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Galton Institute

Exploring Human Heredity

The Galton Review

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Front Cover Image: Professors Bartha Knoppers and Veronica van Heyningen with the silver Galton Plate

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EDITORIAL

It has become fashionable in recent years to disparage the achievements of those in the not so recent past. Every week, the newspapers are full of stories in which someone is outraged that an historical figure is still celebrated in the name of a building or a statue which has stood for decades. Consider the cases of William Gladstone in Liverpool and Cecil Rhodes in Oxford, both giants of their time.

How nice therefore, that we were able to celebrate the legacy of Francis Galton in our recent Annual Conference. Of course Galton has also been subjected to recent scorn at UCL, so to hear notable academics celebrate his accomplishments was most gratifying. We are of course all aware that he was the epitome of a true polymath but to listen to so many talks about modern advances in science, ALL of which can trace their origins to the work of this one remarkable man, was frankly astonishing. A full report of this year's conference can be found on page 4. The highlight was the 101st Galton Lecture, delivered by **Professor Bartha Knoppers** from Canada and you can see a video of this on our website. Our 2018 conference certainly looks to be something special as it will concern the fast-moving field of 'Genome Editing'. Details will appear on our website in due course.

Also to be found on our website is a report on our most recent Teachers' Conference held in Manchester which was again very well-attended and received excellent feedback from the delegates. You can also find links to most of the speakers' presentations.

Finally, 2018 marks the 100th anniversary of RA Fisher's iconic paper on "The correlation between relatives on the supposition of Mendelian inheritance". In this paper, Fisher introduced the term 'variance' and proposed its formal analysis. To mark the occasion, we are awarding an Essay Prize for post-16 secondary students on the topic of **"The role of statistics in medical and scientific research, especially in genetics".** Please pass this on to interested parties.

Robert Johnston

The Galton Institute Annual Conference
Surveying Galton's Legacy
15 November 2017 at the Royal Society

This year's conference attracted over 200 delegates to listen to a diverse range of experts considering the impact Francis Galton had in his time and the legacy he left behind. The full programme is available on our website. It was organised by the President, **Professor Veronica van Heyningen, FRS, Professor John Beardmore** and **Professor Dian Donnai.** The President started proceedings with a brief account of the aims and activities of the Galton Institute, details of which can be found at www.galtoninstitute.org.

The first session was chaired by **Professor Melinda Mills** who introduced the first speaker, **Professor Gregory Radick** (University of Leeds) who discussed **'The Meaning of the Quincunx'**. He believes that re-visiting a legacy is important because legacies change in the light of new discoveries. Even now, Galton is sometimes seen as something of a 'pantomime villain', an arch-determinist who led genetics down the ruinous road of eugenics. Professor Radick argues that the opposite is true. In Galton's famous book 'Hereditary Genius', he labours the point that gifted parents frequently produce children who are far from gifted. In his quincunx, identical pellets, starting from the same point, end up in very different positions.


Professor Gregory Radick

Galton believed that the same is true of offspring – other agencies have a profound effect on final phenotype. For the early geneticists, there seemed to be a choice between Mendel and Galton; Mendel, with the strong support

of Bateson won the argument and ever since, genetics courses, at all levels have begun with Mendel and his peas. Professor Radick believes Mendelism is a special case and that for most traits strict determinism is not applicable. Perhaps schools and universities should reconsider the way they teach genetics in the 21st century.

The second session was chaired by **Professor John Beardmore** and the first to speak was **Professor Ian Deary** (Edinburgh) on **'Quantitative phenotyping and population genomics of cognitive function and ageing'**. He presented, step by step, an evaluation of the legacy of Galton's research and writings on the inheritance of ability, as viewed through the eyes of the 21st century. He used studies on the unique longitudinal Scottish birth cohorts started in the middle of the 20th Century to evaluate the extent to which Galton's ideas have endured. From Galton's important observations on distributions ('deviations from an average,' namely the bell curve) he saw that what applied to height and other physical features should apply to 'natural ability'. He recognised that zeal and capacity for labour were also important and were 'a gift of inheritance'. Galton was able to make the link between sensory discrimination and intelligence and also observed that many abilities and traits were likely to be correlated, both of which have since been confirmed. Indeed it is now shown that some 40-50% of variation in intelligence is 'general' while a quarter is specific to particular domains (reasoning, speed, memory, spatial) and a further quarter to highly specific subdomains. On the other hand Galton was wrong about sex differences: modern data shows that mean IQs of boys and girls are exactly the same. However, there are differences: girls outperform boys in the middle range of ability but boys are

Professor Ian Deary

much overrepresented at the extremes of the ranges of IQ. Galton correctly anticipated the value of collecting multiple measurements and the value of a national biobank, which took a century to transpire. He even suggested that four yearly data collection might be suitable, and proposed February 29th!

