk. Several such variants were already known: the ApoE*4 allele, a risk factor for Alzheimer's disease, the Factor 5 Leiden variant, a risk factor for thrombosis, or the CCR5Δ32 variant, frequent in African populations, that conferred resistance to HIV infection. The expectation was that the Human Genome Project would yield a cornucopia of such variants.

Professor David Hunter

However, the promised flood of risk variants has not materialised. Such variants have unquestioned clinical validity as risk factors but

the question is about their *clinical utility*: what is the value of knowing that somebody carries such a variant? He used Alzheimer's disease and haemochromatosis as examples. In both cases there were known non-genetic ways of reducing a person's risk, and these were effective regardless of the level of genetic risk. His conclusion was that knowing one's genetic risk added little value. Population screening would not be justified, but if a person's high-risk genotype was discovered as an incidental finding from some other investigation, it might be useful to refer them to their GP for discussion on whether they should adopt relevant lifestyle changes.

Most common diseases are truly polygenic, with innumerable variants each conferring a minute change in risk. The polygenic risk score, summarising the effect of all such variants for a given disease, is just another risk factor, most useful for diseases where there are few known non-genetic risk factors. Importantly, these are risk factors, not screening tools, combined with the non-genetic risk factors they may be useful for modifying thresholds for screening e.g. refining for individual women at what age to enrol in routine mammographic screening.

Professor Hunter concluded by talking about the NHS 10-year plan and the Our Future Health initiative. This aims to recruit 5 million adults, of all ages and ethnicities, for genome sequencing and other investigations. Subjects consent to being recontacted if any findings suggest it. He highlighted unresolved logistical problems – who would handle the vast amount of data generated, and how would it be protected against hackers and other unauthorised access? He ended on a positive note by encouraging researchers to make full use of this unprecedented data source.

Following lunch, the first afternoon session was chaired by **Professor Dian Donnai** who introduced the speaker, **Professor**

Aroon Hingorani (University College London). He discussed **"Polygenic Risk Scores in Population Screening and Disease Prediction"**. He approached the question of the potential contribution of population risk scores (PRS) to screening and disease prediction from the perspective of a genetic epidemiologist.

He explained that PRS is essentially the sum of the effects of multiple independent DNA sequence variants found to show an association with a specific disease, the weight of which depends on the degree of association with the disease in question. There is currently a desire to determine the utility of PRS scores for disease prediction. This motivation is reinforced by social media and has already attracted significant interest from academia, industry and health service strategists. Many genetic testing companies have been set up, and their work is likely to influence the healthcare agenda, so that the use of PRS is included in the NHS ten year plan. This raises questions about how such tests might be used for disease prevention, and how they will be funded. Screening is defined as the systematic application of a test performed on asymptomatic individuals to identify those assessed to be at sufficiently increased risk of disease to justify interventions to lower the risk. Professor Hingorani went on to explain how PRS is used in risk calculations. A useful test would have a sufficient separation between values in unaffected and affected individuals such that a cut-off of test false positives of 5% would identify 80% of aff-

Professor Aroon Hingorani

ected individuals; however, this is rarely seen. Using the example of coronary artery disease (CAD), he explained that the detection rate of individuals who will develop CAD at a 5% false positive rate using only clinical risk criteria parameters is 11%; adding PRS may increase the detection rate to 14%, but this only negligibly improves outcomes and requires genotyping hundreds of individuals. Preventative treatment is cheap and convenient, and arguably it would be better only to use age as the risk factor to use to treat all individuals over the age of 50 with statins and blood pressure lowering medication if required. Even when an improved PRS was introduced, it only increased the detection rate at 5% false positive rate to 14%, which is insufficient for clinical utility. In general, in order to obtain a detection rate of 80% at 5% false positive rate, an odds ratio of at least 12, and possibly much higher, would be required.

