The purpose of this role will be to have specific responsibility for research, for developing research objectives and proposals for a research project in “Targeting refractory and dormant stem cells in childhood leukaemia”. This position is an exciting interdisciplinary project funded by the Little Princess Fund within the Children's Cancer and Leukaemia Group (CCLG). You will be expected to plan and conduct work using approaches or methodologies and techniques appropriate to the type of research, and will be responsible for writing up the work for publication.

You will join an established team, led by Dr Alex Thompson and Dr Claire Seedhouse, whose main areas of research interest include pre-clinical modelling of blood cancers and evaluation of novel therapies.

This post will be based within the new purpose-built expansion of the Centre for Biomolecular Sciences (CBS) (https://www.nottingham.ac.uk/ccs/cancer-research/cancer-research.aspx) that houses the Centre for Cancer Sciences within the University of Nottingham. This building brings together interdisciplinary groups from within and outside the Division of Cancer and Stem cells including Cancer, Stem Cells, Immunology, Pathology, Bioengineering and Pharmacy relevant to the project. The project builds on existing work in which candidate drugs that potentially target dormant and refractory stem cells in leukaemia have been identified but now need to be validated in advanced models of childhood disease. In partnership with Professor Ken Mills (Queen’s University Belfast) and in collaboration with Dr Jasper de Boer (University College London) and Professor Robert Wynn (Chair of the Cell Bank Steering Committee Bloodwise Childhood Leukaemia Cell Bank), the project will combine stem cell technology, 3D and in vivo modelling and clinical samples, to evaluate the efficacy of a cohort of drugs against leukaemia and other blood cancers. De-risking of such drugs will provide the basis for future development within a therapy-accelerated programme of current and future clinical trials.

For background, the summary of the original proposal is provided here:
A major challenge to curative therapy of cancer is identifying and targeting cancer-specific or cancer-dependent pathways that are non-toxic to normal tissue. This is particularly important in childhood cancer to reduce the risk of long-term, life altering side effects. Leukaemia is the most common cancer in children. Translocations in the Mixed Lineage Leukaemia (MLL) gene results in formation of a fusion protein that drives leukaemia generation and development. Childhood leukaemia patients that harbour this translocation have a particularly dismal prognosis and are in urgent need of better therapies.

Over the last decade, advanced diagnosis and precision medicine has dramatically improved survival rates for children with acute lymphoid but not acute myeloid leukaemia. Despite initial remission, acute myeloid leukaemia patients exhibit higher rates of relapse caused by greater
numbers of resistant or refractory leukaemia stem cells that remain dormant within a defined microenvironment during treatment. We have recently developed individual models of (a) dormancy that identify or mimic leukaemia stem cells and (b) MLL-AF9 leukaemia. Using bioinformatics, we have identified candidate FDA-approved drugs and small molecules that (a) potentially reverse dormancy in acute myeloid leukaemia and (b) target the key oncogenic HOX pathway in MLL-AF9. In addition, we have developed a patient-based assay to examine drug sensitivity of dormant versus proliferating primary leukaemia cells.

This proposal aims to further examine FDA-approved drugs specifically targeted to leukaemia stem cells in both traditional and novel models of acute myeloid leukaemia. In this way, we aim to de-risk a subset of candidate FDA-approved drugs with low toxicity for acceleration into PhaseI/II clinical trials.

The successful candidate will combine excellence in research, collaboration, communication and meeting deadlines. It is a particular need for the project that that candidate has experience in blood cancer cell and/or patient tissue culturing and analysis and an ability to learn new techniques. This may include, for example, skills in qPCR / RNA profiling, high content imaging (e.g. confocal plate reader), flow cytometry, CRISPR/Cas9 editing, generating dose response curves and use of in vivo imaging systems.

You will have the opportunity to use their initiative and creativity to identify areas for research, develop research methods and extend your research portfolio.

<table>
<thead>
<tr>
<th>Main responsibilities</th>
<th>% time per year</th>
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<tbody>
<tr>
<td><strong>Research Responsibilities:</strong></td>
<td>70 %</td>
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<tr>
<td>To manage, plan and conduct own research activity using recognised approaches, methodologies and techniques within the research area. To resolve problems, in meeting research objectives and deadlines in collaboration with others.</td>
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<tr>
<td>Develop advanced pre-clinical models of leukaemia to further validate candidate drugs and de-risk such therapies for future incorporation into clinical trials.</td>
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<tr>
<td>Validate and identify existing, novel or repurposed therapies, either singly or in combination, to target blood cancers using systems involving combination drug screening approaches in current models of leukaemia</td>
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<tr>
<td>To identify opportunities and assist in writing bids for research grant applications. Prepare proposals and applications to both external and/or internal bodies for funding, contractual or accreditation purposes.</td>
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<tr>
<td>Read academic papers, journals and textbooks to keep abreast of developments in own specialism and related disciplines and formulate, write and submit grants for fellowship awards, project and travel support to attend and present new experimental data at national and international meetings.</td>
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</table>
2 Engagement, Communication and Continuation Responsibilities:
- To write up research work for publication and/or contribute to the dissemination at national/international conferences, resulting in successful research outputs.
- To collaborate with academic colleagues on areas of shared interest for example, course development, collaborative or joint research projects.
- Prepare data and regular progress reports to members of the Haematology and Blood Cancer Research Group, internal and external audiences and partners. Achieve milestones / deadlines, which will be continuously evaluated and actively engage with the funding agency.