The final speaker before lunch was **Dr Cristoffer Nellåker** (University of Oxford) who discussed **'Facial measurements and analysis'**. Although rare genetic diseases are by definition 'rare', collectively they are remarkably common accounting for about 8% of live births. However, most clinicians rarely if ever encounter some of these conditions making them notoriously difficult to diagnose. However, a significant number result in a cranio-facial manifestation which can help with diagnosis and accelerate treatment. Dr Nellåker's team are therefore developing technology to identify these conditions from facial appearance. They are building up a database of photographs of patients with rare disorders and have produced software for describing features digitally. A new website, 'Minerva and Me' allows participants to upload family photos so that the computer models can 'learn' more about the inevitable variation within a given disease cohort. However, Dr Nellåker acknowledges the need for global collaboration to ensure ethical and legal loopholes are covered. The technique could also be used for paternity testing and ancestral studies. Galton, of course, was the first to seriously study facial measurements and link appearance with disease and status.

Dr Christoffer Nellåker

The session after lunch was chaired by **Professor Nicholas Wood** who introduced **Professor Mark Jobling** (University of Leicester) to talk about **'Fingerprinting and Identity'**. He explained that Francis Galton was not the first to study fingerprints. Early work by William Herschel (1833-1917) who was a British Indian Civil Service Officer in India used fingerprints for identifi-

cation of individuals on contracts. Early researchers studied 3 types of fingerprints, arch, loop and whorl structures and showed that they could discriminate amongst individuals and relatives. Fingerprinting is still in use and the UK database has ~7.1 million people on it. It is now done electronically and countries such as Russia use it routinely before issuing a visa.

Professor Mark Jobling

A newer development was to use DNA 'fingerprinting' where the 4 nucleotide bases act as the markers. It uses multiple regions of minisatelites that are tracts of repetitive DNA in which certain DNA motifs (ranging in length from 10–60 base pairs) are typically repeated 5-50 times. They occur at more than 1,000 locations in the human genome and they are notable for their high mutation rate and high diversity in the population. They are cut out and radiolabelled with P^{32} then electrophoresed on gels and autoradiographed to produce a banded pattern rather like a bar code. It has been successfully used to identify criminals to aid their prosecution and to establish family relationships in disputed maternity or paternity cases. The technique can now be done on microsatellites that are scattered throughout the genome using very small blood drops.

A problem arises as to who should be on the UK National DNA database. It was hoped that being on the database might act as a deterrent to crime; but this did not appear to occur. If innocent people are kept on the database this might have implications for racial discrimination or medical insurance. The debate about this continues.

The next speaker was **Professor Tim Spector** (King's College, London) who in discussing **'Lessons from Twin Studies'** started by giving details of the Twins UK Bioresource facility; this was following on from the pioneering work of Francis Galton on twins at the end of the 19th century. Genetics has

advanced out of all recognition since then and Professor Spector showed us some of the developments from his own department. His results on the heritability of common traits showed values of around 30-50% for conditions that are not generally thought to be inherited at all, such as osteoporosis, migraine, and traits such as daily physical activity, alcohol intake and predilection to consume junk food! He then gave examples of molecular phenotypes that were intermediates to disease states and these too showed high degrees of heritability.

Professor Tim Spector

One of the most interesting examples of his current work is the human microbiome of the gut which is composed of bacteria, archaea, viruses and eukaryotic microbes that reside in our intestines. These microbes have tremendous potential to impact on our physiology, both in health and in disease. They contribute metabolic functions, protect against pathogens, educate the immune system, and, through these basic functions, affect directly or indirectly most of our physiology and some disease states. They act like an additional body organ and using twin studies, it was found that the gut microbiome can be genetically determined. Thus 'thin' twins have a different gut microbiome to 'fat' twins. Furthermore, this trait is transmissible: colonization of germ-free mice with an 'obese microbiota' results in a significantly greater increase in total body fat than colonization with a 'lean microbiota'. These results identify the gut microbiota as an additional contributing factor to the pathophysiology of obesity.

The highlight of the day was The Galton Lecture, given by **Professor Bartha Knoppers** (McGill University) and introduced by the President, **Professor Veronica van Heyningen, FRS**. Professor Knoppers' talk was on **'Eugenics: the (Un)Ethical Trump card?'** and she started from the premise

that just because the word 'eugenics' has acquired such a bad name, mainly due to its past history, particularly in Nazi Germany, it should not be dropped from our vocabulary. This is because many of the new Assisted Reproductive Technologies are eugenic in nature (defining eugenic as obtaining a good birth; eu- good; genesis- birth). Pre-implantation genetic screening, for severe metabolic and other genetic defects, is now routinely done and the embryo is discarded if found to be defective. Cloning is on the horizon for humans if ethical and regulatory bodies can agree and gene editing has taken a new lease of life with the introduction of the CRISPR–cas 9 technologies.

