The Institute of Cancer Therapeutics is excited to announce its first **three fully-funded studentships** (3.5 years) at its newly created **Doctoral Training Centre**. Focused on the generation of new anticancer prodrugs, the ICT-DTC has been created following a major £2m investment by ICT spin-out company Incanthera Ltd.

We are now looking for applications from outstanding potential PhD candidates.

**Why study with us?**

- Fully-funded PhD studentships at a leading UK research institute focused on cancer drug discovery
- Join a multi-disciplinary research environment, with facilities for cancer drug design and synthesis, *in vitro* pharmacology and molecular biology, and *in vivo* biology
- Join an academic team with a track record of success in translational research, commercialisation, and delivering drug candidates to the clinic.

**What do we offer?**

Doctoral level training in a unique multidisciplinary environment at the interfaces between medicinal chemistry and pharmacology. Cutting-edge research projects focused on exciting new anticancer prodrugs. Modern facilities. Extensive support: an experienced supervisory team, an independent mentor, dedicated medicinal chemistry and pharmacology research support (two active senior laboratory-based researchers working alongside you, and providing training), a strongly-focused team environment. Each studentship benefits from a full training package in techniques for compound synthesis, analysis, and for *in vitro* screening for pharmacology and drug metabolism.

**Who should apply?**

Applicants with a passion for cancer drug discovery, medicinal chemistry and pharmacology. Candidates should have, or expect to obtain, a first or good upper second class degree (or non-UK equivalent) in a relevant science subject (see individual projects overleaf) or an appropriate Masters qualification. Applications are invited from UK and EU citizens. Outstanding international students may be eligible for a University bursary and will be considered - please enquire.

**Funding**

Studentships cover tuition fees, a tax free stipend (at standard MRC rates) for the duration programme and writing-up (3.5 years total) and a generous research budget. A travel fund is also provided for each student to guarantee participation in a national and international conference. Funding for specific training courses is also included in the DTC.

**How to apply**

For further information or informal enquiries about the ICT DTC, please contact Dr Robert Falconer, (email: r.a.falconer1@bradford.ac.uk) or take a look at our website [www.bradford.ac.uk/ict/](http://www.bradford.ac.uk/ict/)

Applications should be submitted to the main contact associated with the individual project (see project descriptors overleaf).

You should submit a **CV** (max. 2 pages) and a **covering letter** outlining your background and interest in the project(s). Applicants may indicate that they wish to be considered for more than one of the studentships.

Application deadline: we will continue to accept applications until all places are filled. We will initially consider all applications received by 30 April 2019 for shortlisting and interview.
# Project #1: Novel targeted cytotoxic chemotherapy for prostate cancer

**Background** Taxanes (docetaxel, paclitaxel) are the single most important treatment for men with advanced prostate cancer, but consistently cause dose-limiting toxicities. There is, therefore, a need to develop novel strategies to optimise taxane therapy. Membrane-type matrix metalloproteinases (MT-MMPs) are functionally active at high levels in prostate cancer tissue, have negligible activity in normal tissue, and selectively cleave specific peptide sequences. In preliminary studies, we demonstrated proof-of-concept for an MT-MMP-activated taxane (paclitaxel) prodrug, ICT3205, in a prostate cancer model.

**Aim** To develop a new non-toxic prodrug therapy for prostate cancer

**Focus** Optimisation of our prototype prodrug, ICT3205. Fine-tuning of MT-MMP peptide sequence selectivity, and chemical modifications to enhance aqueous solubility. Evaluation of prodrug stability in normal tissues, prodrug activation in tumour tissues; MMP cleavage; assessment of aqueous solubility. Pilot pharmacokinetics study in mice for most promising compound.

**Main skills** Medicinal chemistry; peptide chemistry; compound analysis; pharmacological assays; drug metabolism


**Background required** Chemistry, Medicinal Chemistry, Pharmacy or related subjects

**Contact**: Prof Paul Loadman ([p.m.loadman@bradford.ac.uk](mailto:p.m.loadman@bradford.ac.uk)); Dr Robert Falconer ([r.a.falconer1@bradford.ac.uk](mailto:r.a.falconer1@bradford.ac.uk))

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# Project #2: Novel targeted cytotoxic chemotherapy for colorectal cancer

**Background** Metastatic colorectal cancer (CRC) is largely incurable by conventional approaches and requiring the development of better therapeutics. Clinical studies indicate that increased levels of an enzyme known as cytochrome P450 2W1 (CYP2W1) positively correlate with the degree of tumour malignancy, as well as with decreased 10-year survival in patients with CRC. We have developed prodrugs of the duocarmycin family of natural products and shown in proof-of-concept studies that a lead prodrug (ICT2706) is selectively activated in CRC in vitro and in vivo.

**Aim** To develop a new non-toxic prodrug therapy for colorectal cancer

**Focus** Re-engineering of the duocarmycin scaffold through design and synthetic manipulations to discover novel prodrugs with clinical potential. Compounds with high affinity for CYP2W1 will be co-crystallised with the enzyme to provide mechanistic insight into the active site and function of the enzyme. Lead prodrug will be investigated in an appropriate in vivo CRC model.

**Main skills** Organic/medicinal chemistry; compound analysis; pharmacological assays; drug metabolism


**Background required** Chemistry, Medicinal Chemistry, Pharmacy or related subjects

**Contact**: Dr Klaus Pors ([k.pors1@bradford.ac.uk](mailto:k.pors1@bradford.ac.uk))

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# Project #3: Novel prodrug anti-metastatic therapy for neuroblastoma

**Background** Neuroblastoma is a paediatric cancer with a desperate need of new non-toxic therapies to combat relapse, which occurs in 50-60% of children, despite an initially good response to chemotherapy and surgery. Current treatments to prevent and/or treat relapse lack efficacy in some patients, and cause significant side-effects. We previously demonstrated that cytidine monophosphate (CMP) inhibits polysialyltransferase, the enzyme that regulates biosynthesis of polysialic acid on neuroblastoma cells, promoting tumour migration, invasion and metastasis. CMP, while an effective inhibitor, lacks potency due to very poor tumour cell penetration and in vivo instability.

**Aim** To develop a new type of non-toxic prodrug therapy for neuroblastoma, which will inhibit tumour spread (metastasis)

**Project** Synthesis of novel prodrugs of CMP, using clinically proven technology, to address these shortcomings. Evaluation of prodrug stability in blood, neuroblastoma cell penetration and subsequent prodrug release, and effects on tumour cell polysialylation, migration and invasion. Pilot pharmacokinetics study in mice for most promising compound.


**Main skills** Medicinal chemistry; compound analysis; pharmacological assays; cell culture; drug metabolism

**Background required** Chemistry, Medicinal Chemistry, Pharmacy or related subjects

**Contact**: Dr Robert Falconer ([r.a.falconer1@bradford.ac.uk](mailto:r.a.falconer1@bradford.ac.uk))