He explained that PRS risk assessment has been suggested for the stratification of risk for public health measures, such as when to initiate mammographic screening for breast cancer in women. It has been suggested that those at the upper level of risk, say the top 5%, could be offered screening ten years younger than it is in the general population. However, calculations show that this would be of minimal benefit over just screening women over a certain age, taking into account other clinical and genetic variables, and adding PRS would require offering genotyping to thousands of women.

In general, the change in risk derived using such tests is not great, and the risk alterations as reported are often presented as “high risk” or “normal risk” which is hard to explain to the person taking the test. In conclusion, Professor Hingorani said that the performance of PRS in altering risk prediction is too weak by several orders of magnitude to justify their use for screening, risk stratification or individual risk assessment. They were also open to misrepresentation and misunderstanding.

Next, **Dr Philip Ball (Science Writer)** discussed **"Challenges of Communicating the Complexities of Genomic Data"**. Dr Ball began by arguing that the 'instruction book' concept of genes is wrong and that the complexity of genomes is fundamental. The simple stories are misleading and we need to re-think the old ideas. Watson and Crick's original message that the genes just have to be 'read' is now completely outdated but the general population doesn't appreciate this.

Many people imagine that one's future is fixed by your genes which make you what you are. This is genetic determinism and is becoming an increasingly acceptable view driven by the media, education and even the scientific establishment. Behavioural traits, however, seem to be regarded differently in that one's up-bringing is more important.

However, Dr Ball has found that, among the geneticists, even Crick's Central Dogma is being challenged. For example, many genes yield proteins which perform different roles in different tissues and epigenetics has offered liberation from the disturbing view of determinism. The 'one gene – one trait' view of Mendelism is now regarded as the exception, as so many genes now appear to be pleiotropic, whereas in the past this was regarded as a rarity. Also, most traits are in fact polygenic so it becomes impossible to say one variant is good while another is bad as it will depend on the influence of other genes. Many deleterious mutations now appear to be not in the coding region of genes, but in regulatory sections. All of this tells us that genes and genomes do not function in the simplistic way it was once thought and yet we're still teaching the same story in schools, so it's inevitable that people go through life believing this.

He then moved on to consider this alongside today's theme — genetic screening. He argues that this understanding would wo-

rk for monogenic conditions e.g. when screening IVF embryos for some well-established traits. But how would we screen for complex polygenic traits whose effects are summative? What about screening for genes which give a higher risk of cancer in later life? Decades of work on the genetic origins of tumour formation have been disappointing so that most cancer screening is anatomical, biochemical or physiological.


Dr Philip Ball

He closed by suggesting that there is no need to over-simplify genetics in schools but rather start from the perspective that living systems are complex and therefore so are the genetic systems that control them. Why not compare genomics with Generative AI? Thus, the genome is a source of molecular resources that allows cells and organisms to grow and function.

Following afternoon tea, the Vice-President, **Professor Dian Donnai** chaired the final talk, the 4th Adelphi Lecture (107th Galton Lecture), given by **Dr Margaret McCartney (University of St Andrews)** on **"Challenges of Population Screening"**. The first challenge raised was ***Evidence***. Dr McCartney quoted the work of Dr James Lind, the ship surgeon from Edinburgh who is credited with the first Random Clinical Trial proving that citrus fruits could prevent scurvy. He wrote that "before the subject could be set in a clear and proper light, it was necessary to remove a great deal of rubbish". She also mentioned the work of Dr Benjamin Spock who, without evidence, recommended that infants be put to sleep on their front, which remained accepted

dogma for half a century, until data from 1970 suggested that this was likely to be harmful.

The second challenge was ***Humans***. Clinicians overestimate the benefits and underestimate the harms of commonly used medical interventions – what she called optimism bias. The third challenge was ***Definitions*** where she proposed people were confused by terms such as screening, symptomatic diagnosis, early diagnosis and what was actually needed was helpful or optimal diagnosis. She also made the point that one hears about the benefits of early diagnosis but not often about the harmful or negative side effects.