All these methods are eugenic in nature with the aim of getting a good live birth for the family. However the world regulatory bodies disagree on how these methods should be used. Some countries such as Germany will not authorize assisted reproductive techniques that are allowed in other countries such as China; and even within the same UK jurisdiction, abortion is legal in England, but not in Northern Ireland. What is needed is a common ethical and legal system that provides something like a Universal Declaration on Human Rights in the field of Assisted Reproduction and Science that all countries can adopt.

Professor Bartha Knoppers

At the conclusion of her lecture, Professor Knoppers was presented with the Galton Plate by the President.

The final talk was given by **Professor Han Brunner** (Maastricht, Netherlands) on **'Intellectual ability and disability: genes and genetics'** and focussed mainly on educational **dis**ability. In contrast to heritability of intelligence within the normal range, which seems to be affected by many genetic

variants with very small effect, most severe disability is monogenic (Structural Variants and simple nucleotide changes leading to loss of function of critical proteins). Recent studies by Brunner's group on 50 trios in which both parents of the affected child were intellectually normal, searched for de novo mutations by whole genome sequencing. In as many as 40% of the trios of this previously well studied cohort, they were able to find good candidates located within plausible genes. The frequency of disability caused by such de novo events is rather higher than the frequency of Down's syndrome, with an overrepresentation of older fathers because of the mutations that accumulate in the many cell divisions in the male germ line. The fact that most of these compromising mutations arise in patients with older fathers leads to an interesting discussion point: namely should all males freeze their sperm at age 17, to be used later?


Professor Han Brunner

This survey also surprisingly uncovered many fewer recessively acting mutations than might have been expected from the number identified in consanguineous families. Brunner suggested that there may have been selection against alleles with unrecognised effects in heterozygotes. He also reported that, consistent with Galton's claims, there is some relationship between intellectual (dis)ability and brain/head size. Recent studies have shown that tight control of brain size is mediated through the mTOR signalling pathways.
Mutations in the gene RAC1 for example, in which many de novo mutations have been found, can cause either smaller or larger head size, depending on whether they are 'inactivating' or 'activating' mutations.

Dallas Swallow
David J Galton
Robert Johnston

Biology and Chemistry of Vision Conference

June 2017, Steamboat Springs, Colorado

Every two years, the top researchers in 'vision science' from around the world come together to discuss their most recent data at the FASEB Biology and Chemistry of Vision Conference. This year the event, organised by Marie Burns and David Williams, took place in Steamboat Springs, Colorado, USA – a quaint city best known for its Ski Resorts. In June however, there was little snow to be seen and the city was instead surrounded by lush green mountains, providing a beautiful backdrop for an exciting few days. The conference was held in the Steamboat Grand Hotel where the majority of attendees also stayed, providing a welcoming and inclusive atmosphere. Sessions ranged from the basic science of phototransduction to the latest advances in the treatment of patients with blinding diseases. The conference consisted of eight chaired sessions and two poster sessions, each supplemented with DataBlitz presentations. These fast-paced sessions allowed each participant a maximum of two slides and three minutes to describe their most exciting findings, giving trainee scientists an opportunity to sell their poster and encourage other attendees to visit.

The conference began with a keynote address from **Samuel Jacobson**, detailing his seminal work which led to the first human clinical trial of a gene therapy for inherited retinal degenerations, and introduced the translational theme that ran throughout the meeting. The first session covered the latest research into how the photoreceptor cell functions. A particularly striking talk was delivered by **Yoshikazu Imanishi**, who detailed the use of Dendra 2 photoconversion to distinguish between old and newly synthesised rhodopsin molecules in Xenopus Rod cells and stunned the audience with beautiful

images obtained by this technique. Dendra 2 photoconversion will no doubt prove useful for many of the researchers present, seeking to locate their protein of interest in the photoreceptor outer segment. The remaining sessions covered a vast number of topics, from new developments in understanding phototransduction to mouse models of human retinal disease. **Roxana Radu** presented her recent work using ABCA4 knockout mouse as a model of Starsgardt's disease. She observed partial rescue of the retinal degeneration phenotype by re-introducing the ABCA4 gene exclusively to the RPE cells. This work highlighted the complex relationships between cell types within the retina and the importance of considering this when designing new therapeutic strategies. The focus on treatment strategies continued, with talks examining the application of CRISPR and stem cell therapies to treat human retinopathies. In the final keynote address, **Paul Sieving** described his work with the 'audacious goals initiative' from the National Eye Institute, which seeks to restore vision by regenerating the human retina.

This meeting excellently highlighted the substantial progress that has been made in our understanding of the science of vision and how these findings may lead to new treatments for patients suffering from devastating blinding diseases. The strong collective atmosphere of this meeting will no doubt encourage new collaborations between researchers and aid progress in the field. The next FASEB Biology and Chemistry meeting is scheduled for 2019 and is set to be another exceptional meeting. I for one am excited to see the developments in the field over the next two years.

