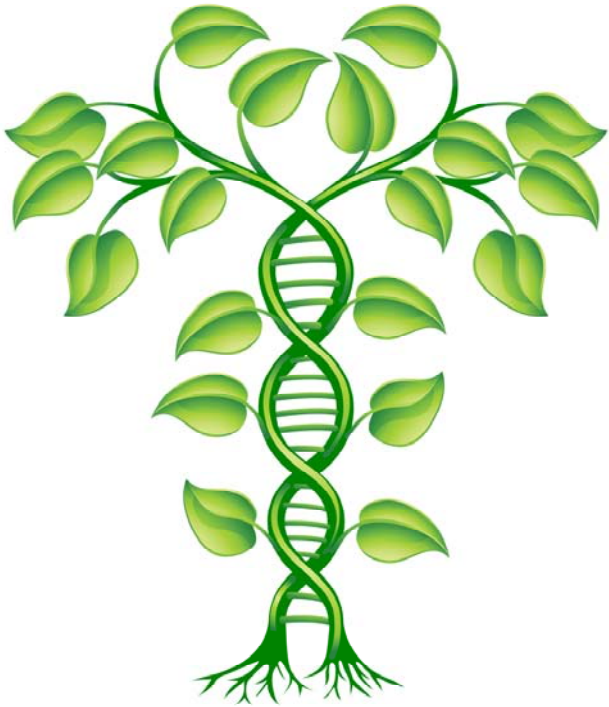
ISSN 2397-9917

Issue 13
Summer 2020

Galton Institute

Exploring Human Heredity

The Galton Review



www.galtoninstitute.org.uk

CONTENTS

Front Cover Image: Depositphotos.com

Published by:

The Galton Institute, 19 Northfields Prospect, London, SW18 1PE

Tel: 020 8874 7257 www.galtoninstitute.org.uk

General Secretary: Mrs Betty Nixon

executiveoffice@galtoninstitute.org.uk

Review Editor: Mr Robert Johnston

EDITORIAL

On page four you'll find a short introduction to our new President, **Professor Turi King,** who took over from **Professor Veronica van Heyningen** in June. Some of you will no doubt remember her from our 2019 Annual Conference and we were delighted when she agreed to take on this role during these challenging times. She has already proposed some innovative changes and we look forward to hearing much more from her in the coming years.

On page six we have the latest in our 'My Life in Genetics' series and this time it's the turn of our Librarian, **Professor David Galton**. In this, he freely admits to being something of a rebel in his younger years but his career story would be an inspiration to any young geneticist.

This issue's Book Review concerns Adam Rutherford's *How to argue with a racist: history, science, race and reality.* I'm sure many of you will have read this and I'd be interested to know if you agree with the opinion of our reviewer, **Professor Dallas Swallow**.

Hopefully I'll see many of you at next year's Annual Conference when, with any luck, some degree of normality will have returned.

Robert Johnston

President of the Galton Institute

We are delighted to announce that **Professor Turi King** became the Galton Institute's new President in June 2020. Turi is Professor of Public Engagement and Reader in Genetics and Archaeology at the University of Leicester. Those who attended our annual conference last October, 'New Light on Old Britons', will remember Turi's insightful talk on how DNA can be used as a 'window on the past'. This included a fascinating account of her leading role in the identification of King Richard III's bones, found buried under a car park in Leicester in 2012. (Podcasts featuring interviews with Turi and other speakers at this event are available on our website at **http://www.galtoninstitute.org.uk/podcasts/**).

Turi is a Canadian who started her career in Archaeology and Anthropology at the University of Cambridge. She then joined the University of Leicester to study for an MSc in molecular genetics to complement this background, with the aim of applying interdisciplinary approaches to human evolutionary genetics and to answer questions in history and archaeology. For her PhD, she discovered that British men who share a surname are more likely to share sections of Y-chromosome DNA, a novel finding that sparked a huge amount of public and media interest.

Turi's research has since centred around combining genetics with forensics, history and archaeology. Throughout her career, Turi has continued to carry out outreach work with schools, societies, museums and the media. For the King Richard III project, Turi was well placed to both lead the crucial genetic analysis of the remains, and also to communicate the results to relatives and the public. She has received several accolades and widespread recognition for both her research and her public engagement work. We look forward to working with Turi to continue communicating scientific advances in human heredity to a wide range of audiences.

