Job title	Laboratory Technician - Membrane Protein and Nanobody Production
Division	Medical Sciences
Department	Nuffield Department of Medicine, Structural Genomics Consortium
Location	Old Road Campus Research Building, Old Road Campus, Roosevelt Drive, Headington, Oxford, OX3 7DQ
Grade and salary	Grade 4: £22,417 - £25,941 per annum
Hours	Full time. We would also consider part time working for this post.
Contract type	Fixed-term contract to 31st August 2022 in the first instance
Reporting to	Liz Carpenter, Professor of Membrane Proteins Structural Biology, Integral Membrane Proteins Group
Vacancy reference	*143944*
Additional information	Funded by Innovative Medicines Initiative and BBSRC
Research topic	Generation of reagents for the study of proteins involved in genetic disease, including production of proteins, antibodies, nanobodies, structures and assays for ion channels and solute carriers associated with pain, neurological and metabolic disorders
Principal Investigator / supervisor	Liz Carpenter, Professor of Membrane Protein Structural Biology.
Project team	Integral Membrane Proteins Group
Project web site	http://www.thesgc.org/node/9498
Funding partner	The funds supporting this research project are provided by Innovative Medicines Initiative and BBSRC
Recent publications	**Structure and function of human membrane proteins** Rödström, K.E.J., Kiper, A.K., Zhang, W., Rinné, S., Pike, A.C.W., Goldstein, M., Conrad, L., Delbeck, M., Hahn, M., Meier, H., Platzk, M., Quigley, A., Speedman, D., Shrestha, L., Mukhopadhyay, S.M.M., Burgess-Brown, N.A., Tucker, S.J., Mueller, T., Decher, N., Carpenter, E.P. (2019). "A unique lower X-gate in TASK channels traps inhibitors within the vestibule". BioRxiv DOI: https://doi.org/10.1101/706168.

Bushell, S.R., Pike, A.C.W., Falzone, M.E., Rorsman, N.J.G., Ta, C.M., Corey, R.A., Newport, T.D., Shintre, C.A., Tessitore, A., Chu, A., Wang, Q., Shrestha, L., Mukhopadhyay, S., Love, J.D., Burgess-Brown, N.A., Sitsapesan, R., Stansfeld, P.J., Huiskonen, J.T., Tammaro, P., Accardi, A., Carpenter, E.P., (2019), "The structural basis of lipid scrambling and inactivation in the endoplasmic reticulum scramblase TMEM16K". Nature Communications, 10:3956, 1-16, (https://doi.org/10.1038/s41467-019-11753-1).

Schewe, M., Sun, H., Mert, Ü., Mackenzie, A., Pike, A.C.W., Schulz, F., Constantin, C., Vowinkel, K., Conrad, L.J., Kiper, A.K., Gonzalez, W., Musinszki, M., Tegtmeier, M., Pryde, D.C., Belabed, H., Nazare, M., de Groot, B.L., Decher, N., Akler, B., Carpenter, E.P., Tucker, S.J., Baukrowitz, T. A (2019), "Pharmacological Master Key Mechanism that Unlocks the Selectivity Filter Gate in K+ Channels". Science, 363, 6429, 875-880.

Dong, Y.Y., Wang, H., Pike, A.C.W., Cochrane, S.J., Hamedzade, S., Wyszynsk, F.J., Bushell, S.R., Royer, S.F., Widdick, D.A., Sajid, A., Boshoff, H.I., Lucas, R., Liu, W.-M., Lee, S.S., Machida, T., Mehmood, S., Liu, W.-W., Belaya, K., Chu, A., Shrestha, L., Mukhopadhyay, S., Burgess-Brown, N.A., Bibb, M.J., Barry, C.E., Robinson, C.V., Beeson, D., Davis, B.G., Carpenter, E.P., (2018), "Structures of DPAGT1 explain glycosylation disease mechanisms and advance TB antibiotic design". Cell, 175, 1045-1058.

Grieben, M., Pike, A.C.W., Shintre, C., Venturi, E., El-Ajouz, S., Tessitore, A., Shrestha, L., Mukhopadhyay, S., Mahajan, P., Chalk, R., Burgess-Brown, N.A., Sitsapesan, R., Huiskonen, J.T., & Carpenter, E.P., (2017), "Structure of the polycystic kidney disease TRP channel Polycystin-2/PC2.", Nature Structure and Molecular Biology, 24, 114-122.

Wilkes, M., Madej, M.G., Kreuter, L., Rhinow, D., Heinz, V., Sanctis, S., Ruppel, S., Richter, R.M., Joos, F., Grieben, M., Pike, A.C.W., Huiskonen, J.T., Carpenter, E.P., Witzgall, R., Kühlbrandt, W. and Ziegler, C., (2017), "Structures of the TRP channel Polycystin-2 in complex with lipids and cations", Nature Structure and Molecular Biology, , 24, 123-130.