Science was the fourth challenge. There needs to be a clear rationale for why a test is being carried out. ***Statistics*** was the fifth challenge. Here one of the main issues discussed is lead time bias which is a form of systematic error in diagnostic and screening studies that creates an artificial appearance of increased survival time among individuals whose disease is detected early, even if their actual life span is not prolonged. The sixth challenge was ***Fear and Persuasion***. Using examples from bowel, prostate and breast cancer, she demonstrated that screening is not always beneficial. For example, 5 women out of every 1000 die from breast cancer without screening compared to 4 women with screening. By screening, out of every 1000 women, 100 women were exposed to false alarms and received additional treatments or had biopsies and 5 women without non-progressive cancer had unnecessary partial or complete breast removal. The seventh challenge was ***Money***. She suggested that there are potential conflicts of interest where companies are offering massive investments for interventions for which outcome measures might not have patient benefits written into them. There is also evidence of financial conflicts of interest.

More is not necessarily better was the eighth challenge. She reviewed the NHS plans to DNA test all babies in the UK to assess disease risk and questioned whether this was beneficial and useful to prevent illness. The ninth challenge was **The real world**. The NHS has limited resources which are not equitably distributed. The most vulnerable miss out more and deprived areas are exposed to more health harming products. Industry's approach to health care prevails – for example the food industry promotes obesity while the weight loss drugs industry promotes thinness. The final challenge was **What really matters**. She suggested that continuity of care matters and strong GP-patient relationships results in fewer emergency admissions, GPs are more satisfied with their work, patients feel safer and fewer tests are carried out. She concluded by inviting the audience to participate at the Centre for Evidence and Values in Healthcare - helping people to make better decisions in healthcare - at the University of St Andrews.

At the conclusion, the Vice-President presented Dr McCartney with the new Adelphi Vase

My Life in Genetics An Interview with Dr Sarah Wynn, Trustee of the Adelphi Genetics Forum

Tell us about growing up and what first drew you into studying genetics.

All through my early teenage years I was obsessed with science and its potential to unravel the answers to absolutely everything! I had a chemistry set, a microscope and read lots of science books as well as devouring science stories in newspapers. As I got older this general interest became more specifically targeted at biology, genetics and the future of medicine. I knew I wanted nothing other than to do research to understand how humans formed, grew, developed, functioned and, with the naïve optimism of youth, how we might be able to put that knowledge to work in curing disease.

What was the topic of your PhD and what did it involve?

While an undergraduate I spent a summer working on SOX genes in the laboratory of Robin Lovell-Badge at the National Institute for Medical Research (NIMR, now relocated to become part of The Francis Crick Institute). I absolutely loved the lab work and so after my first degree in Bristol I moved to Imperial College to undertake a PhD. My project involved using a mouse model to understand more about how the individual genes on human chromosome 21 (mouse chromosome 16!) contribute to the features

of Down's syndrome. Advances in science mean that it is now possible to sequence a person's whole genome (around 20,000 genes) in a matter of hours, but back in 1995 when I started my PhD, Next Generation Sequencing was yet to be invented. We were excited to be able to do semi-automated Sanger sequencing in a newly formed sequencing centre! I spent 3 years doing a great deal of sequencing - of just two genes! One had not yet been sequenced and it was such a thrill to be the first person to deposit the mouse sequence of the gene DONSON in GenBank (the international genetic database). The sequencing of these genes was the precursor to making mouse knockout models to try to understand the function of these genes and their possible role in Down's syndrome. After my PhD, I continued working at Imperial as a postdoctoral researcher until an opportunity came to go to and live and work in Hong Kong. There followed a wonderful experience of living in a new country and working in the lab of Kathy Cheah at the University of Hong Kong, working once again on SOX genes. After 3 and half years we returned to London and I took up a new postdoc back in Robin's lab at the NIMR.

Tell us about your involvement with Unique and its role.