Galton Institute Annual Conference

Due to the current Covid-19 pandemic we have rescheduled our 2020 annual conference and plan to present this year's programme in the autumn of 2021.

The conference title will be:

Genetic studies of populations:
Insights into health and social outcomes

My Life in Genetics

An Interview with Professor David J Galton
Librarian of the Galton Institute

Who first inspired you to study Genetics?

J B S Haldane (1892-1964) was professor of Genetics and Biometry at University College London where I was studying medicine (1955-1964). He gave some of the worst lectures on genetics (or any other subject for that matter) that I ever heard. He stood up, face to the blackboard, completely ignored his undergraduate audience and started to do quite complex mathematics on what I assumed were permutations and combinations with a stick of chalk on the board. It was all about bean-bag genetics, a conceptual model of genetics which was

used by him and Ronald A Fisher to keep coloured beans in bags as a way of tracking Mendelian ratios. A beanbag full of coloured beads would be considered the gene pool for the whole population. I found it quite boring. Professor Haldane appealed to me in other ways. He was an ardent Marxist writing enthusiastically that 'Marxism is true' (whilst I was an ardent junior Trotskyite at the time) and he had been on the Editorial Board of the *Daily Worker*, quite unusual for an ex-Etonian. He also published a wide range of very stimulating essays on scientific issues such as biochemistry, genetics, evolution and the origin of life. One relevant to the Galton Institute's work was his essay on 'Eugenics and Social Reform'. In it he concluded 'teach voluntary eugenics by all means; but if you desire to check the increase of any population or section of it, either massacre it, or force upon it the greatest practicable amount of liberty, education and wealth' when they will destroy themselves by excess of luxury and lechery, he seemed to imply. Quite different from the dictatorial politicians who enforced eugenics by sterilizing everyone with traits they did not approve or forbidding them to reproduce e.g. China's one-child policy starting in 1979.

.

Another inspiration for me was Professor A E Garrod (1857-1936). I was appointed as Consultant Physician to St. Bartholomew's Hospital and Senior Lecturer to the Medical School where Garrod did his ground breaking work. It was inspiring stuff and he gave me some ideas on which I could spend the rest of my scientific career. He was especially brilliant by showing that Mendelian rules apply not only to garden peas but to humans as well. He demonstrated that the human disease alkaptonuria was inherited along the lines proposed by Mendel using dominant and recessive inheritance and yielded about a 1:3 ratio of affected individuals versus those unaffected in first cousin marriages in families where the disease is segregating. He also showed that if he fed about 1 gram of the metabolite homo-

gentisic acid to his patients with the disease he could recover almost the same amount excreted in the urine; whereas in controls he recovered none. Homogentisic acid or 2,5dihydroxy phenylacetic acid was made for him by Professor Gowland Hopkins. Garrod wrote that there may be a faulty enzyme at the step catalysed by the enzyme homogentisic acid oxidase to block further metabolism which accounted for the disease. He called it in 1908 ‘an inborn error of metabolism’ and included three other diseases albinism, pentosuria and cystinuria in the group.

He also wrote in 1908: ‘the liability to develop diabetes or gout is often inherited but the diseases themselves are not inherited...’. This for me was a career defining sentence. Where are the inherited liability factor(s) that predispose to disease and how do they work?

Who has been the greatest influence in your work?

I won a prize essay competition from the Mental Health Research Fund that awarded me a Travelling Fellowship to go to any Academic Department in the world for a year. The conventional place for me to go was Professor George Cahill at the Joslin Diabetic Clinic at Harvard USA. But his Laboratory was full for at least another 3 years with visiting Fellows. I had to choose somewhere else. The work of Martin Rodbell at the National Institutes of Health USA appealed to me because he had just found a way of isolating the rat adipose cell from the epididymal fat pad and was writing a series of papers in the *Journal of Biochemistry* on its properties (sensitivity to insulin and other hormones etc.) and he was now up to writing Paper III. This was well before he won the Nobel Prize in 1994 for elucidating the membrane bound G-proteins of the rat adipose cell. His Laboratory had no visiting overseas Fellows when I applied so I was spoilt for expert company.