I would like to thank the **Galton Institute** and the **Genetics Society** who made it possible for me to attend this conference with the award of a Junior Scientist Conference grant

Abigail Little

Primary Care Genetics Workshop
Sharing Best Practice: Equipping European Primary Care Health Professionals to Deal with Genetics
5 May 2017, London

Introduction

The Gen-Equip project [www.primarycare genetics.org] is co-funded by the EU Erasmus+ programme and is the work of partners from six European countries. We have developed a programme of online learning modules and tools to support practice with patients at risk of genetic conditions seen in primary care. This workshop was organised to disseminate the project, obtain feedback, and create a network of interested persons to ensure ongoing support and sustainability of the educational programme.

The aims of the workshop were to:

- Share best practice on facilitating good standards of genetic healthcare in primary care practice
- Introduce the series of online educational material available to primary care professionals and discuss how they can be used.

Participants

This workshop was planned to provide a forum for sharing experiences regarding genetics education in primary care across a wide range of stakeholders. Invited participants included primary care professionals (general practitioners, community paediatricians, midwives, primary care nurses), genetics professionals (medical geneticists, genetic counsellors), relevant patient group representatives and those involved in provision of education for primary care professionals. In total, there were 78 participants from 15 different countries.

Programme

The aim of the programme was to enable participants to:

1. Learn more about genetics education in primary care
2. Share their own challenges and successes in providing genetic education for primary care professionals
3. Share a range of different educational tools
4. Provide feedback and direction for the Gen-Equip project.

The programme was divided into presentations and guided group work sessions. Time was also allowed for informal networking and discussion. All formal presentations were made available to all participants after the Workshop and a participant contact list was circulated to encourage post-Workshop networking.

Results of the group work

During the first group work session, participants were asked to work in groups with colleagues from different countries: each group included representatives of both primary care and genetics. The task was to determine the opportunities and challenges involved in providing genetics education for primary care from the perspective of primary care, and opportunities and challenges from the perspective of the genetics specialist.

In the afternoon, the Gen-Equip and a range of other resources for primary care education in genetics were presented. Participants were then asked to form groups according to country or region, and were asked to address the following questions:

1. How can you use the resources in your own setting?
2. Are there gaps to be filled? Where are the gaps?
3. Can you give suggestions for improvement of the resources?
4. Can you provide suggestions for dissemination of the resources?

After working in groups, the questions were discussed generally. As organisers, we had a sense that participants were very engaged in the topic. There were numerous questions asked, and in the group work sessions there was a high level of discussion, debate and contribution from participants. In the refreshment breaks, the level of animated conversation continued between participants from different countries and disciplines.

Evaluation and feedback by participants

All participants were asked to complete an evaluation form, in which they were asked to rate the Workshop and also the Gen-Equip resources. While the lectures were all rated well, the participants seemed particularly to appreciate the group work sessions, where they were able to exchange ideas in discussion with peers.

We consider that the aims of the Workshop were achieved. The Gen-Equip resources were publicised and since the Workshop we have noted increased numbers accessing the modules. However, one of the major outcomes was that a group of professionals who were interested in this topic were able to discuss it and form new professional networks. We hope that new professional alliances will result from the event, to further genetics education in primary care in Europe.

Our sincere thanks to the **Galton Institute** for their support for this work.

Professor Heather Skirton
Plymouth University

The material in this article reflects only the author's views and the European Commission and Ecorys UK are not responsible for any use that may be made of the information it contains.

Wales Gene Park Genetics and Genomics for the Third Generation (3G) Public Conferences
21st June 2017 in Cardiff and 24th October 2017 in Wrexham

Wales Gene Park is very grateful to the **Galton Institute** for supporting our second annual ***G****enetics and* ***G****enomics for the Third* ***G****eneration*, or 3G, conference through its *Small Grants* scheme. The event aims to promote learning and engagement around genetics and genomics amongst members of the public over the age of fifty in an informal and friendly environment.

The South Wales event took place in Cardiff, where around 120 members of the public heard expert talks including *The Genomics Revolution* by **Rachel Butler** of All Wales Medical Genetics Laboratory, *Eat to Fit Your Genes* by **Dr Maninder Ahluwalia** of Cardiff Metropolitan University, *Working with Bees to Discover New Antibiotics* by **Professor Les Baillie** from Cardiff University, *How can the Public Voice Make a Difference?* by **Barbara Moore** of Health and Care Research Wales Support Centre and **Sian Jones** an Involving People Network member, *The People of the British Isles: where do we come from and why does it matter* by **Dr Bruce Winney,** *Bowel Cancer in Wales: challenges and opportunities* by **Dr Lee Campbell** of Cancer Research Wales and *Using DNA in Wildlife Crime* by **Dr Rhys Jones** of Cardiff University.

There were interactive stands for the public to enjoy, which included information and hands-on activities, from BRAIN, Cancer Research UK, Cancer Research Wales, Cardiff University Libraries, HealthWise Wales, National Centre for Mental Health, Tenovus Cancer Care, Wales Cancer Research Centre, and Wales Gene Park.