While in Hong Kong and trying to start a family, I had multiple miscarriages and we subsequently discovered my husband has a balanced translocation involving chromosomes 5 and 7. This information was given to me over the phone while at work in the lab and is etched in my memory as a moment when my personal life and work life collided. The obstetrician who gave me the results knew little about genetics and had no idea what a balanced translocation was! I felt a sense of relief that I did know and understood what it meant for us, but I couldn't help but wonder how this news would have been even more difficult to take in if the person receiving it did not know what it was and how it might impact their life. So, in what is now a daily part of my role working at a patient organisation, I learned how to explain geneti-

cs and genetic conditions in a clear and understandable way.

A common feature among scientists is a desire for data and information, so once we had the lab report documenting the details of the translocation, I went on a deep dive into the scientific and medical literature looking for reports of anyone who had the same translocation. My search led me to Unique, who held (and still hold) a large database of people around the world with chromosome disorders, including balanced translocations. While the Unique database did not hold a match, I was incredibly impressed by the response I received from the then CEO, Beverly Searle. She was kind and empathetic and sent enormously detailed and helpful information. It turned out that she too has a PhD in genetics and had become involved with Unique after the birth of her daughter Jenny, who had a chromosome 18p deletion. I offered to volunteer for Unique while continuing to postdoc and starting a family. While on maternity leave with my second daughter, Unique advertised for someone to join their small team and I leapt at the opportunity to put my background and personal experience to a new purpose. I worked first as an information officer and then became the CEO in 2021.

Unique is a charity that provides accurate and accessible information. As I mentioned earlier, we help make important, and often complicated, medical information easier to understand. Through sharing knowledge and lived experience, Unique helps families and professionals navigate the world of chromosome and gene disorders. We work with anyone that has been affected by, or wants to know more about, rare chromosome or gene disorders - whether that's an individual, a family, a parent or carer, a doctor or a scientist. We act as a facilitator, helping people connect with each other to share their experiences. Unique now has over 30,000 members (individuals, families and professionals) globally and are growing every day.

Working with such families must be difficult but rewarding.
Some of the children in the families we support don't survive infancy or childhood and the loss for these families is immense, often overwhelming. Other families face enormous struggles getting a diagnosis for their child or the right support and care after diagnosis. We see how parents become experts in their child's rare condition - with no scientific or medical training – and advocate on behalf of them daily. It is humbling and inspiring. The overriding feeling that I, and I think my colleagues at Unique, have is how incredible people are at dealing with unexpected events and adversity, finding love and resources to do their very best for their child. That is not to say that it is easy – it often isn't. It can be frustrating, time consuming and frankly hard work to care for a child with a rare condition but the sense of love and hope together with sharing experiences and knowledge can be very powerful. It's a privilege to have our wonderful Unique families share their stories with us.

What roles do you think the AGF should play?
One of the biggest challenges that exists when a person or family receive a result from genetic testing is that the information is complex and not always easy to understand. With rare conditions this is exacerbated. Public understanding of genetics can be low with the perception that genetic results are more deterministic and binary than they often are in practice. Organisations like the Adelphi Genetics Forum have a vital role in education and awareness raising. Advances in genomics (for screening, diagnosis, monitoring and treatments) are hugely exciting but there are also limitations, uncertainty and many ethical concerns. The NHS 10-year plan published a few months ago predicts that 50% of healthcare interactions will have a genomics/genetics element. This means it is even more vital that public engagement and understanding of genetics grows and there are plenty of opportunities for thoughtful and informed discussions. The AGF is well placed to help with this.

Tell us something about yourself that isn't widely known.
I gave Derren Brown an early career break! I was the entertainments rep for my hall of residence at the University of Bristol back in 1992. One of the events I organised was a hypnotist stage show for the students. We paid him just £50! However, it was a bit more exciting than we anticipated when one of the students was hypnotised so thoroughly that he could not be roused. Eventually he did wake up but not before we had called an ambulance! After that stressful evening, events organising was not on my career wish list!

