



Job title	Postdoctoral Researcher in genetic disorders of chromatin function
Division	Medical Sciences
Department	Nuffield Department of Medicine
Location	Centre for Human Genetics, Building for Genomic Medicine, Roosevelt Drive, Old Road Campus, Oxford, OX3 7BN
Grade and salary	Grade 7: Salary in range £36,024 - £40,521 per annum
Hours	Full time (part time hours considered, at minimum of 60% FTE)
Contract type	Fixed-term contract for 2 years Funding is provided by Wellcome
Reporting to	Robert Beagrie, Sir Henry Dale Fellow
Vacancy reference	174376

Additional information	This role meets the eligibility requirements for a Skilled Worker Certificate of Sponsorship or a Global Talent Visa under UK Visas and Immigration legislation. Therefore, the Nuffield Department of Medicine welcomes applications from international applicants who require a visa.
About us	 University of Oxford - <u>www.ox.ac.uk/about/organisation</u> Nuffield Department of Medicine (NDM) - <u>https://www.ndm.ox.ac.uk</u> Unit - <u>www.chg.ox.ac.uk</u>
What we offer	 https://hr.admin.ox.ac.uk/staff-benefits An excellent contributory pension scheme 38 days annual leave A comprehensive range of childcare services Family leave schemes Cycle loan scheme Discounted bus travel and Season Ticket travel loans Membership to a variety of social and sports clubs A welcoming and diverse community

Research topic	Congenital defects caused by mutations in Nipbl, a component of the cohesin complex
Principal Investigator / supervisor	Dr Robert Beagrie, Sir Henry Dale Fellow



Project team	Beagrie Group
Project web site	beagrielab.comandwww.well.ox.ac.uk/research/research-groups/beagrie-group
Funding partner	The funds supporting this research project are provided by Wellcome
Key publications	 Beagrie, R. A. <i>et al.</i> Complex multi-enhancer contacts captured by genome architecture mapping. Nature 543, 519–524 (2017). Chea, S. <i>et al.</i> Gastrulation-stage gene expression in Nipbl+/– mouse embryos foreshadows the development of syndromic birth defects. Science Advances 10 – 12 (2024).

Background

More than 100 chromatin proteins have been identified as causative genes in human genetic disease. Most of these genes are broadly expressed and many have fundamental roles in transcriptional regulation, yet their disruption causes tissue-specific effects. We do not understand the molecular basis of this tissue-specificity, as it has been challenging to identify the specific cell types affected and to study the consequences of these mutations in the proper tissue context.

The Beagrie lab studies genetic disorders of chromatin function, focussing on heart and brain development because these tissues are very commonly affected in chromatin disorders. We use stateof-the art experimental and computational approaches to address why mutations in chromatin organising complexes lead to intellectual disability and/or congenital heart defects.

The role

This position is open to either an experimental or computational researcher. This project will involve investigating the consequences of mutations in *Nipbl*. Nipbl is responsible for loading the cohesin complex onto chromatin and therefore has a major role in establishing proper 3D chromatin folding. Heterozygous loss-of-function mutations in *Nipbl* are the most common cause of Cornelia de Lange Syndrome, but it is not clear whether this is primarily due to disruption of sister chromatid cohesion during cell division or disruption of gene expression programs due to loss of cohesin-mediated enhancer-promoter loops during interphase.

The aim of the project is to characterise the transcriptional, epigenetic and 3D-chromatin consequences of Nipbl disruption using animal models and cell lines. You will do this by applying advanced techniques including single-cell RNA-seq, single-cell ATAC-seq and Genome Architecture Mapping (GAM). You may apply experimental approaches, computational analysis, or both, depending on your skill set. Training will be available for the successful candidate to improve computational and/or wet-lab biology skills and further world-leading training opportunities will be available both within the Centre for Human Genetics and the wider University.