The North Wales conference was held in Wrexham, where around 50 members of the public enjoyed talks on *Same But Different: The Rare Project* by

Ceri Hughes, *The ABC of DNA* by **Dr Sue Assinder** of Liverpool School of Tropical Medicine, *Feeding and Healing the World through Plant Genetic Technologies* by **Dr Geraint Parry** of GARNet community, Cardiff University, *The 100,000 Genomes Project and the Future of Healthcare* by **Paul Evans** of North West Coast Genomics Medicine Centre, *Bowel Cancer in Wales* by **Dr Lee Campbell** of Cancer Research Wales, and *DNA analysis in forensic science* by **Amy Rattenbury** of Glyndwr University. Delegates also enjoyed interactive stands from Same but Different: Rare Beauty, Cancer Research UK, and Cancer Research Wales.

Feedback from the events, through evaluation questionnaires, was extremely positive with 62% of all respondents rating the quality of the event as 'excellent' and 38% as 'very good'. Eighty seven per cent of respondents 'agreed strongly' that they felt more informed about genetics after attending. Comments from delegates included '*unmissable*', '*excellent programme. I highly recommend it to everyone*' and '*a brilliant day!*'

Rhian Morgan
Cardiff University

The Galton Institute Essay Prize 2018

- **Prize: for post-16 secondary students**
- **Topic: 'The role of statistics in medical and scientific research, especially in genetics'**
- **Deadline: 5 February, 2018**
- **Prizes: First £500, with two runner-up prizes of £100**
- **Full Details: see website: www.galtoninstitute.org.uk**

SITraN
Sheffield Institute for Translational Neuroscience

Sheffield Rare Disease Study Day

8 September 2017

The day was organised and chaired by Dr Alisdair McNeill (University of Sheffield). It was held in the Sheffield Institute for Translational Neuroscience (University of Sheffield). The purpose was to provide an update on rare disease research to clinicians (both specialists and non-specialists) and also to provide information to families affected by rare disease.

Around 50 people attended, from diverse backgrounds: Consultants in medical specialties, doctors in training in genetics, laboratory scientists, nurses and families affected by a rare disease. In the morning talks were given by **Dr Alison Foster** (Birmingham Womens Hospital) on overgrowth disorders and **Dr Hannah Titheridge** (Birmingham Womens Hospital) on rare genetic, autoimmune conditions. **Dr Derek Lim** (Birmingham Womens Hospital) spoke on a rare cancer causing condition called Birt-Hogg-Dube syndrome.

Following a buffet lunch, there was a detailed discussion of current management of ataxia-telangiectasia by **Dr Mohnish Suri**, who runs the national paediatric ataxia-telangiectasia clinic in Nottingham. The keynote address was given by **Dr Beverly Searle**, the chief operating officer of the charity Unique which produces information resources for families affected

by rare genetic diseases. **Dr Alisdair McNeill** (Sheffield) then gave a talk on his research into neurological manifestations in adults with 22q11 deletion syndrome. As part of the day several people with 22q11 deletion syndrome who had participated in the research attended so they could understand the outcome of the work. We are grateful for the funding from the **Galton Institute** which permitted us to invite a diverse range of speakers and families affected by rare disease.

Dr Alisdair McNeill PhD MRCP (UK) DCH
INSIGNEO Senior Clinical Fellow
University of Sheffield and
Honorary Consultant in Clinical Genetics, Sheffield Children's Hospital

Grants from the Artemis Trust of The Galton Institute

The objectives of the grant are to help preserve and protect the physical and mental health of people, particularly but not only those from poorer communities, in particular by:

- **Assisting in the provision of fertility control and other measures to improve reproductive and sexual health; and**
- **Advancing education in all aspects of reproductive and sexual health.**

Maximum Grant: £15,000 p.a.
Details and application form: www.galtoninstitute.org.uk

British Society for Population Studies Conference 2017
6-8 September, University of Liverpool

Over the course of three days, over 220 people attended and over 140 papers were presented in 45 strand sessions, with six sessions running simultaneously. Additionally, there were two contributed sessions from ONS on developments in official population statistics, and a very informative and well-received workshop from **Esther Roughsedge** and **Vicky Avila** from National Records of Scotland *on Infographics & interactive visualisations*. **Rebecca Sear**, **Wendy Sigle** and **Alina Pelikh** ran a session on *Good practice in peer review: how to review journal articles* which was also very popular, with excellent feedback from those attending. **Natalia Permyakova** and **Sam Wilding** were responsible for a panel session on *Building a career in academia in the UK* and **Chris Lloyd** contributed a training session on *Using the PopChange resource to explore population change in Britain*. To add to the packed programme, there were two plenary sessions from **Professor Michael Anderson** (University of Edinburgh) and **Professor Clara Mulder** (University of Groningen).