Dong, Y. Y, Pike, A. C.*, Mackenzie, A., McClenaghan, C., Aryal, P., Dong, L., Quigley, A., Grieben, M., Goubin, S., Mukhopadhyay, S., Ruda, G. F., Clausen, M. V., Cao, L., Brennan, P. E., Burgess-Brown, N. A., Sansom, M. S., Tucker, S. J.† & Carpenter, E. P.† "K2P channel gating mechanisms revealed by structures of TREK-2 and a complex with Prozac" (2015). Science, 347, 1256-1259.

Quigley, A., Dong, Y. Y., Pike, A. C. W., Goubin, S., Shrestha, L., Yang, J., Berridge, G., Edwards, A., Bountra, C., Marsden, B., von Delft, F., Bullock, A. N., Burgess-Brown, N. A. and **Carpenter, E. P.** "The structural basis of ZMPSTE24 dependent laminopathies", (2013), Science, 339 (6127), 1604-1607.

	Technical skills Preparing large scale cultures of insect and mammalian cells for protein purification, purification of integral membrane proteins, production and characterisation of antibodies and nanobodies, biophysical studies of membrane proteins and their interactions with protein binders, mutagenesis and other molecular biology methods. Crystallisation and grid preparation for cryo-EM.

The role
The role

Liz Carpenter's Integral Membrane Protein (IMP) group at the Structural Genomics Consortium in Oxford has created a high-throughput system and methods for purification, crystallisation and structural studies of human integral membrane proteins. We aim to solve structures and understand the function of proteins involved in genetic diseases including neuropsychiatry, cancer, rare and metabolic disease, as well as inflammation related disease. We work with a range of proteins including ion channels, solute carriers (SLCs), ABC transporters and integral membrane enzymes. We use heterologous expression of proteins in insect and mammalian cells to produce these proteins. We have assessed more than 400 human IMPs for purification behaviour, in a range of conditions, including varying detergent and buffer systems, followed by large-scale purification and crystallisation using vapour diffusion, LCP and other techniques. The group have purified more than 50 human membrane proteins and have solved the structures of twelve of these challenging proteins in 10 years. Antibodies and nanobodies are essential reagents for both structural and functional studies. These binders allow us to obtain crystals and usable samples for cryo electron microscopy, so we can understand the structures of these proteins. They also allow us to find where the protein resides in a cell and in some cases control the function of the protein. We aim to produce and characterise a range of nanobobies and antibodies for both ion channels and solute carriers.

The Carpenter group is seeking a technician to assist the team with production and crystallisation of integral membrane proteins and their associated antibodies and nanobodies. This position would involve extensive preparation of large-scale (6 to 24 Litres) cultures of insect and mammalian cells for protein purification. You will assist with screening constructs to identify suitable conditions for protein purification, by screening a range of detergents, lipids and buffers. You would then purify proteins to use as antigens for generation of antibodies and nanobodies. You would help with production of the resulting binders and characterisation of their behaviour. You would perform complete purification experiments, and also help other members of the group with their purifications, including spinning down cells, doing membrane preps and preparing buffers. You would use a range of biophysical methods to characterise the interaction between nanobodies/antibodies and their target proteins. You will be required to perform mutagenesis, cloning and other molecular biology techniques. You will be expected to assist with stock keeping, ordering and equipment maintenance.

You will be joining a team of highly motivated and enthusiastic membrane protein scientists, who work closely together to achieve the objectives of the group. You will receive extensive training from experienced members of the group in all necessary techniques. Due to the challenge of delivering the group's objectives, you must be keen to acquire new skills. The Carpenter group also work extensively with colleagues at the SGC, including the Biotech group,

the Research Informatics group and the Crystallography group. Excellent communication and interpersonal skills are therefore essential.

Responsibilities

1. Preparation of recombinant baculoviruses and plasmids for insect cell and mammalian cultures.
2. Maintenance and large scale grow-ups (6 – 24 Litres) of insect cell, mammalian and yeast cultures for protein purification, including harvesting cells.
3. Assisting with screening constructs of membrane proteins for expression and purification using SDS-PAGE and high-throughput purification methods to test constructs in a series of purification conditions.
4. Purifying proteins and assisting the post-doctoral scientists in the group with protein purification, using metal affinity chromatography, size exclusion chromatography (SEC) and other techniques. For this work the technician could be responsible for individual steps of the process, such as spinning down cells, membrane purification or preparing buffers, or a complete purification of a protein.
5. Sending protein samples to collaborators who will generate antibodies and nanobodies.
6. Working with others at the SGC to develop in house screening of libraries for antibodies and nanobodies.
7. Helping with nanobody and antibody production by subcloning, screening nanobodies and antibodies to see if they bind to the required proteins using techniques such as bilayer interferometry (BLI), size exclusion chromatography (SEC) and Western Blots.
8. Performing mutagenesis experiments and subcloning into expression vectors.
9. Assisting with general laboratory and equipment maintenance, including assisting with consumables stock keeping and purchasing for the Carpenter group.
10. Keeping accurate, complete and up-to-date records of all experiments performed, using the SGC's database and electronic notebook system.
11. Interacting with other groups in the SGC and elsewhere.
12. To carry out any other relevant duties as may reasonably be associated with the post and which may be required from time to time.