You will report to Dr. Robert Beagrie at the Centre for Human Genetics. This is a great opportunity for a motivated scientist to conduct state-of-the-art research and to collaboratively build an inclusive, sustainable, and conscientious working environment in a growing lab.

The post is offered on a full-time basis for 24 months with the possibility of extension, however parttime working arrangements could be accommodated if required (minimum 60% FTE).

Responsibilities

You will:

- Contribute to the research group's goal of understanding how mutations in chromatin organising genes cause disease by conducting laboratory experiments to test hypotheses, reviewing and refining working hypotheses as appropriate, contributing ideas for new research projects and developing ideas for generating research income.
- Manage your own academic research and administrative activities, including small scale project management and co-ordinating multiple aspects of work to meet deadlines.
- Adapt existing and develop new scientific techniques, computational approaches and/or experimental protocols.
- Keep detailed, accurate and comprehensible electronic records of experimental and computational work and communicate progress and difficulties in the research project to Dr. Beagrie and the wider research group.
- Identify appropriate computational pipelines and statistical approaches to analyse scientific data from a variety of sources.
- Contribute to general laboratory management, including administration of laboratory consumables, organisation of experimental reagents and management of scientific data.
- Collaborate in the preparation of scientific reports and journal articles and occasionally present papers and posters.
- Use specialist scientific equipment in a laboratory environment.
- Remain up-to-date with developments in the field and act as a source of information and advice to other members of the group on scientific protocols and experimental techniques.
- Represent the research group at external meetings/seminars, either with other members of the group or alone.
- Carry out collaborative projects with colleagues in partner institutions, and research groups.
- Participate in and support the public engagement and widening access activities of the Department and the University. This is anticipated to be not more than 2 days per year.
- Undertake mandatory training as required by the University, Division and Department. The specific list of training courses may change from time-to-time, in response to both legal and internal University requirements.

Selection criteria

Essential

- Hold a PhD/DPhil (or be close to completion) in biology, biochemistry, genetics, bioinformatics, or other related subject.
- Strong research experience in at least one of the following areas:
 - Chromatin organisation: the establishment, maintenance and function of 3D chromatin folding, nucleosome positioning, histone variants and/or modifications, DNA methylation etc.
 - **Gene regulation:** how enhancers, boundary elements and other DNA elements coordinate the activities of transcription factors and transcriptional co-activators to

establish normal gene-expression programmes, and how these processes are disrupted in disease;

- Congenital disease (especially intellectual disability or congenital heart disease).
- Hands-on experience generating and/or analysing genomics datasets.
- Demonstrate a clear interest in learning how to generate Genome Architecture Mapping data and integrate it with single-cell and/or spatial transcriptomics data.
- Ability to work collaboratively as part of a team and manage the day-to-day running of a research project including assisting the work of junior researchers.
- Ability to organise and prioritise own work with minimal supervision.
- Previous experience of contributing to publications/presentations.
- Excellent communication skills, including the ability to write for publication, present research proposals and results, and represent the research group at meetings.

Desirable

- Experience generating and/or analysing any of the following:
 - Genome folding data (e.g. Hi-C, Capture-C, SPRITE, GAM);
 - o RNA-seq data;
 - Single cell data (e.g. single-cell RNA-seq, single-cell ATAC-seq, single-cell Hi-C);
 - Spatial transcriptomics data;
 - Epigenetic data (e.g. ChIP-seq, CUT&RUN, CUT&TAG, ATAC-seq).
- Working knowledge of Python or R programming languages;
- Experience applying molecular biology techniques in solid tissue samples.
- Experience analysing imaging data.
- Demonstrated commitment to addressing EDI and/or sustainability issues in research.

Pre-employment screening

Standard checks

If you are offered the post, the offer will be subject to standard pre-employment checks. You will be asked to provide: proof of your right-to-work in the UK; proof of your identity; and (if we haven't done so already) we will contact the referees you have nominated. You will also be asked to complete a health declaration so that you can tell us about any health conditions or disabilities for which you may need us to make appropriate adjustments.