The poster session saw over forty posters on display. The annual poster prize was awarded to **Anna Rybinska** (University of North Carolina at Chapel Hill) for her poster *Childbearing intentions in early adulthood*. Abstracts for all presentations, both oral and in poster form, can be found on the Society's website at **www.bsps.org.uk.**

Plenary reports

Plenary 1 – Professor Michael Anderson (University of Edinburgh) "Scottish Migration: who, when, where and why: from the mid-nineteenth century to the present day?"

Professor Michael Anderson gave the first plenary talk and dedicated it to the principal matter of migration that has been extensively researched in qualitative

studies but has been relatively overlooked in population geography. As researchers focus on matters of migration, it is important that we understand not only the current patterns of migration but also look at the historical changes throughout the past century. As Professor Anderson's talk got underway, it was noticeable the significance of the historical dimension to his explanation and disentanglement of Scottish migration that made use of the recently digitalised Census data stretching back to 1851.

He reminded the audience of the unique topology of the Scottish landscape and how this influenced Scots settlement patterns. He noted the massive concentration of the population in a band running from Dundee to Ayrshire and that this area formed the heartland of Scotland's industrial economy. However, there was a large area of near emptiness in the land to the north-west of the central belt. While a common explanation has been that the areas relatively emptiness was the result of massive clearances, actually it was the product of the hilly and mountainous regions that made the area less habitable. Professor Anderson's talk continued with the relatively unique case of Scottish migration and pointed to the patterns of emigration throughout the twentieth century. He explained that compared to other Western European countries and the constituent countries of the UK, Scotland had a higher rate of emigration. He remarked that his talk was intent on trying to answer the significant questions of who was moving, where were they moving to, and why were they moving?

Using the newly digitalised Census data, he began by considering who had moved from Scotland. His talk mentioned that many professionals and skilled workers, as well as rural workers of all ages, left Scotland. Comparing the population change to England and Wales, he remarked that for much of the 19th century Scotland's population was growing at a slow rate and after the First World War had almost stopped growing. Statistics showed that approximately 680,000 Scottish men emigrated overseas and this was, in fact, more than were killed in the First World War. He mentioned that the US was significant to Scottish migration, but this only told a partial account of the story. He suggested that we also needed to consider England in the wider picture of Scottish migration. The consideration was because England acted as a major destination for Scot-

tish migrants. The Census data revealed that in 1851 4.1% of Scots were living in England and this had risen to 16.2% in 2001.

Professor Anderson noted that the Scottish Story cannot be understood by emigration alone and we also needed to look at churn and turnover that were intimately linked to the economy. Remarking of specific examples, he noted specific demographic differences in migration by age cohort were related to specific industries that were concentrated in specific areas. Noting the demographic characteristics of residents in the coal-mining sector, he pointed out that there was an abundance of work for young men but that there was also a net out migration of girls and adolescent women. However, he then noted an in-migration of young women that he explained was as a result of cohabitation and coal miners wanting and forming intimate relationships with young women. He observed that the same types of patterns were observed in the textile industry but vice versa with the initial out-migration of young men and with an abundance of work for women across the age categories. Meanwhile, there was a noticeable in-migration of men at a certain age as they began to form intimate relationships with women in the textile sector. He showed that there was evidence across Scotland of these types of local demographic patterns that were gendered and intersect age for specific industries and could explain a lot about local churn and internal migration patterns.

Professor Anderson then turned his attention to why Scottish international migration had gathered pace in the twentieth century, often at a faster rate than other Western European countries. His evidence focused on some key factors. First, low wages and this was because it was often assumed that low wages were the principal factor for Scots to emigrate. However Scottish wages were relatively high compared to other European countries but at a lower level than the US. Second, differences in the welfare system where in Scotland the Poor Law did not offer as much protection to laid-off workers during economic slumps as it did for workers in England and Wales. The problem is especially evident given the dominant sectors in Scotland were the heavy industries that were very sensitive to changes in the economy. Third, the different industrial structure in Scotland was dependent on shipbuilding, heavy engineering and mining and during the

late nineteenth century, there was too little investment in new plants that meant that Scottish firms became increasingly uncompetitive. Fourth, the demographic dynamics whereby natural growth increased the number of children who entered professions where there were not enough jobs to support them. Lastly, the Scottish diaspora and emigration that has often been written about as attracting newer migrants to move abroad and these also included recruitment agencies and Commonwealth recruitment schemes, but he noted that these accounts have virtually ignored the largest group of Scots located in England. There has also been a lack of attention to the specific recruitment schemes in England that were aimed at attracting Scots to come and work in the labour market.

In conclusion Professor Anderson remarked that insecurity mainly linked to the economy was ever present in Scotland, and it would not take much to tip Scotland back into net emigration and thus population decline. The availability of new digitalised Census data and the need to make other historical data digitalised has opened up more questions than answers about the dimensions of Scottish migration that he had only begun to attempt to answer in his forthcoming book. The question of why Scots moved and some of the local dimensions he states offered exciting opportunities for those interested in Scottish migration to investigate in the future.

