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1. **Research Fellow - Cell/Molecular Biology (Ref. NB/rf)**
2. **Postdoctoral Scientist – Cell/Molecular Biology (Ref. NB/pds)**
3. **Research Fellow – Bioanalytical Mass Spectrometry (Ref. JB/rf)**
4. **Postdoctoral Scientist – Bioanalytical Mass Spectrometry (Ref. JB/pds)**

Project Overview:

There is very significant interest in Gene Therapy approaches to disease treatment currently. Adeno-associated virus (AAV)-based gene therapies represent an exciting new wave of advanced therapy medicinal products (ATMPs) that are being generated for the treatment of ailments caused by a defective gene within certain patient populations. AAV based gene therapy is used to deliver a correctly functioning copy of the gene to the patient. Very promising results have been reported in a number of genetic diseases including haemophilia and ocular degeneration.

However, current yields of AAV from the manufacturing process mean that supplying patients with the required quantities of medicine will be challenging.

This project – a collaboration between NIBRT and Allergan Biologics – will address the following challenges in AAV production:

- To optimise a cell culture process for generation of infectious AAV particles of various serotypes
- To establish vectors and transfection/transduction conditions to minimise incorrect packaging events
- To investigate sensitive analytical methods for the characterisation of the resulting AAV particles that enable differentiation between full and empty AAV capsids

NIBRT is hiring two **Research Fellows** and two **Postdoctoral Scientists** to address these areas of interest.

Tenure

Appointments will be made on a full-time, temporary basis for up to 24 months.

Research Fellow (Cell/Molecular Biology)

Role: We are seeking to hire a highly experienced scientist to investigate the generation of high quality AAV packaged vector using alternative expression systems. The goal will be to find optimal conditions for AAV yield without compromising the infectivity of the particles. Furthermore, the challenge of minimizing empty capsid formation will be addressed using various molecular biology and cell culture format approaches including the development of a scaled-down process for medium-throughput AAV production. The Research Fellow will be responsible for planning lab activities in conjunction with the PI, executing the experiments, managing the activities of a postdoctoral scientist and reporting on project outcomes to the PI and industry collaborators.

Qualifications:

The successful candidate will have the following essential qualifications and experience:

- PhD in Molecular Biology/Cell Biology/Virology or closely-related discipline
- Minimum 5 years postdoctoral experience – ideally including viral vector generation
- Expert knowledge and experience with mammalian cell culture, molecular biology techniques including DNA cloning, qPCR, virus preparation, transfection, and other cell-based analytical techniques including flow cytometry and imaging
- A proven ability to work within a team focused on different elements of a project
- Evidence of excellent communications skills – report writing, conference presentations, senior author on scientific publications

The successful candidate will have the following desirable qualifications and experience:

- Experience working on industry-focused projects with tight deadlines
- Knowledge and experience of protein/virus analytical techniques
- Experience managing other scientists in order to meet project deliverables
- Experience with Next Generation Sequencing library generation and analysis

Enquiries: niall.barron@nibrt.ie

Postdoctoral Scientist (Cell/Molecular Biology)

Role: This element of the project will address AAV viral particle packaging accuracy and efficiency. Current AAV production platforms are notorious for the large number of empty capsids generated. The presence of these reduces the efficacy of the medicine and creates problems measuring dosage. Furthermore, it has been shown that some particles can contain mis-incorporated DNA – often from the host cell or packaging plasmids. This aspect of the project will attempt to reduce the incidence of empty or mis-packaged AAV particles by manipulation of the packaging vectors used in the transfection. The appointed postdoc will work closely with Research Fellow 1 to address these challenges.

