Horizon 2020 Pitch
Topic of interest: SC1-BHC-09-2018: Innovation platforms for advanced therapies of the future

What we do? Our research is focussed on identifying novel immunotherapeutic targets, with a particular interest in inflammation-driven cancer and obesity-associated morbidities such as non-alcohol fatty liver disease (NAFLD). We are highly experienced in translational research studies and are well-published in the space of obesity, inflammation, cancer and T and NK cells. Our group's extensive experience in leading human research studies together with access to fresh and biobanked tumour tissue, adjacent normal tissue, blood, serum, plasma, adipose tissue and liver from cancer patients have been integral in the generation of high quality data outputs. A well-established multidisciplinary consenting, sampling, biobanking and processing system exists within our department. Dedicated biobank managers collect and manage patient samples and data. Blood and tissue samples are delivered to the research team for immediate processing while additional samples of serum, tissue and tissue conditioned media are stored in secure dedicated biobanking freezers with sophisticated temperature monitoring systems. All samples are linked to clinical data for subsequent analysis including age, sex, tumour stage, lymph node involvement and metastasis, treatment regime and pathological response. To date, our department have acquired blood and tissue samples from over 950 upper and lower GI cancer patients. These samples facilitate highly translational and cutting edge research across the spaces of immunology, metabolism, radiobiology and theranostics.

Scope identified in the call topic	**How our expertise meets this scope**
Studying the basic biology of the potential therapy and investigating its mode of action, proof of concept (*in vitro*, in animal models – where necessary - or first-in–man studies); safety, efficacy, characterisation, refinement and manufacturing of the product could be considered.	Amidst a tidal wave of FDA approvals for checkpoint inhibitors, a number of undesirable inflammatory conditions have emerged during their systemic administration. Therefore, it is becoming more apparent that it is crucial to study their basic biology, off-target effects and their susceptibility to loss during chemo-radiotherapy (CRT). This can all be achieved by our team using **pre-optimised functional assays and patient samples**. So far, our team have completed collaborative and productive projects with industry partners to identify the potential of novel immunotherapeutics by profiling their immunogenicity in human tissue samples and to contribute to the safety profile of approved immunotherapeutics in inflammation driven cancer and obesity-associated disease.
Sex and gender differences should be investigated, where relevant.	Our biobank houses **serum, tissue and conditioned media from both male and female cancer patients** and all samples are linked to clinical data for subsequent analysis including age and sex. Furthermore, our biobank also contains age and sex matched serum and conditioned media samples from non-cancer patients. Therefore, any sex and gender differences can be studied within and outside the context of cancer.

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Examples of issues that have been identified as holding back the field include; 1) Immunogenicity of potential new therapies	1) Our team has initiated collaboration with pharmacists within our institution to elucidate the immunogenicity of their novel anti-cancer agents and we shall be seeking further funding to propel such testing forward. We can perform such studies to assess drug efficacy using cancer patient samples under the conditions of the tumour microenvironment (hypoxia, nutrient deprivation, acidosis). This facilitates the completion of state-of-the-art human studies *ex vivo* and permits rigorous testing prior to costly *in vivo* preclinical studies.
2) Cell homing and tracking	2) Inadequate cell homing has been the downfall of many adoptive transfer treatments and our team has focussed on elucidating and manipulating the migratory patterns of T and NK cells in cancer and inflammation. Such studies have been used to test novel drugs from our industry collaborators Chemocentryx. Furthermore, the lead compound has been progressed to proof-of-concept *in vivo* testing funded by Irish Research Council and European Association for Cancer Research.
Platforms should comprise the components and expertise necessary to create a solid foundation on which to build possible new therapeutic approaches and/or aim to overcome particular development bottlenecks.	Bottlenecks in treatment development regarding off-target effects of immune enhancing agents, incorrect timing of immunotherapy in combination with regimens of chemotherapy or CRT, insufficient receptor coverage in receptor antagonist trials and poor cell homing following adoptive cell transfer trials **can all be pre-empted using our immune function platform. This comprises a unique combination of assays using invaluable cancer patient blood and tissue samples. It is also possible to extend such testing to 3D human cancer models**. By conducting such testing prior to progression into preclinical models, novel treatments can be rigorously assessed, doses can be refined and optimal timing can be determined in a human *ex vivo* model and more sophisticated treatment regimens can be designed for subsequent *in vivo* testing.

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Impact set out in the call topic	How our expertise can contribute to the impact
Strengthened competitive position of European advanced therapy research and development.	If Europe is to strengthen its position in advanced therapy research then the increased prevalence of complex inflammation-driven and obesity-associated cancers must be considered and targeted treatments must be carefully integrated into current treatment regimens to a) maximise efficacy and b) both minimise and manage toxicities. Our team can test the potential toxicity and efficacy of novel drugs pre- and post-chemo-radiotherapy because we have access to cancer patient samples at both time points. In the absence of preliminary data, our team can generate pilot data using *in vitro* cancer models, commercially available chemotherapies and a state of the art irradiation facility which is housed within our institute. Subsequently, the drugs can be progressed into immune function platforms using patient samples. Therefore, we can contribute to Europe's standing in the new era of integrating cancer immunotherapies into current multimodal treatment regimens by publishing high quality data outputs in both rare and validated human *ex vivo* models that will inform and advance clinical treatment design.

Brief Bio:
I am an immunologist and Irish Research Council-funded Senior Research Fellow in the Department of Surgery at Trinity College Dublin. I lead several translational research projects in immunology, cancer, inflammation and liver disease and have published peer-reviewed articles and procured funding across these research themes. I have a background in clinical trial database design and management, team leadership, project management, biobank management, multidisciplinary team coordination and GCP-compliant processes having spent several years as a Data Team Lead in multinational contract research organisation Quintiles and as the Upper Gastrointestinal Biobank Manager at St. James's Hospital, Dublin.

My research investigates immunological mechanisms in inflammation and cancer and examines how we might therapeutically target the underlying immune processes in pathological inflammation in obesity, cancer and liver disease. The overarching objective of my translational research is to identify novel immunotherapies in this disease space with a focus on lymphocyte trafficking and chemokine networks. Specifically, my studies address how specific chemokine pathways might be manipulated to enhance anti-tumour immunity and alleviate pathological inflammation in obesity and cancer. Another strand of my research assesses how immune checkpoint inhibitors might augment anti-tumour immune responses in upper gastrointestinal cancer and examines the safety of such therapeutics in inflammation-driven malignancy. Such studies are conducted in collaboration with industry partners and international scientists. My goals in this space are to develop novel immunotherapies and examine the optimal conditions for integrating existing immunotherapies into current treatment regimens to ultimately improve outcomes for millions of patients worldwide and enhance Ireland and Europe's standing in the cancer treatment and chemoprevention space.

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