Plenary report - **William Shankley**
(University of Manchester)

Plenary 2 – Professor Clara H. Mulder (University of Groningen) - "Putting family centre-stage: Family ties and spatial mobility".

In her presentation, Professor Mulder illustrated the research project for which she was recently awarded a European Research Council (ERC) Advanced Grant, and that she will be working on for the next five years The project is entitled: "Family ties that bind: A new view of internal migration, immobility and labour market outcomes". It aims to propose a new perspective to the analysis of internal migration called the "family ties" perspective. The perspective introduces family ties into the study of internal migration flows. This is important because,

while family ties have been widely studied in relation to international migration and internal migration in the Global South, no comprehensive analysis of how family ties shape internal migration flow exists for the Global North. She used her talk to present the Family ties perspective, to illustrate how it differs from conventional perspectives on internal migration, and to reflect on what may go wrong if family ties are neglected from the analysis of internal migration.

First of all, she clarified that the family ties perspective is not meant to oppose, but rather to complement conventional views on internal migration. Existing perspectives have focussed on the analysis of why people do (or do not) migrate, and where migrants go. In particular, the cost-benefit approach hypothesises that people will migrate if the benefits of doing so outweigh the costs. Costs and benefits may relate to increasing one's human capital or the economic returns to it. Thus, people may migrate mainly towards educational institutions and employment centres, or towards places with favourable amenities.

The Family ties perspective introduces the study of ties outside the potential migrants' households as factors motivating – or inhibiting – internal migration. It builds on three main premises, that have been empirically tested: first, that family members are important for social networks and for the exchange of support; second, that despite rapid technological developments in communications, face-to-face contact remains important for people; and third, that geographical proximity is crucial for contact and the exchange of support. Thus, local family ties even outside the household are expected to be a potential deterrent to migration, and the presence of family ties in the place of destination is expected to be an additional attraction factor.

Professor Mulder demonstrated how the conventional cost-benefit approach to migration can be extended and integrated using the Family ties perspective. In this extended view, severing ties represents an additional cost, while strengthening ties an additional benefit of migrating. And the benefits of staying or migrating are augmented by the additional social benefit provided by family ties. These relationships are difficult to test empirically, because costs and benefits arising from family ties are likely to intersect with those related to costs and opportunities in education and in the job market.

Professor Mulder also illustrated the importance of family ties using the concept of "linked lives". She argued that family ties are stronger than other ties, such as friendships, because they last for a lifetime, and cannot be replaced. Commitment to lifetime partners should also be considered, as spouses' decisions to migrate are usually jointly made.

When studying the impact of family ties on internal migration it is also important to consider differentiations among individuals and among contexts. In fact, different individuals are expected to have different needs and preferences for contact. The importance of family ties relative to competing costs and benefits of migrating will depend on individual preferences, which can vary according to gender, age, socioeconomic and health status, marital status, the presence of children and ethnic or cultural background. In terms of differentiation by context, it is also important to consider the role of welfare states and support systems to families, in particular by comparing individualistic and familistic societies.

Professor Mulder concluded her talk by summarising what is gained from the Family ties perspective on internal migration. She argued that taking family ties into consideration in the study of internal migration will lead to an improved, more complete understanding of migration and immobility. At the same time, it will also improve understanding of the individual outcomes from internal migration, as family ties are likely to play a role alongside educational and labour market benefits. She also moved on to reflect on what we may lose in terms of understanding of migration if we ignore the role of family ties. In particular, if the effect of family ties on migration is related to the effect of individual costs and benefits, then the results from the existing literature may suffer from 'omitted variable bias', and thus may overestimate or underestimate the importance of individual push and pull factors by ignoring the mediating effect of family ties. These are empirical questions and hypotheses that the results from the Family ties project will reveal the answer to, in a few years' time.

Plenary report – **Ginevra Floridi**
(London School of Economics)

Thanks to the **Galton Institute** and to the Centre for Spatial Demographic Research at the University of Liverpool for sponsoring this event.

BOOK REVIEW

Jennifer Doudna and Samuel Sternberg:
A Crack in Creation: the new power to control evolution
Pub: Bodley Head

Professor Doudna, a truly remarkable woman, has helped to uncover a truly remarkable bacterial defence mechanism against invading viruses (phage), the CRISPR system. Apart from elucidating some of the science, she has now written a much needed popular science book about her work. This reads like an autobiography, despite a co-author, a former PhD student whose .contribution is not entirely clear. However, the book provides a much needed comprehensible account of the CRISPR system, of what was used before it to edit genes (the ZFN and TALENs systems), the history of how CRISPR was discovered, how it works, what are the molecules involved, what its applications might be and the ethical considerations of editing DNA in human germ cells.