His Laboratory was a revelation to me. Coming from London Departments which I found stuffy, rather sanctimonious, and really mean spirited regarding colleagues, Martin Rodbell's Lab was like stepping into a sunlit world of fresh air. It all seemed so free and easy, everyone was relaxed, Marty (familiarity terms from the start) would be drinking from a can of Coke whilst giving us a seminar, he freely communicated his work and could not keep any data under wraps at the large national Science Meetings at Atlantic City where piracy was rife. He was friendly from the start and intellectually alive (and his shoes were almost always dirty).

My plan was to learn all the adipose cell techniques and then do the same for the human adipose cell. The adipose cell is a pivotal centre for glucose, triglyceride and free fatty acid metabolism; and this would naturally lead in humans to studying diabetes m. (ketoacidosis of Type 1; obesity and hypertriglyceridemia of Type 2).

However the Vietnam War was at its height and since I was on an immigrant visa I was inducted into the Maryland light Infantry. I did not burn my call-up papers but refused to attend my health checks. My wife and I agreed although England had much less opportunities than the States, it was a nicer and quieter place to live with no wars going on at the time (Falkland's and Iraq were still to come). So we sailed back to England on the Queen Elizabeth.

Did your work achieve anything?

That is an interesting question that I have often asked myself. Good scientists are meant to make important discoveries or new developments to the field they choose. I will just submit one item from our work and let you, the reader, decide if it was either good or important. In 1983 we were one of the first (not

boasting, but if untrue please contact me) to publish the use of a common single nucleotide polymorphisms (SNP for short) to identify susceptibility genes for a common disease, hypertriglyceridemia. This followed from theoretical considerations by David Botstein and Walter Bodmer on the use of polymorphic DNA markers to construct a genetic linkage map for human DNA. We found a C3175>G transversion in the 3'UTR of the apoC3 gene at nucleotide 3175, where the rare S2 allele was associated with plasma levels of apolipoprotein C3, plasma levels of triglycerides and the occurrence of coronary atherosclerosis with the G allele. Nobody really believed us at the time: the numbers (<80) in the groups and controls were small, not everyone could confirm our results, our methods were not sensitive enough etc. We just kept on doing more experiments on the ApC3 system (>14 published papers up to 1990 that all seemed to corroborate). Then a metanalysis by Ordovas et.al. published in 1990 showed that comparing the frequency of the above mutation in 2,223 Caucasian controls to 1,170 Caucasians with either hypertriglyceridemia or coronary heart disease gave values of 0.072± 0.04 and 0.14±.10(SD) respectively with a p-value for difference of <0.001. So we felt somewhat vindicated and even more so when our results relating to hypertriglyceridemia and coronary artery disease were confirmed by Genome Wide Association Studies (GWAS for short) in 2009 for ours and many other SNPs in the gene region. A final verification of our work came from the Drug Industry that developed an antisense oligonucleotide (volanesorsen) knocking down apoC3 messenger RNA which has now regulatory approval in the USA (early access programme), Canada, the European Union and the UK (by NICE) for treatment of severe hypertriglyceridemia.

So it amounts to just another disease with just another new therapy; but a reader might not realize the amount of hard work that goes into such a project!

I like to think that our initial approach of studying SNP-trait associations helped to lead to the development of Genome Wide Association Studies (GWAS) that in 2009 confirmed our initial observations and identifying a further > 57,000 such SNP -trait associations for many different diseases; but happy to accept that the HLA-protein association studies for autoimmune disease was the real fore-runner. What I had not appreciated is that it takes so long for an observation made in 1983 being put to practical use in 2019 for therapy.

The Role of the Galton Institute

I have always wondered whether Francis Galton really deserves an Institute for himself. Charles Darwin has a Research Station on Galapagos. The Mendel Institute was founded in 2000 in Vienna and Galton was an exact contemporary of Gregor Mendel, both born in 1822. Both set out on the same scientific quest to clarify the nature of inheritance.