Previous contributors to the *My Life in Genetics* series:

Published in the ***Adelphi Review***

Professor Gregory Radick	Issue 8
Professor Shirley Hodgson	Issue 6
Dr George Burghel	Issue 5
Dr Helen Middleton-Price	Issue 4
Professor Nick Mascie-Taylor	Issue 3
Mr Robert Johnston	Issue 2
Dr Jess Buxton	Issue 1

Published in the ***Galton Review***:

Professor Nicholas Wood	Issue 15
Professor Dallas Swallow	Issue 14
Professor David Galton	Issue 13
Professor Andrew Read	Issue 12
Professor Veronica van Heyningen	Issue 11
Professor Dian Donnai	Issue 10

BOOK REVIEW

How Life Works – A User's Guide to the New Biology - Philip Ball, Picador 2023.

This must be science writer Philip Ball's most ambitious book yet. Drawing widely on 21st century developments in molecular genetics and cell biology, he aims to disabuse us of the idea that DNA is any sort of a blueprint. Genomes are certainly interesting and

important, but they don't explain very much about how life works. Since the blueprint was a key concept in 20th century biology, he has set himself a very substantial challenge. So, what has changed so much?

In many ways the rot started with the Human Genome Project. It did indeed deliver on its promise to produce massive amounts of data. But there was a more subversive second effect. For decades geneticists had speculated about the total number of genes in the human genome. It became a topic for bar-room sweepstakes at genetics conferences. Most guesses hovered around 50,000 – 100,000 genes. The thinking was that we knew the prokaryotic *E. coli* bacterium had around 4,000 genes, while the eukaryotic single-cell yeast had around 6,000. The more complex an organism was, the more genes it needed. We are so much more complex, so we must have correspondingly more genes. Therefore, it was a major surprise when the actual number turned out to be scarcely over 20,000 – no more than the 1mm long nematode worm *Caenorhabditis elegans*, widely studied as one of the very simplest multicellular organisms.

This surprising result triggered a rethink. Crudely put, the default view pre-2000 could be summed up by three propositions:

(Protein-coding) genes are the major functional component of the human genome.

There are lots of genes in our genome: lots more than flies (13,000) or worms (20,000) because we are much more complex.

Genes are thinly scattered among long stretches of 'junk DNA'.

None of these ideas survived. If complexity was not to be explained by the number of genes, instead it must depend on increasingly complex regulation of a fairly modest set of genes. Ball sets out the progress made in understanding all this – but he goes much further, arguing that there must be a clear break from the determin-

istic past. “You can’t compute from the genome how an organism will turn out, not even in principle.... from a single protein-coding gene, you can’t even tell what the product of its expression will be, let alone what function that product will serve in the cell” (p.94). He takes aim at the idea of ‘molecular machines’ – multiprotein complexes with defined functions: “In reality a well-defined entity like this has a vanishing probability of forming and remaining stable in a real cell” (p.189). Outcomes are context dependent, which “is hard to reconcile with the idea that molecular communication depends on highly selective recognition and binding processes – in which case either you have the right match or you don’t” (p.209). The principles and processes of self-organisation also make higher-level phenomena less determined by lower-level details such as genomic sequences.

So, what does the new cell biology look like? The old metaphors of cells as machines or computers must be abandoned. For the most part, changes in cell behaviour are not the result of a single, decisive, switch-like signal. Rather, they *emerge* as the combinatorial effect of multiple relatively weak and somewhat non-specific interactions. Ball’s preferred metaphor is a committee. The committee weighs up evidence and viewpoints to reach a final decision that is not closely determined (‘caused’) by any individual lower-level detail. A key concept is *causal emergence*. In complex multi-layered systems like living organisms, truly causal factors must be sought at higher levels of organisation; they do not depend in any simple way on details at the lower levels. Indeed, behaviours at the higher level are largely insulated from variations in the lower levels.