Professor Doudna is a laboratory based scientist and not the usual popular science writer dealing with the concepts of science but reporting the critical experiments of others to support these ideas. She takes you through the ups-and-downs of life in the laboratory with her co-workers, the results of successful experiments, the failures of others and the meetings she had with many inspiring colleagues at International Conferences. Fortunately, Professor Doudna is an enthusiast, indeed she encourages (or warns) you "*I'm incredibly enthusiastic about the promise of gene editing",* and her enthusiasm carries the text along with zest and *elan*. You can feel this enthusiasm coming in waves off the pages which is exhilarating for the reader.

At the start of the book CRISPR and gene editing is going to solve all our urgent problems of agricultural yields both quantity and quality (for animals and plants), cure all the diseases that involve genes, and give us the power to control evolution etc. By the end of the book she gives perhaps more realistic expectations. After all we have had such 'hypes' before with gene therapy and RNA interference being extolled as fundamental advances to transform medicine which in the end did not fulfil their early promise. Further work revealed insuperable difficulties such as getting the transplanted genes under the correct regulatory con-

trols which are as important as the transplanted genes themselves for correct functioning. However these techniques have found a niche in restricted fields such as gene therapy to cure severe combined immunodeficiency syndrome. Professor Doudna points out situations where gene editing would be the only option, e.g. if both parents suffered from cystic fibrosis (or other homozygous recessive conditions) the mutation would be found on both copies of both parents' chromosomes so their children following natural reproduction would be bound to inherit the disease. She admits this would be a rare occurrence as up to 98% of men with cystic fibrosis may be infertile.

Fortunately to counterweigh former enthusiasms, towards the end of her book, Professor Doudna points out some of the emerging problems with gene editing, one chief one being off-target effects. The specificity of the technique relies on a 20 base RNA sequence that exactly finds and matches its complementary sequence of DNA in the target gene to be altered. This guides a "killer" enzyme *Cas* 9 to cut both strands of the defective DNA in half and then for editing to repair the gap with the correct DNA sequence. But what if there are similar DNA sequences elsewhere in the genome, will they be cut too and lead to genetic defects elsewhere? Cystic fibrosis is one the diseases that Professor Doudna wishes to treat by gene editing. This is the simplest possible task for CRISPR. Just one base has to be corrected out of the 6 billion and it's not a needle in a haystack: CRISPR can find, cut and repair it. But I personally would prefer to implant a 'normal' embryo, selected by pre-implantation genetic diagnosis untouched by the CRISPR machinery, rather than treat a diseased embryo with CRISPR to correct the faulty DNA sequence and then have to worry about what other genes might have been altered too. When the CRISPR system evolved in bacteria to disable phage DNA, 100% accuracy was not required for success; so why should it be 100% accurate when working in human cells? Ways and means to reduce off target effects are currently being sought. Nevertheless Professor Doudna is still "....*extremely excited and enthusiastic about virtually all the phenomenal progress being made with CRISPR*". She may be right – time will tell. Time also induces a certain amount of scepticism in promises made before practice. Even a sure-fire discovery such as insulin, the hormone that patients with Type 1 diabetes lack, are not cured by insulin replacement. It revealed a new problem of accurately timing the delivery of insulin in relation to

food consumption which is much more difficult to achieve. As a result, patients still develop complications in the eyes, kidneys, nerves etc.

There is a more inglorious (which she calls "*disheartening")* aspect to her story which she briefly alludes too. With her talent for clear exposition of ideas it might prove as instructive and certainly more relevant to the general public than knowing the molecular details of CRISPR. It concerns money, power and conflict.

At the start, all the pioneers of CRISPR agreed to work together as founding members of the project. They then decided to set up a biotech company to exploit CRISPR-based therapies to treat genetic disease and to make money. So they started a company, Editas Medicine with $34 million in finance from 3 venture capital firms. Soon another biotech company was set up by one of Professor Doudna's co-workers named CRISPR Therapeutics, bankrolled with $25 million and then a third company, Intella Therapeutics joined the scene with $15 million in funding. All were to use CRISPR technology that "*Emmananuelle and I had first developed and described."* So a battle for priority and patents began concerning who was the first to do what and when? Publication dates of hers and her main rival, Feng Zhang, working at the Broad Institute, Boston were dissected before the US Patent Trial and Appeal Board to establish precedence. After a bitter battle, with rival camps belittling each other, the Appeal Board ruled in favour of the Broad Institute where Feng Zhang works. Professor Doudna's Institute, the University of California may appeal.

The true credit for CRISPR should go to the bacteria which evolved the system in the first place to destroy phage. Many people stumbled on bits of it by chance and eventually found a use for it other than altering the DNA of phage. If CRISPR is so good why did eukaryotes not retain the system during evolution from our prokaryote ancestors like so much else? The suggestion that CRISPR can now be used as a powerful tool to control our evolution sounds a little far-fetched to me.

David J Galton
Wolfson Institute of Preventive Medicine

Professor Doudna will be the Galton Lecturer at our conference this year at The Royal Society in London on 31 October, 2018.