% time per year

20%

Main responsibilities
(Primary accountabilities and responsibilities expected to fulfil the role)

3 Teaching:
- To supervise undergraduate and/or postgraduate students projects as appropriate.
- To participate in the assessment of student knowledge and co-supervise projects at Masters level.
- You are expected to make a contribution to teaching that is in balance with wider contributions to research and other activities.

10%

4 Other:
- Any duties as required in accordance with the nature and grade of the post

N/A

Person specification

<table>
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<th>Essential</th>
<th>Desirable</th>
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<tr>
<td>Skills</td>
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<tr>
<td>• Excellent oral and written communication skills, including the ability to communicate with clarity on complex information.</td>
<td>• Previous experience in haematology/cancer biology.</td>
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<tr>
<td>• Ability to creatively apply relevant research approaches, models, techniques and methods.</td>
<td>• Experience in stem cell culture and CRISPR/Cas9 genome editing.</td>
</tr>
<tr>
<td>• Ability to build relationships and collaborate with others, both internally and externally.</td>
<td>• Experience in bioinformatics.</td>
</tr>
<tr>
<td>• High analytical ability to analyse and illuminate data, interpret reports, evaluate and criticise texts and bring new insights.</td>
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</table>
### Role profile

**Knowledge and experience**

- Ability to assess and organise resource requirements and deploy effectively.
- Some practical experience of applying the specialist skills and approaches and techniques required for the role.
- Experience in use of research methodologies and techniques to work within area.
- These include skills in:
  - Tissue culture and in-vitro drug treatment of primary cells or cell lines.
  - Cellular analysis such as fluorescence microscopy, flow cytometry and colony assays and use of biochemical techniques such as protein analysis, cell cycle apoptosis.
- Previous success in gaining support for externally funded research projects.
- Experience of developing new approaches, models, techniques or methods in research area.
- Knowledge of GLP working procedures.
- Experience in assay development.

### Qualifications, certification and training (relevant to role)

**Essential**

- PhD or equivalent in Haematology, Biochemistry, Pharmacy or Biomedical Science related subject, or the equivalent in professional qualifications and experience in research area OR near to completion of a PhD.

**Desirable**

- 1st Class undergraduate degree in science.
- Hold a personal animal licence.

### Statutory, legal or special requirements

- Knowledge of Health and Safety regulations and ability to put them into practice.
- Adherence to relevant codes of practice and ethical requirements for working with patient tissues and animals.

### Other

- Willingness to adopt the Ethos and Principles of the School of Medicine.
- Scientific memberships e.g. AACR.
- Experience in working with industry.
- Evidence of winning awards.
- Be willing to work irregular hours when necessary for the progress of the research project.
Role profile

The University of Nottingham is focused on embedding equality, diversity and inclusion in all that we do. As part of this, we welcome a diverse population to join our work force and therefore encourage applicants from all communities, particularly those with protected characteristics under the Equality Act 2010. The School of Medicine holds a Silver Athena SWAN award in recognition of our achievements in promoting and advancing these principles. Please see http://www.nottingham.ac.uk/medicine/about/athena-swan.aspx

Expectations and behaviours

The University has developed a clear set of core expectations and behaviours that our people should be demonstrating in their work, and as ambassadors of the University's strategy, vision and values. The following are essential to the role:

**Valuing people**
Is always equitable and fair and works with integrity. Proactively looks for ways to develop the team and is comfortable providing clarity by explaining the rationale behind decisions.

**Taking ownership**
Is highly self-aware, looking for ways to improve, both taking on board and offering constructive feedback. Inspires others to take accountability for their own areas.

**Forward thinking**
Driven to question the status quo and explore new ideas, supporting the team to “lead the way” in terms of know-how and learning.

**Professional pride**
Sets the bar high with quality systems and control measures in place. Demands high standards of others identifying and addressing any gaps to enhance the overall performance.

**Always inclusive**
Ensures accessibility to the wider community, actively encouraging inclusion and seeking to involve others. Ensures others always consider the wider context when sharing information making full use of networks and connections.
Key relationships with others

- **Line manager**: 
- **Role holder**: 
  - **Associate Professor in Stem Cell Technology**
  - **Research Fellow**
  - **Key stakeholder relationships**
    - Partners and Collaborators
    - Colleagues
    - Students