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 (OHS), 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:

Selection criteria

Essential selection criteria

1. Proven experience as a research technician or student in academic or industrial laboratories.
2. Experience in protein purification.
3. Basic experience in molecular biology, including techniques such as PCR, cloning, mutagenesis.
4. The ability to work as part of a team and to collaborate with colleagues on a range of projects.
5. Excellent oral, presentation and written communication skills in order to provide reliable and precise reports.
6. Well organized, familiar with good laboratory practices and safety requirements.
7. Familiarity with MS Office products, such as Word, Excel, and PowerPoint.
8. A qualification in biology or chemistry, either awarded, or to be completed soon.

Desirable selection criteria

1. Experience in maintenance and large scale grow-ups of insect or mammalian cell cultures.
2. Experience in generation, production and characterisation of antibodies and/or nanobodies.
3. Experience in purification and crystallisation of membrane proteins.
4. Experience in maintaining and using complex equipment such as high-throughput HPLC systems, crystallisation robots etc.
5. Experience working in a high-throughput environment.
6. Previous experience of working under tight timelines.

All employees will have to ensure that their work in the laboratory is conducted safely at all times and, in particular, that work is undertaken following the appropriate health and safety policies and procedures for the particular area, without compromise to their own safety or that of others who may be affected.

About the University of Oxford

Welcome to the University of Oxford. We aim to lead the world in research and education for the benefit of society both in the UK and globally. Oxford’s researchers engage with academic, commercial and cultural partners across the world to stimulate high-quality research and enable innovation through a broad range of social, policy and economic impacts.

We believe our strengths lie both in empowering individuals and teams to address fundamental questions of global significance, while providing all our staff with a welcoming and inclusive workplace that enables everyone to develop and do their best work. Recognising that diversity is our strength, vital for innovation and creativity, we aspire to build a truly diverse community which values and respects every individual’s unique contribution.

While we have long traditions of scholarship, we are also forward-looking, creative and cutting-edge. Oxford is one of Europe's most entrepreneurial universities. Income from external research contracts in 2016/17 exceeded £564m and we rank first in the UK for university spin-

outs, with more than 130 companies created to date. We are also recognised as leaders in support for social enterprise.

Join us and you will find a unique, democratic and international community, a great range of staff benefits and access to a vibrant array of cultural activities in the beautiful city of Oxford.

For more information, please visit www.ox.ac.uk/about/organisation.

Medical Sciences

The Medical Sciences Division is an internationally recognized centre of excellence for biomedical and clinical research and teaching. We are the largest academic division in the University of Oxford

World-leading programmes, housed in state-of-the-art facilities, cover the full range of scientific endeavour from the molecule to the population. With our NHS partners we also foster the highest possible standards in patient care.

For more information please visit: www.medsci.ox.ac.uk

Nuffield Department of Clinical Medicine (NDM)…fostering your career in science

The Nuffield Department of Clinical Medicine (NDM) is one of the largest departments of the University of Oxford and is part of the Medical Sciences Division, with responsibility for a significant part of the teaching of clinical students within the Medical School.

NDM has significant financial turnover and complexity, resulting from its diverse research portfolio, its geographical spread and its close links with NHS funding and strategic teams involved in the development and delivery of increasingly integrated clinical research platforms. For more information please visit: http://www.ndm.ox.ac.uk/home

The Nuffield Department of Clinical Medicine has been presented with a Departmental Athena SWAN Silver award in recognition of the commitment made to promote gender equality through our organisational and cultural practices and our efforts to improve the working environment for both men and women. For more information please see our Departmental Athena SWAN pages: www.ndm.ox.ac.uk/working-for-ndm/aboutndmatheneswan/ .

Structural Genomics Consortium (SGC)

The Structural Genomics Consortium (SGC), a not-for-profit, public-private partnership funds pre-competitive research that contributes to new hypotheses in understanding and treating human disease, and the subsequent identification of new targets for drug discovery. The SGC supports pioneering research at the University of Oxford (UK), University of Toronto (Canada), University of Campinas (Brazil), and University of North Carolina (USA). The reagents and knowledge related to human proteins that the SGC supports are made openly accessible to researchers around the world to accelerate the discovery of new medicines in order to bring potentially life-saving drugs to market faster and at a lower cost.