Please read the candidate notes on the University's pre-employment screening procedures at: https://www.jobs.ox.ac.uk/pre-employment-checks

Hazard-specific / Safety-critical duties

This job includes hazards or safety-critical activities. If you are offered the post, you will be asked to complete a health questionnaire which will be assessed by our Occupational Health Service, and the offer of employment will be subject a successful outcome of this assessment.

The hazards or safety-critical duties involved are as follows:

- Lone Working
- Work with any substance which has any of the following pictograms on their MSDS:



How to apply

Applications are made through our e-recruitment system and you will find all the information you need about how to apply on our Jobs website <u>https://www.jobs.ox.ac.uk/how-to-apply.</u>

If you would like to apply, **click on the Apply Now button** on the 'Job Details' page and follow the onscreen instructions to register as a new user or log-in if you have applied previously.

As part of your application you will be asked to provide details of two referees and indicate whether we can contact them now. You will be asked to upload a CV and a supporting statement. The supporting statement must explain how you meet each of the selection criteria for the post using examples of your skills and experience. This may include experience gained in employment, education, or during career breaks (such as time out to care for dependants). Your application will be judged solely on the basis of how you demonstrate that you meet the selection criteria stated in the job description.

Please upload all documents **as PDF files** with your name and the document type in the filename. Please note using a long file name may prevent you from uploading your documents.

http://www.ox.ac.uk/about_the_university/jobs/research/

All applications must be received by **midday** UK time on the closing date stated in the online advertisement

Information for priority candidates

A priority candidate is a University employee who is seeking redeployment because they have been advised that they are at risk of redundancy, or on grounds of ill-health/disability. Priority candidates are issued with a redeployment letter by their employing department(s).

If you are a priority candidate, please ensure that you attach your redeployment letter to your application (or email it to the contact address on the advert if the application form used for the vacancy does not allow attachments).

If you need help

Application FAQs, including technical troubleshooting advice is available at: <u>https://staff.web.ox.ac.uk/recruitment-support-faqs.</u> Non-technical questions about this job should be addressed to the recruiting department directly <u>recruitment@ndm.ox.ac.uk</u>

To return to the online application at any stage, please go to: www.recruit.ox.ac.uk.

Please note that you will receive an automated email from our online recruitment portal to confirm receipt of your application. **Please check your spam/junk mail** if you do not receive this email. Important information for candidates

Data Privacy

Please note that any personal data submitted to the University as part of the job application process will be processed in accordance with the GDPR and related UK data protection legislation. For further information, please see the University's Privacy Notice for Job Applicants at: https://compliance.admin.ox.ac.uk/job-applicant-privacy-policy. The University's Policy on Data Protection is available at: https://compliance.admin.ox.ac.uk/job-applicant-privacy-policy. The University's Policy on Data

The University's policy on retirement

The University operates an Employer Justified Retirement Age (EJRA) for very senior research posts at **grade RSIV/D35 and clinical equivalents E62 and E82**, which with effect from 1 October 2023 will be 30 September before the 70th birthday. The justification for this is explained at: <u>https://hr.admin.ox.ac.uk/the-ejra.</u>

For **existing** employees on these grades, any employment beyond the retirement age is subject to approval through the procedures: <u>https://hr.admin.ox.ac.uk/the-ejra.</u>

There is no normal or fixed age at which staff in posts at other grades have to retire. Staff at these grades may elect to retire in accordance with the rules of the applicable pension scheme, as may be amended from time to time.

Equality of opportunity

Entry into employment with the University and progression within employment will be determined only by personal merit and the application of criteria which are related to the duties of each particular post and the relevant salary structure. In all cases, ability to perform the job will be the primary consideration. No applicant or member of staff shall be discriminated against because of age, disability, gender reassignment, marriage or civil partnership, pregnancy or maternity, race, religion or belief, sex, or sexual orientation.