After several chapters setting out these iconoclastic ideas about cells, there follow fairly orthodox explanations of how cells collaborate to form tissues, organs and organisms. Then a long philosophical chapter addresses the ‘What is Life?’ question. He

quotes approvingly Schrödinger's idea that living organisms feed off negative entropy from their surroundings. For me, this exemplifies the way physicists think differently from us ordinary mortals. I always had real problems with that idea. Doesn't your domestic fridge provide a far more comprehensible analogy? (OK, back in 1944 Schrödinger probably didn't have a fridge, but that's no excuse now). Given a working compressor and a power source, your fridge happily pumps heat up the thermal gradient, from its cold interior to the warm kitchen. Which is surely exactly how life works: it just needs an appropriate mechanism and an energy source. But then comes the Big Idea. What really distinguishes living organisms from non-living things, argues Ball, is that they show *agency*: that is, they act in purposeful ways to achieve goals. This, he says, is the real criterion for deciding if a system is living. Controversially, he argues that even bacteria show a basic form of agency, albeit without conscious purpose, when they migrate up a concentration gradient of nutrients.

This all makes quite challenging reading. The old mechanistic ideas were much easier to get one's head fully around than these more fuzzy and abstract concepts, especially for people like me who tend to think in highly analytic ways. I did just wonder how much more of the immense complexity might some future super-powerful AI be able to explain at the level of gene interactions? Interestingly, Eric Topol raised exactly this question in an article about AI in cell biology (*Science* 30th January 2025), mentioning this book specifically. Well, we must wait to see, but I can't see AI ever replacing the new vision of cells that Ball sets out. His criticism of the idea of cells as machines or computers programmed by DNA is very cogent. It always was just too simple to be the whole truth. As for bacteria having agency – well, you must read the book and make up your own mind, you will meet very many interesting facts and ideas on the way.

Andrew P Read

Betty Nixon

To many of us the existence of the Adelphi Genetics Forum (AGF) without the calm and effective guidance of our General Secretary, Betty Nixon, is unimaginable. Betty admits to around 30 years of administering the organisation. She steered it unobtrusively but brilliantly throughout this time. Over the years she worked with a wide range of officers and council members: most of them assiduous, but some difficult! Her knowledge and insight into the history and evolution of AGF from its complex antecedents is, I believe, unmatched. I have only known Betty since 2014 when, as a very untutored and ignorant newcomer, I took on the role of President of the Galton Institute, the previous incarnation of AGF. From the outset Betty's professionalism and quietly knowledgeable approach was clear. When I was just starting, she provided a brilliant brief tutorial of the organisation's history, supported with

the necessary documentation and highlighting key details. Betty's organisational abilities were obvious. All the administration was flawless, minutes of meetings were meticulous and timely. She dealt single-handedly with all the organisational complexities of the annual conference.

Throughout my six years as President, we were embroiled in the many debates, particularly at Galton's academic home, UCL, about the history of eugenics. Betty's insight into the issues was obvious, and her gentle guidance to Council on how we might resolve them was impressive and reassuring. What stood out was her emotional intelligence, her deep instinctive understanding of how to interact effectively with different people. Her discretion was also legendary. And now Betty has told us that the time has come for her to retire. Typically she has prolonged the stepping down time to help with the change-over. We have managed to appoint someone we expect to be an excellent successor, but we shall miss Betty. Her indelible contributions will be embedded in the annals of the organisation.

On behalf of the Adelphi Genetics Forum, its succession of council members and all its fellows and members: Thank you, Betty! We hope you will adapt to retirement smoothly and life will flow enjoyably, in the company of family and friends.

Veronica van Heyningen

European Human Behaviour and Evolution Association Conference April 14-17 2025 at Newcastle upon Tyne

EHBEA 2025 brought together over 180 delegates from over 16 countries across Europe and beyond for four days of scientific exchange. The programme featured plenary lectures, themed talk sessions, panels, poster presentations, and social events, offering numerous opportunities for collaboration, discussion, and networking across career stages and disciplines. Post-conference evaluations showed that 90% of respondents were satisfied with the overall conference experience.