Qualifications:

The successful candidate will have the following essential qualifications and experience:

- PhD in Molecular Biology/Cell Biology/Virology or closely-related discipline
- Experience with mammalian cell culture and molecular biology techniques including DNA cloning, qPCR and transfection
- A proven ability to work within a team focused on different elements of a project
- Excellent communications skills – report writing, oral presentations, scientific publications

The successful candidate will have the following desirable qualifications and experience:

- 2+ years postdoctoral experience – ideally including viral vector generation
- Knowledge and experience of cell/protein/virus analytical techniques

- Self-motivated and capable of working with other scientists in order to meet project deliverables
- Knowledge of Next Generation Sequencing technology

Enquiries: niall.barron@nibrt.ie

Research Fellow (Bioanalytical Mass Spectrometry)

Role: Applications are sought from experienced and motivated scientists to investigate the use of native high-resolution mass spectrometry and native LC-MS for the characterisation of AAV product related impurities. The successful candidate will develop and apply native MS and native LC-MS methods for the characterisation of fully, partially full and empty AAV particles to support the molecular biology and bioproduction aspects of the project. The successful candidate will have experience with the use of high resolution Orbitrap mass spectrometry for the characterisation of proteins, protein complexes or viruses under native conditions. The successful candidate will also have experience in the development and application of liquid phase separation strategies for profiling the heterogeneity of these biomolecules, ideally with hyphenation to high resolution mass spectrometry. The Research Fellow will be responsible for planning lab activities in conjunction with the PI, executing the experiments, managing the activities of a postdoctoral scientist and reporting on project outcomes to the PIs and industry collaborators.

Qualifications:

The successful candidate will have the following essential qualifications and experience:

- PhD in Analytical Chemistry, Bioanalytical Chemistry, Structural Biology or closely-related discipline
- Minimum 5 years experience characterising proteins, protein complexes or viral particles using mass spectrometry, ideally native mass spectrometry
- Expert knowledge and experience liquid chromatography method development for the separation of proteins, protein complexes or viral particles
- Proven experience in the analysis of native mass spectrometry data using appropriate software tools
- A proven ability to work within a team focused on different elements of a project
- Evidence of excellent communications skills – report writing, conference presentations, senior author on scientific publications

The successful candidate will have the following desirable qualifications and experience:

- Experience working on industry-focused projects with tight deadlines
- Knowledge and experience of other protein/virus analytical techniques
- Experience managing other scientists in order to meet project deliverables
- Experience with molecular modelling and protein structural bioinformatics tools

Enquiries: jonathan.bones@nibrt.ie

Postdoctoral Scientist (Bioanalytical Mass Spectrometry)

Role: Applications are sought from a motivated postdoctoral scientist to develop LC-MS based methods for the confirmation of viral particle identity and also to understand the role of conformational changes associated with the potency of AAV based gene therapies. The successful candidate will develop and apply peptide mapping and top-down LC-MS approaches for the characterisation of viral particle proteins. Additionally, the successful candidate will use hydrogen-deuterium exchange mass spectrometry to probe conformational changes necessary to ensure that the produced AAV particles exhibit high potency. The appointed postdoc will work closely with Research Fellow 2 and the project PI and will be responsible for planning lab activities, executing the experiments and reporting on project outcomes to the PIs and industry collaborators.

Qualifications:

The successful candidate will have the following essential qualifications and experience:

- PhD in Analytical Chemistry, Bioanalytical Chemistry, Protein Characterisation, Proteomics, Structural Biology or closely-related discipline
- Proven practical experience in the use of LC-MS methodologies for protein identification, quantitation and structural comparability assessment
- Proven experience in the analysis of mass spectrometry data using appropriate software tools
- A proven ability to work within a team focused on different elements of a project
- Excellent communications skills – report writing, oral presentations, scientific publications

The successful candidate will have the following desirable qualifications and experience:

- 2+ years postdoctoral experience – ideally including LC-MS method development for protein characterisation
- Knowledge and experience of other protein/virus analytical techniques
- Self-motivated and capable of working with other scientists in order to meet project deliverables
- Knowledge of molecular modelling and protein structural bioinformatics tools

Enquiries: jonathan.bones@nibrt.ie

How To Apply:

To apply for a position(s) please email your CV, cover letter and the names and contact details of two referees in a combined PDF document to careers@nibrt.ie.

Please include '*Your Name, the position(s) you are applying for & the Ref.*' in the subject line.

Closing date is 20th August 2019.

Applicants must be eligible to work in Ireland and hold an up-to-date relevant Visa entitling them to work in Ireland.