**Summary pitch for long term positions:**

New opportunities in Geneva to pursue your career in human genetics . These opportunities include **permanent positions** (after an initial 2 years of 2 x 12 month contracts) where you will either i) lead the development of reproducible analytical pipelines and [products](https://www.tidyverse.org/blog/2017/12/workflow-vs-script/) , both in local systems and in secure data environments, as an experienced computer scientist - in this role your main outputs will be computational and disseminated via github and [DeSci](https://desci.com/nodes) labs or similar platforms; or ii) lead the analysis of genetic data linked to metabolic disease related phenotypes as a statistical geneticist/analyst. A combination of these roles is also possible.

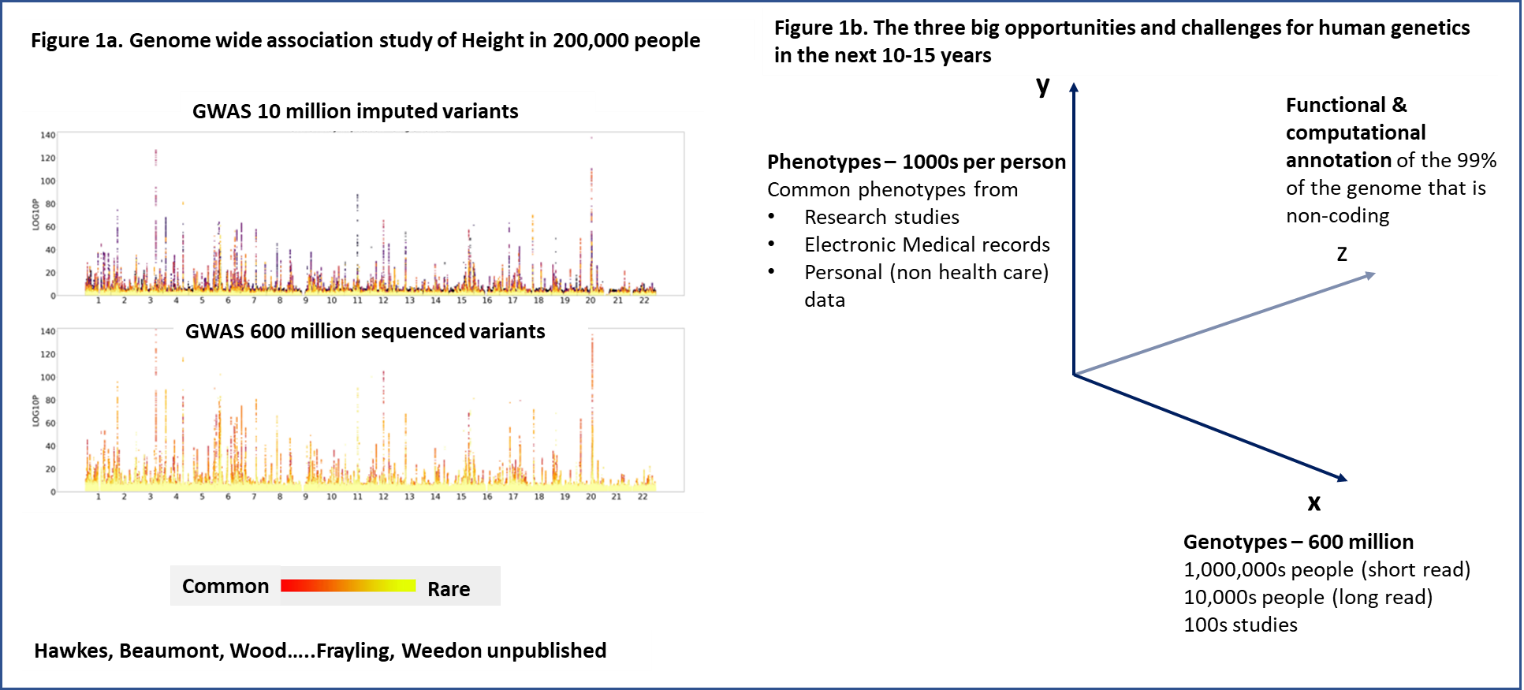
Salaries will start from 80,000 CHF (PhD <2 years ago). Progress your career in the way you want, i) as a traditional postdoctoral researcher building towards independence, or ii) as a staff data scientist supporting wider research as well as your own, or iii) a blend of the two, but all options with the security of long term stable employment in human genetics research in a Faculty of Medicine Hospital setting. There are also excellent ongoing PhD and fellowship opportunities available. PhD students are employed starting on 48,000 CHF and contribute to their pension. The Lake Geneva region brings additional benefits, including an excellent funding environment through the [Swiss National Science Foundation](https://snf.ch/en/ORgUpoSFePiH6QCp/page/get-a-grant) (with approximately 30% grant success rate), the [Swiss Bioinformatics Institute](https://www.sib.swiss/), an excellent health data environment, (including all hospital in-patients being offered the chance to [participate in research](https://www.hug.ch/sites/interhug/files/documents/consentement-general.pdf) that includes genetics, a federated system that allows patient queries across hospitals, and a [network of biobanks](https://ecat-biobank.sib.swiss/search)), leading [statistical genetics groups](https://wp.unil.ch/sgg/), [a leading diabetes and obesity research centre](https://www.unige.ch/medecine/diabetescentre/fr/), excellent core scientific support, with core genotyping, in vivo, sequencing and [bioinformatics](https://www.unige.ch/medecine/bioinformatics/home) support as well as a clinical research facility and separate [Genome centre](https://campusbiotech.ch/en/platforms/dna-sequencing) at [Campus Biotech](https://campusbiotech.ch/). For more information please contact Tim Frayling [t.m.frayling@exeter.ac.uk](mailto:t.m.frayling@exeter.ac.uk) More details: the post is *not a tenured academic position*, and will be part of a research team in common disease genetics led by a PI, but does provide long term stability, a large degree of independence and academic freedom.