Mendel laid an excellent foundation by discovering the 'gene' leading to such things as DNA structure, sequence and function by using such tools as PCR and CRISPR cas9. Galton did some interesting statistics which have been developed but nothing as brilliant as Mendel's basic work. Galton also had some crack-pot ideas like inventing composite photography of criminal faces to determine what the average criminal face should look like! I have remained a Trustee of the Galton Institute for the last ten years mainly for Galton's founding ideas on Eugenics. Eugenics raises the tricky issues of integrating the new knowledge of genetics into society and a liberal democracy. We all know what dictators can do with eugenics. Like J B S Haldane, my mentor, I think this is a very important topic and should be the major focus of the Galton Institute, leaving basic research projects to the large Research Foundations. I have written two books on the subject of eugenics. One

entitled ‘Eugenics: The future of human life in the 21st. C publ. 2001, Abacus Press’ which to my surprise was well received. I was expecting internet trolls to accuse me of Nazism, and Swastikas to be painted on my front door. But no: ‘A clearly written book that gives a guarded welcome to the *New Eugenics’* was the Daily Telegraph’s comment.

I think that this is going to be a major battle-field for the future with all the new ‘eugenic’ (eu - good; genesis - birth) techniques coming along using DNA biochemistry.

Tell us something about yourself not generally known

I failed my ABRSM exam grade 3 for piano at 8 years. You may think so what, why is that worth recording? Well music has remained a passion throughout my life and I play the piano every day, however badly (much to my wife’s annoyance!). Some things are a joy to do for their own sake and not just for the rewards and artificial diplomas that may come from them.

Creating patient friendly information resources for the most common cause of intellectual disability (22q11 deletion syndrome)

Report for Artemis Trust Grant 2018-2019

We interviewed 15 adults with 22q11 deletion syndrome using an inductive, semi-structured technique. Interviews were audio recorded (with consent) and transcribed. Thematic analysis was performed using Nvivo 12. Three overarching themes emerged: (1) Impact of 22q11 deletion on family life, (2) Views on reproductive medicine options and (3) Lack of accessible information resources on reproductive medicine options. The

interview findings helped to define the content of the information leaflet we produced.

To ascertain clinicians' views on the type of reproductive medicine information which should be discussed with people with 22q11 deletion syndrome and how it should be delivered, a Delphi method study was undertaken. Two Consultant Clinical Geneticists, two Genetic counsellors, a General Practitioner with a special interest in sexual health and a sonographer (fetal medicine ultrasound) took part. Participants were asked to rank options for the content of the information leaflet and the means of delivering the information, in order of importance.

The interview study identified the content for the information leaflet. Participants expressed a desire to be informed of all the available reproductive medicine options. Participants also made negative comments about the currently available information resources: that the language used was too technical, that they were not specifically designed for 22q11 deletion syndrome and that they were too long. This helped us to design a leaflet which would be useful for adults with 22q11 deletion syndrome. The results of the Delphi process indicated that an easy read information leaflet was felt to be the best option by clinicians, but that it should be used in conjunction with a face-face consultation. The clinicians felt it was important to include information on a range of reproductive topics such as adverse health effects of pregnancy in a woman with 22q11 deletion as well as reproductive medicine options (such as amniocentesis and preimplantation genetic diagnosis).

The first draft of the information leaflet was produced by **Alisdair McNeill**. The text was then edited according to "easy read" principles by **Mr Ian Christie** ("easy read" consultant). Alisdair McNeill and Ian Christie then iteratively selected appropriate Photosymbols to place in the leaflet (these provide a vis-

ual illustration of the subject matter to aid understanding). A focus group of adults with intellectual disability was then held by Mr Ian Christie. The feedback was incorporated into a final version of the information leaflet. The role of **the Artemis Trust** in funding production of this leaflet is acknowledged on the leaflet.

The charity 'Unique' produces and disseminates information resources on chromosome disorders and genetic conditions. The leaflets are freely distributed via a website www.rarechromo.org. The information leaflet on reproductive medicine options for adults with 22q11 deletion syndrome will be disseminated via this website.

Outputs 1. A research paper in the American Journal of Medical Genetics Part A describing the findings of our qualitative interview study (enclosed). 2. A patient friendly information leaflet to guide adults with 22q11 deletion syndrome on reproductive medicine options (enclosed). This will be made available free of charge through the Unique charity website (www.rarechromo.org). 3. The work will be presented at the Sheffield Rare Disease Study Day 2020. 4. We will submit the work for presentation at the British Society of Genomic Medicine meeting in October 2020.