SGC Oxford, a part of the Nuffield Department of Clinical Medicine, receives funding from public, charitable and private sector organisations such as the European Commission, UK Research Councils, Wellcome Trust, and pharmaceutical companies. Research in SGC Oxford is focused on the production and characterisation of the 3-dimensional structures of soluble and

of integral membrane proteins, the discovery of selective chemical probes that can modulate protein function, and the development of target enabling packages that transform genetic hits into starting points for drug discovery. SGC Oxford shares its research outputs through collaborations with researchers worldwide.

For more information please visit: http://www.thesgc.org/scientists/groups/oxford/

How to apply

Before submitting an application, you may find it helpful to read the 'Tips on applying for a job at the University of Oxford' document, at

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

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

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

If you would like to apply, click on the **Apply Now** button on the 'Job Details' page and follow the on-screen instructions to register as a new user or log-in if you have applied previously. Please provide details of two referees and indicate whether we can contact them now.

You will also 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.

All applications must be received by **midday** 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).

Should you experience any difficulties using the online application system, please email recruitment.support@admin.ox.ac.uk. Further help and support is available from www.ox.ac.uk/about_the_university/jobs/support/. 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 e-recruitment system 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: www.admin.ox.ac.uk/councilsec/compliance/gdpr/privacynotices/job/. The University's Policy on Data Protection is available at: www.admin.ox.ac.uk/councilsec/compliance/gdpr/universitypolicyondataprotection/.

The University's policy on retirement

The University operates an Employer Justified Retirement Age (EJRA) for all academic posts and some academic-related posts. The University has adopted an EJRA of 30 September before the 69th birthday for all academic and academic-related staff in posts at **grade 8 and above**. The justification for this is explained at: www.admin.ox.ac.uk/personnel/end/retirement/acrelretire8+/.

For **existing** employees, any employment beyond the retirement age is subject to approval through the procedures: www.admin.ox.ac.uk/personnel/end/retirement/acrelretire8+/.

There is no normal or fixed age at which staff in posts at **grades 1–7** 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.

Benefits of working at the University

Employee benefits

University employees enjoy 38 days' paid holiday, generous pension schemes, travel discounts, and a variety of professional development opportunities. Our range of other employee benefits and discounts also includes free entry to the Botanic Gardens and University colleges, and discounts at University museums. See www.admin.ox.ac.uk/personnel/staffinfo/benefits.

University Club and sports facilities

Membership of the University Club is free for all University staff. The University Club offers social, sporting, and hospitality facilities. Staff can also use the University Sports Centre on Iffley Road at discounted rates, including a fitness centre, powerlifting room, and swimming pool. See www.club.ox.ac.uk and www.sport.ox.ac.uk/oxford-university-sports-facilities.

Information for staff new to Oxford

If you are relocating to Oxfordshire from overseas or elsewhere in the UK, the University's Welcome Service website includes practical information about settling in the area, including advice on relocation, accommodation, and local schools. See www.welcome.ox.ac.uk.
There is also a visa loan scheme to cover the costs of UK visa applications for staff and their dependents. See www.admin.ox.ac.uk/personnel/permits/reimburse&loanscheme/.

Family-friendly benefits

With one of the most generous family leave schemes in the Higher Education sector, and a range of flexible working options, Oxford aims to be a family-friendly employer. We also subscribe to My Family Care, a service that provides practical advice and support for employees who have caring responsibilities. The service offers a free telephone advice line, and the ability to book emergency back-up care for children, adult dependents and elderly relatives. See www.admin.ox.ac.uk/personnel/staffinfo/benefits/family/mfc/.

Childcare

The University has excellent childcare services, including five University nurseries as well as University-supported places at many other private nurseries.
For full details, including how to apply and the costs, see www.admin.ox.ac.uk/childcare/.

Disabled staff

We are committed to supporting members of staff with disabilities or long-term health conditions. For further details, including information about how to make contact, in confidence, with the University's Staff Disability Advisor, see www.admin.ox.ac.uk/eop/disab/staff.

Staff networks

The University has a number of staff networks including the Oxford Research Staff Society, BME staff network, LGBT+ staff network and a disabled staff network. You can find more information at www.admin.ox.ac.uk/eop/inpractice/networks/.

The University of Oxford Newcomers' Club

The University of Oxford Newcomers' Club is an organisation run by volunteers that aims to assist the partners of new staff settle into Oxford, and provides them with an opportunity to meet people and make connections in the local area. See www.newcomers.ox.ac.uk.