**Common disease genetics and genomics in Geneva.**

**Common disease genomics in an era of whole genome sequencing at scale**

There has never been a more exciting time to study common disease using human genetics. This excitement stems from the advances in technology that means we will soon be able to work with whole genome sequence (WGS) data in millions of people (based on short read sequencing) or 10,000s of people (based on long read sequencing). This use of sequence level data in the context of common disease is still in its infancy but, for the first time, provides us with the ability to identify rarer variants with relatively large effects on common phenotypes. Early studies by the Exeter team (in which Prof Frayling has a key role) indicate that WGS studies will lead to the identification of alleles present in 1 in 50 to 1 in 5000 people with effect sizes of >0.5 SDs, or odds ratios > 2.0, with common phenotypes (Fig 1a). The discovery of such alleles will facilitate greater understanding of biology and disease, through more direct functional studies and clinical studies and more opportunities for personalised medicine. Whilst this type of study is ongoing at scale with exome data, financed by industry with a view to informing drug design, these studies usually neglect the 99% of the genome that is non-coding.

The advances in genome sequencing are occurring in parallel to two other broad major advances. First, those in functional genomics, where technologies such as single cell RNA sequencing and chromatin accessibility assays means we will have a much greater understanding of the role of the non-coding genome. Second, in the linkage of human genetic and genomic information to routinely collected medical and health information, including, potentially, that outside the health care setting such as from [wearables](https://www.hdruk.ac.uk/news/have-your-say-can-you-help-develop-a-smartphone-app-to-track-heart-health/). These 3 big challenges – genotypes, phenotypes and functional information are illustrated as a notional 3 axis graph in Fig 1b.



**Obesity and its causes and consequences in the general population.**

The team’s broad disease focus is metabolic disease, notably the causes and consequences of excess weight. For the first time in human history, people will be living into old age having spent their whole adult lives overweight. In groups under-represented in genetic studies, such as people living in developing countries, the prevalence and impact of obesity is increasing. The consequences on health and social care are profound and go beyond metabolic disease and include Musculo-skeletal disease and cancer. In parallel, new therapies will provide us with the opportunity to study at scale why some people are better able to lose weight compared to others, given certain interventions such as the use of anti-diabetic incretin based drugs for many people living with excess weight.