Future work We are developing a grant proposal to fund production of an online decision support aid for people with intellectual disability regarding reproductive medicine decisions.

Dr Alisdair McNeill
Senior Clinical Lecturer in Clinical Genetics,
The University of Sheffield

Evolution Evolving. Process, Mechanism and Theory
Conference 2019, Churchill College, Cambridge

The conference was organized by **Paul Brakefield FRS, PLS** (Zoology, Cambridge University), **Kevin Laland** (Biology, University of St Andrews), **Tobias Uller** (Biology, Lund University), **Katrina Falkenberg** (Biology, University of St Andrews) and **Andrew Buskell** (History and Philosophy of Science, Cambridge University). Approximately 200 delegates attended the meeting with 80 from the UK and 120 from other countries, and there were 67 talks and 51 poster presentations. Representatives of the media (Nature Ecology and Evolution, New Scientist) also attended.

The title of the meeting – *Evolution Evolving* – was designed to highlight both that the evolutionary process itself evolves over time (an idea encapsulated in the concept of 'evolvability', which was one focus of the meeting) and that evolutionary biology is itself a vibrant field of enquiry with a theoretical framework that also evolves. There is no question that evolutionary biology is a vigorous and dynamic field that is changing. Currently, ideas are flooding into it from evo devo, epigenetics, ecology, genomics, and many other disciplines. The organisers began with the premise that this plurality of perspective is healthy, and that it would be fruitful to encourage discussion of these new or changing ideas and concepts, in an open-minded spirit.

Central to this conference was the idea that knowledge of how organisms develop, grow, and interact with their environment, helps researchers to account for both the diversity

of life and the processes of adaptation. ‘Evolvability’ was just one of several themes of the conference. Additional topics include the evolutionary causes and consequences of ‘developmental bias’, ‘developmental plasticity’, ‘niche construction’ and ‘extra-genetic inheritance’. In his opening address, Kevin Laland described two factors that these topics have in common: (i) they are all regarded, by some researchers, at least, as central to attempts to integrate development and evolution, and (ii) the evolutionary significance of all of them is contentious, for a particular reason – they are of interest precisely because they highlight differences in how researchers think about and understand evolution. That is why, for instance, they are the focus of the extended evolutionary synthesis.

The organisers set out to encourage inter-disciplinarity and an integrative spirit at the meeting, for which they regarded a conference structure with a single session and a diverse portfolio of talks, optimal. However, they also recognized the value of having symposia focused on particular topics, and wanted lots of people to get the opportunity to present their work. The unusual structure of this meeting was designed to try and balance those conflicting demands: there was a single general session in the mornings, where delegates heard talks on a wide range of topics, followed by more focused twin parallel sessions in the afternoons. The six symposia were on the topics of developmental plasticity, philosophy of biology, developmental bias, niche construction, evolvability and mathematical models. Morning sessions and one of the afternoon parallel sessions were held in Churchill College’s Wolfson Hall, with the other set of afternoon sessions in the college’s Fellows Dining Room. All sessions were very well attended. There were also two dedicated poster sessions.

The organisers set out to ensure that the meeting had a balanced program of talks and posters, a mix of empirical and theoretical work, and presentations from researchers of all genders, career stages, and backgrounds. To encourage early career researchers, prizes were awarded to the best two talk and poster presentations, awards going to **Alfredo Rago** (Southampton University), **Illiam Jackson** (Lund University) and two to **Ahva Potticary** (University of Arizona).

Amongst the highlights of the conference were talks given by invited speakers **Alex Badyaev** (Arizona), **Renee Duckworth** (Arizona), **Laurel Fogarty** (MPI Leipzig), **Jukka Jernvall** (Helsinki), **Joanna Masel** (Arizona), **Armin Moczek** (Indiana) and **Sean Rice** (Texas Tech. Together they addressed a range of biological topics including control theory, maternal effects, niche construction, developmental bias, evolvability and incorporating developmental processes into mathematical models of evolution. Another highlight was a talk given by **Bruce Damer** that, for the first time, connected origin of life research to evolutionary biology using niche construction theory.