A core aim of EHBEA 2025 was to promote equity, diversity, and inclusion in science. The grant from the Adelphi Genetics Forum helped us offset costs and maintain affordable registration fees, particularly for students and early-career researchers. Travel Grants were also provided by EHBEA to several students. We implemented a double-blind abstract review process to ensure fairness in presentation selection, and a buddy system to support first-time attendees and early-career researchers. These initiatives helped create a supportive atmosphere that was highlighted in participant feedback. Finally, the conference included a “Stand up for science panel” session to discuss practical ways in which we can stand up for science by resisting the misuse, and repression of, research.

The conference covered a wide array of themes, including co-operation, cognition, animal behaviour, evolutionary health, cultural and behavioural ecology. This interdisciplinarity promoted valuable cross-field discussions that we hope will continue well beyond the meeting.

We thank you once again for your support and look forward to future collaborations.

ADELPHI GENETICS FORUM

Conference 2026

Thursday 22 October 2026 at
The Royal Society
6-9 Carlton House Terrace
London SW1Y 5AG

Complexity of Neural Function – the Brain in Charge

Studying how the human brain works and malfunctions has revealed rich detail about the development, organisation and function of the brain. In the 2026 annual conference of the Adelphi Genetics Forum we aim to explore how our understanding of brain function, and more generally biological mechanisms, has evolved through the study of neural diseases. Neural functionality is dependent on the action of genes and their interaction with environment and even requires some stochastic activity.

The complexity of neural function, and the myriad genes implicated in the smooth working of the systems, means that things can go wrong in many different ways. Study of neurodevelopmental disorders has uncovered many genes and different mechanisms of disruption. Dissecting the function of these genes helps us build a picture of the complex pathways and regulatory networks involved. Epilepsy has been recognised since

biblical times. We now know that many forms are associated with mutations in ion channels and ways to treat this group of distressing and often progressive diseases have been developed. Novel therapeutic approaches are emerging with increasing understanding of molecular mechanisms.

Understanding pain and managing different aspects has a long history too. With increasing molecular insight into the genesis of pain, new drugs are now being developed.

With increasing brain complexity novel mechanisms of communication evolved and speech and language development is a key human attribute, although, increasingly, related animal communication systems are now recognised.

Movement disorders are distressing conditions often caused by anomalous neural control; some are congenital while other forms develop in later life. Identifying disease associated genes can provide insight into mechanisms and permit the development of therapeutic approaches. This is of course of huge interest to those affected by conditions such as Parkinson's disease. We look forward to hearing a discussion between a clinician scientist working to understand and ameliorate this disease and a high profile, knowledgeable, affected individual.

Many complex behaviours are increasingly understood at the neuro-molecular level. Our final focus will be on the fascinating topic of the neural control of appetite.

Veronica van Heyningen

ADELPHI
GENETICS FORUM

Sixth Teachers' Conference

Further Advances in Genetics

Free conference for A-level science teachers at
The Nowgen Centre, Grafton Street, Manchester
26 June, 2026

Topics included in the programme:

Professor Andrew Read (University of Manchester):
The Human Genome Project – 20 years on

Dr Sarah Wynn (CEO at Unique): **The Promises and Challenges of Genomics for Patients and Families Affected by Rare Conditions**

Professor Siddharth Banka (Manchester Centre for Genomic Medicine)**: *Epigenetics and Genome Imprinting***

Dr David Craufurd** (Manchester)**: Huntington's Disease and Recent Progress

Dr Coreen McGuire** (Durham)**: History of Eugenics

Professor Sue Kimber** (Manchester): **Using Human Pluripotent Stem Cells to Discover New Therapies

Admission is **FREE**, but strictly by ticket, available from:

The Executive Secretary, Adelphi Genetics Forum

executiveoffice@adelphigenetics.org
www.adelphigenetics.org