**An excellent data centric and “team science” approach to human genetics**

The team

PI Tim Frayling. I have an excellent track record of investing time and energy in training the next generation of human geneticists and health data scientists. Early career researchers in my team are encouraged and supported to develop their own ideas and projects, and this freedom has often led to last authorship on key papers for postdoctoral researchers, when , for example they have had a strong role in developing the project and supervising a PhD student or more junior scientist (see for example last author papers from Tyrrell, Wood, Yaghootkar in recent years). My training activities have also included setting up an MSc in Health Data Science, a secondment with HDR UK to support training, and delivering basic data handling training to all medical students.

Principle/Chief Data/Analytical Officer(s) and Research software engineering support. As part of the team in Geneva, we will have strong support for all aspects of data analysis with the appointment of one or two long term Chief Data/Analytical Officers or Senior Research software engineers. These people will have their own research projects but work alongside me to ensure Phd students and junior postdocs have the best data training and support. This type of role is unusual in academia but will be increasingly important given the huge opportunities, but also considerable challenges, of working with large complex datasets, including in trusted research environments such as [DNA nexus](https://www.dnanexus.com/) and the Genomics England (GEL) platform.

**Reproducible analytical pipelines.** We will provide basic training in reproducible data analysis and ensuring our work is FAIR – findable, accessible, inter-operable and reproducible. This includes adhering to basic good data practice, such as:

* keeping newly derived variables as code only, not in new copies of datasets; credit for sharing using gitbub
* Dissemination and version control using git and github repositories
* Working in Trusted Research Environments / Secure Data Environments such as DNA Nexus

**Pursue your research interests within human genetics and metabolic disease.**

New recruits to the team will have the freedom to pursue their research interests with a broad remit of human genetics and metabolic traits and conditions. The shared goals of the team will include helping answer big questions, but examples of specific focused projects could include:

1. How do we effectively use the new era of population scale sequence data to advance understanding of the genetic causes and consequences of metabolic disease ? Specific projects could include:
   1. Testing the hypothesis that aggregates of rare variants in non coding elements of the genome associate with exemplar molecular traits that are proximal to the genes, such as circulating protein levels and metabolites. For many such traits the search space can be narrowed by focusing on cis genes or very strong biological candidates.
   2. Testing the hypothesis that aggregates of rare variants in non coding elements of the genome associate with common phenotypes such as height and BMI and long term metabolic conditions such as obesity and type 2 diabetes.
   3. What can we learn from recruiting patients and members of the public to specific clinical research studies ? “Recruit by genotype” clinical studies have had limited success so far, but as datasets increase to include WGS, we will have the opportunity to study people carrying variants with much larger effects than those of common variants.
   4. How do much larger sequenced reference panels help us impute rarer variation of larger effect ? Should we do more GWAS with improved imputation of rarer variants ? Early studies testing this indicate that reference panels such as TOPMED will capture variants in the 0.01% to 0.5% MAF range much more effectively than HRC and 1000 Genomes, especially in non-European ancestries. See figure 1 in [this study](https://pubmed.ncbi.nlm.nih.gov/35981533/).
   5. How does long read based sequencing in medium sized studies help us understand, and potentially impute complex variants ?
   6. Can we improve the annotation of the non coding genome in collaboration with functional biologists in the department, or using machine learning or similar techniques, to for example, identify highly constrained regions that are more likely to be functional ?
2. How do we continue to use common variation to advance understanding of metabolic disease ? given GWAS in millions, we will have increased statistical power for specific projects such as:
   1. Mendelian randomisation studies that separate temporal and spatial aspects of different general risk factors. Most notably separating the early life from later life, and subcutaneous from visceral, aspects of excess weight.
   2. Genomic SEM and multivariate techniques. These techniques could potentially help identify new mechanisms and pathways involved in two or more phenotypes, an approach that could be especially important for studying multi-morbidity, an increasing clinical problem in ageing populations.
3. How do we use linked medical records in large biobanks to expand risk and disease phenotypes at different life stages and translate advances into clinical practice? Specific projects could include:
   1. Identifying the heterogeneity of genetic effects across the life course. For example, do the genetics of metabolic risk factors and disease in middle age differ from the genetics in older age ? this type of question has been very hard to answer because stratified analyses in GWAS, even by simple factors such as age and sex, has been very time consuming or not possible at all.
   2. Personalised / stratified medicine. Systems set up in [Scotland](https://www.registerforshare.org/), the [BioMe](https://icahn.mssm.edu/research/ipm/programs/biome-biobank) and [BioVU](https://victr.vumc.org/what-is-biovu/) resources will allow faster translation of advances in common disease genetics. E.g. incorporation of polygenic risk scores into care (a recent review [here](https://www.nature.com/articles/s41568-023-00599-x.epdf?sharing_token=WYgD8dvkKO4jcnQDSrwkgNRgN0jAjWel9jnR3ZoTv0OrJqXl7GJxg0AChM3Vud49GvqdpvLl6PcPOfbV-vyn9VFR-Yhvtnqhcw-SBzzgicH6QGugrbHtZTzbu94cpJMSe0OhTIK_yRSKKE-T7z9XzTCv0_5Cwa82b1WvjDKHA4o%3D)), pharmacogenomics and studies of more detailed phenotypes available in hospital data, e.g. identifying genetic components to weight loss interventions such as bariatric surgery and the GLP/GIP based drugs, imaging based phenotypes. All out-patients at the hospital in Geneva are offered the chance to consent for all their routine samples and data to be used, and we are exploring the possibility of doing something similar in Geneva to BioMe and BioVu.
4. How do we ensure our genetic research is more representative and environmentally sustainable ?
   1. Working with local Geneva samples and patients will increase diversity to a certain extent – as 40% of the local population are not Swiss, with large Portuguese, Brazilian and Tamil representation, but we will still need to work hard to ensure representativeness.
   2. High performance computing uses surprising amounts of energy. Efficient computing practices will help reduce the carbon footprint of our research.
5. How do we involve and engage industry, clinicians and patients in our work, to ensure efficient translation ?
   1. We will work closely with the Clinical Research Centre and Geneva Hospital clinicians, to ensure projects involve and engage patients. Notably, for diabetes, we will work with the Diabetes centre. Links to patient groups will ensure we keep our research in the “real world”.
   2. The pharmaceutical and biotech industry are increasingly interested in working closely with human geneticists to identify new and repurpose existing drug therapies. This may create opportunities for exchanges and learning about industry.

**PhD studentships**

**Geneva attracts some of the best PhD students because they** are properly employed – paying tax and contributing to their pension, starting on ~ CHF4800 and taking home minimum 3000 CHF a month after health insurance.

There are two relevant programmes, similar to the Doctoral Training Programmes in the UK. Supervisors submit projects to these schemes and students can apply:

1. Genomics and Digital health [University of Geneva - PhD School of Life Sciences | Genomics and Digital Health (unige.ch)](https://lifesciencesphd.unige.ch/program/genomics-and-digital-health)
2. Biomedical Sciences [University of Geneva - PhD School of Life Sciences | Biomedical Sciences (unige.ch)](https://lifesciencesphd.unige.ch/program/biomedical-sciences)

More details of the full programme here [University of Geneva - PhD School of Life Sciences | Welcome to the PhD School in Life Sciences at the Faculties of Medicine and Science (unige.ch)](https://lifesciencesphd.unige.ch/)