Several delegates were interested in the idea that inheritance occurs not just through the transmission of genes, but through many additional means including transgenerational epigenetic effects, parental effects, and cultural transmission. The latter received particular attention, with multiple talks on cultural transmission in primates, whales and birds, as well as a variety of mathematical treatments of cultural inheritance and its interaction with genes.

Also distinctive of *Evolution Evolving* was the inclusion of contributions to the history and philosophy of evolutionary biology, which the organisers felt are underappreciated but

critically important to the field of evolutionary biology. Indeed, three of the invited speakers – philosophers **Alan Love** (Minnesota) and **Angela Potochnik** (Cincinnati), and historian **Jessica Riskin** (Stanford), gave presentations along these lines. By all accounts the scientists in the audience found those contributions insightful and stimulating.

The Galton Institute were thanked on the conference web-site, in the conference booklet, at the Welcome address by Kevin Laland, and in the Closing address by Paul Brakefield. In addition, in between talks, the two slide projectors cycled through slides including one with the Galton Institute logo.

The organisers received a great deal of positive feedback about the conference, which was widely regarded as a great success. Delegates enjoyed three days listening to some fantastic talks and discussing evolutionary science, and most left the meeting feeling both invigorated and inspired.

Katherine Meacham
University of St Andrews

BOOK REVIEW

Adam Rutherford: ***How to argue with a racist; history, science, race and reality***
Wiedenfeld and Nicholson, ISBN 9781474611244 (hardback**)**

Racism is still all too prevalent in the 21st Century world, and we are reminded of this by recent events in the USA and the Black Lives Matter demonstrations. Most of the people reading this review would consider themselves not to be racists but we can all unconsciously stereotype. Progress in genetics provides

enormous insight into the relatedness and genetic diversity of humans, but also provides fodder for apparently innocent, as well as vicious prejudice.

Adam Rutherford's new book *How to argue with a racist* teaches the fallacy of the very concept of human races from a genetic point of view; it explains the subtlety of the 'within group' diversity and 'between group' comparisons; it reminds us how few genes are involved in determining the visible traits such as skin colour, which largely lead to racial classifications. But genetics tells us how much variability there is in those genes, particularly within the continent where ancestors of those currently described as 'black' came from. The book challenges assumptions made about groups of people on the basis of skin colour—such as that 'black people are inherently better runners than white people'. These associations take no account of socio-economic, environmental and role-model factors, but are fuelled by the knowledge that there are real adaptive genetic differences which for example affect oxygen uptake. Many successful long distance runners come from high altitude parts of Kenya and Ethiopia. Genetic adaptation to high altitude may confer some advantage, as does training at high altitude, but there is no evidence that the high-performance runners carry the relevant variants more frequently than their non-runner neighbours, nor is there evidence of success of people coming from high altitude regions in other parts of the world. In contrast, he notes that there are no black American Olympic swimmers—and comments that it is hardly surprising since a staggering 70% of African Americans never learn to swim.

One chapter addresses the sensitive issue of intelligence and cognitive ability. While modern genetic tools confirm the notion that there is a significant heritability to intelligence within populations, comparing between populations is very much more du-

bious. Likewise, musical aptitude has some genetic component, but the fact that classical music and Jazz segregate by skin colour hardly shows that there are 'genes for' musical styles! To quote: "All human behaviour is a heady mix of genes and culture, of biology and history."

The book also calls into question the limitations of some of the interpretations of genetic ancestry testing; results of 23andMe or similar companies may or may not confirm what we can work out from a traditional investigation of family history (which in my view is a lot more interesting) and the results can certainly be mis-used. For example, white supremacists have been known to interpret their own data to confirm their own prejudices (eg 100% white) or chose to disbelieve them, if the results are not as they wish, giving paranoic explanations for the false results. No-one is 100% anything. Adam uses his own ancestry and also a celebrity example from 'Who do you think you are?' to introduce and explain very clearly how: if you are broadly of British Ancestry you, like Danny Dyer, are highly likely to be descended from Edward III and William the Conqueror; and that all the people currently living on earth share ancestors in common with all others as recently as the 14th Century BCE.

This book is highly readable; it educates us all; described by Peter Frankopan as "Far-reaching, insightful and brilliant". I could not put it better.

Professor Dallas Swallow
University College London