



<b>Research Centre:</b>	National Institute for Cellular Biotechnology
<b>Post title:</b>	Postdoctoral Researcher in the functional assessment of PI3K/AKT pathway mutations as predictors of PI3K inhibitor sensitivity
<b>Level on Framework:</b>	Level 1
<b>Post duration:</b>	Fixed-term contract up to 24 months

As part of this role the researcher will be required to participate in the DCU Research Career Framework. This framework is designed to provide significant professional development opportunities to Researchers and offer the best opportunities in terms of a wider career path.

#### **Background and Role:**

A postdoctoral position is available with the Molecular Therapies for Cancer in Ireland within the National Institute for Cellular Biotechnology at Dublin City University (DCU) to undertake research on the following project: "The impact of mutations in PI3K/AKT pathway gene loci on response to PI3K inhibitors". This postdoctoral position is funded through a Health Research Board Emerging investigator award.

PI3K-inhibitors demonstrate clinical efficacy in the treatment of breast cancer. Oncogenic missense mutations in the PIK3CA gene are the most obvious potential prognostic and therapeutic markers of PI3K-inhibitor sensitivity. However, many patients who don't have a PIK3CA missense mutation also respond to PI3Kinhibitors.

Supporting this, data generated by our lab, as well as published clinical trial results, suggest that an extended cohort of patients who are PIK3CA wild-type could benefit from PI3K-inhibitors. We therefore hypothesise that both coding and non-coding 'regulatory' mutations in the gene loci of members of the PI3K/AKT-pathway, influence how BCs respond to PI3K inhibitors.

Therefore, the key question this proposal will address is "*what is the extended cohort of gene mutations in patients with PIK3CA wild-type tumours that predict responsiveness to PI3K-inhibitors*". To test our hypothesis, we will undertake the following:

**Objective 1:** To identify novel coding and non-coding mutations in the gene loci of members of the PI3K/AKT pathway.

**Objective 2:** To functionally evaluate the oncogenic potential of coding and non-coding mutations which affect the activity of the PI3K/AKT-pathway.

**Objective 3:** To determine the most synergistic combinations of PI3K inhibitors and specific targeted therapies to best treat a cohort of BC patients with PI3K/AKT-pathway mutated cancer.

**Impact on breast cancer:** At the end of this project we will have identified the most oncogenic mutations affecting the PI3K/AKT-pathway and discovered the most synergistic combination of drugs that can be used to effectively treat breast cancers with these mutations.

The project will be supervised by Dr. Alex Eustace, Research lead of Molecular Therapeutics for Cancer in Ireland, DCU.

#### **Principle Duties and Responsibilities:**

Reporting to his/her Principal Investigator the Postdoctoral Researcher will:

- Conduct a specified programme of research under the supervision and direction of the Principal Investigator.
- Engage with internal and external stakeholders including academic and industry partners/collaborators as appropriate.
- Carry out administrative work associated with the programme as necessary.
- Supervise and assist postgraduate students working in this area with their research.
- Document all experimental data, analyses and protocols.
- Report/present regularly at group meetings.
- Attend relevant meetings, seminars, training and conferences.
- Contribute to manuscript preparation relevant to the project.
- Complete a detailed report upon completion of the project.
- Undertake standard laboratory management tasks.
- Monitor and report on project budget expenditure.
- Assist in identifying and developing future research and funding initiatives.
- Undertake other tasks as defined by the project leaders.

#### **Minimum Criteria**

The successful candidate will hold a PhD in the area of cancer/molecular biology or a related discipline.

In addition, it is desirable that the candidate has a subset of the following skills:

- Experience with CRISPR editing (including design, viral transfection, functional assessment)
- Molecular Biology techniques (Cloning/primer design/PCR/luciferase reporter assays)
- Maintenance and quality control of a panel of cancer cell lines
- Assessment of the effect of targeted therapies on cell growth, cell cycle progression and cell death mechanisms
- *In vivo* rodent tumour models and drug delivery
- Experience in working with the R-statistical platform
- Experience in the use of UCSC browser

#### **Mandatory Training:**

The post holder will be required to undertake the following mandatory compliance training: Orientation, Health and Safety and Intellectual Property and Data Protection training. Other training may need to be undertaken when required.

**Candidates will be assessed on the following competencies:**

**Discipline knowledge and Research skills** – Demonstrates knowledge of a research discipline and the ability to conduct a specific programme of research within that discipline

**Understanding the Research Environment** – Demonstrates an awareness of the research environment (for example funding bodies) and the ability to contribute to grant applications

**Communicating Research** – Demonstrates the ability to communicate their research with their peers and the wider research community (for example presenting at conferences and publishing research in relevant journals) and the potential to teach and tutor students

**Managing & Leadership skills** - Demonstrates the potential to manage a research project including the supervision of undergraduate students