**Postdoctoral fellowships**

**The Swiss National Science Foundation has postdoctoral fellowship schemes, including a** [mobility scheme,](https://snf.ch/en/XIZpfY3iVS5KRRoD/funding/careers/postdoc-mobility) [Swiss Postdoctoral Fellowships (snf.ch)](https://snf.ch/en/m1NtWp4nTELQixlu/funding/horizon-europe-swiss-postdoctoral-fellowships)

**Resources**

The team’s programme of research will make use of the incredibly rich resources that are available for human genetics research internationally and within Switzerland. Research funders now insist that all data is open access and “FAIR”. **This open approach means our team’s scientific discoveries will be limited only by our ideas and not by access to large scale data**. This increasingly open approach will be facilitated by moving to working with data in “Safe Data Environments” also known as “Trusted research environments”, a new way of working that will require robust analytical pipelines and training for PhD students and junior postdoctoral researchers. Resources will include:

1. **UK biobank.** Over the next 5 years the [UK Biobank](https://www.ukbiobank.ac.uk/) participants will age so that >80% will be over the age of 70. Linked medical records, especially from secondary care, will provide an unprecedented resource to study ageing and disease in real time. In parallel this resource continues to be augmented with genotype and phenotype information.
2. **AllofUS.** In August 2023 the [AllofUS programme](https://allofus.nih.gov/get-involved/opportunities-researchers) – a study with lots of parallels with the UK Biobank, was released to international researchers from not-for-profit institutions. As of August 2023, whole genome sequencec data from ~250,000 individuals is available, with a target of 1 million.
3. **GWAS consortia.** The team will have strong links to many trait specific consortia, including GIANT, EGG, MAGIC, GLGC, Reprogen.
4. **Local resources**- Switzerland has an excellent health data environment, (including all hospital in-patients being offered the chance to [participate in research](https://www.hug.ch/sites/interhug/files/documents/consentement-general.pdf) in a “general consent” that includes genetics, a federated system that allows patient queries across hospitals, and a [network of biobanks](https://ecat-biobank.sib.swiss/search)). More than 600,000 Swiss residents (100,000 in Geneva) have signed the General consent that allows research with existing samples and data. Although there is no genetics available for this at the moment, patients have agreed that spare blood can be used for genetics research and we are exploring options to create a DNA biobank.
5. **DIRECT** – the University of Geneva is a partner in the EU programme [DIRECT](https://pubmed.ncbi.nlm.nih.gov/31203377/) that includes detailed phenotypes on people at risk of type 2 diabetes and this data will be available.
6. **Our Future Health**. The PI’s team in Exeter team are beta testers of this new resource.
7. **NIHR Bioresource.** This resource includes 200,000 UK volunteers, enriched with rarer diseases and plans to sequence with long read technologies at least 10,000.
8. **Newborn sequencing.** During 2023-2025, 200,000 UK newborn babies will have their whole genomes sequenced. (approx. 20% of all newborns). These individuals will have their genomes linked to medical records and data available for research with Genomics England

**Living in Geneva**

Moving to Geneva is made much easier with the help of a dedicated [Welcome Centre](https://www.welc.ch/en/) . Geneva provides an excellent combination of big city life, whilst also being very child and family friendly. A “5 piece” flat (3 bedrooms, kitchen and living area) will cost ~ 3000 CHF per month, a small studio ~1200 CHF. Primary school children attend class 4 days a week (Wednesdays are off) from 8:00-11:30 and then 13:30-16:00. If you work full time, then you can sign up for “parascolaire” which means they can stay in school over lunch and then until 6pm. It costs CHF 200 per month for 4 days a week and an extra CHF 100 per month for the meals, but you also receive 300 CHF in child benefit costs from the State of Geneva. Below 4 years old the public kindergarten cost roughly 10% of the taxable salary for 1 child full time and ~15% for two children.

On the “rive gauche” (as the river Rhone flows, so South) the Champel area is green and calm, Plainpalais/Eaux-vives is more animated but everything is within 5’ walking, Carouge is very charming, and there are nice little cities like Chene-Bourg, Thonex, Lancy). The Plainpalais and Saint-Jean areas are very child friendly.