TRAining in Cancer mechanisms & Therapeutics

Marie Skłodowska-Curie Actions

Background to the project: TRACT is an international, inter-sectoral, multi-disciplinary project providing Marie Skłodowska-Curie PhD Fellowships to early stage researchers (ESRs) with the potential to become the leaders of tomorrow in cancer research. This project has received funding from the European Union's Horizon 2020 research & innovation programme under the Marie Skłodowska-Curie grant agreement No. 721906. PhD Fellows will complete three year research projects in three critical thematic areas; biomarker discovery, molecular resistance mechanisms and metabolic transformation mechanisms. TRACT will enable Fellows to discover novel insights into the molecular and cellular basis of oral and oesophageal cancer and generate new diagnostic tools and therapeutics that will improve patient response and survival. Through our SME/industrial partners, PhD Fellows will be exposed to next-generation technologies in cancer diagnosis, metabolism, genome scale CRISPR knockout and next generation sequencing, imaging, biomarker identification, exosome isolation/analysis, medicinal chemistry, target identification/validation, bioinformatics and drug development. Fellows trained through the TRACT network will be uniquely positioned for careers in academia, industry or as entrepreneurs. A living allowance of up to €3110 per month subject to local taxes (depending on the country of the host institution) is available for recruited researchers along with a mobility allowance and family allowance. In total, eleven PhD positions are available within a number of Institutions listed below with a **start date of 1st March 2017.**

Essential and desirable criteria: Applicants should hold the necessary qualifications entitling them to undertake PhD study in their chosen country, and should possess a high standard of written and spoken English. Prospective PhD candidates should hold at least a 2:1 BSc or alternatively an MSc degree, or equivalent, in biochemistry, molecular biology, immunology, medicinal chemistry, synthetic organic chemistry or related disciplines. Graduates in dental science with a special interest in oral medicine are also encouraged to apply. Relevant research experience is desirable. Applicants must be in the first 4 years of their career post primary degree and not yet hold a doctoral degree. TRACT is a mobility-based EU project and researchers are required to move country to commence their PhD training project. Applicants must not have been resident in the country where the ESR project is being hosted for more than 12 months in the past 3 years.

How to apply: Applicants should email a single attachment file to Prof. James Murray (**TRACT@tcd.ie**) that includes a covering letter, which should specify your reasons for applying and your suitability as a candidate, a copy of your CV which describes your relevant research training and experience and copies of your degree transcripts in English and English proficiency certificate, if required. Also have two letters of recommendation sent independently in support of your application to the same email address. Please include the title of the ESR project(s) that you are interested in in the body of the email (listing choices in order of preference). **Deadline for receipt of applications is 31st December 2016.** Candidates will be shortlisted based on the quality of degree(s) awarded, the relevance of research training and experience and the supporting references. Shortlisted candidates will be interviewed either in person in the host institution of the relevant country or through Skype.

DO NOT SEND APPLICATIONS DIRECTLY TO THE PROJECT SUPERVISORS.

Further information: Enquiries can be sent to the relevant project supervisor(s) via email. Further details on working conditions and entitlements in the host institution(s) will then be provided along with career development prospects.

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TRACT

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ESR1 - Inflammatory response elements, and glycan and proteome profiles as salivary biomarkers for the early diagnosis of OSCC

Supervisor: Prof. Jose Bagan (Jose.V.Bagan@uv.es)

Host Institution: University of Valencia, Valencia, SPAIN

The objective of this research is to analyse the existence of salivary biomarkers in a group of oral squamous cell carcinoma (OSCC) patients, in different clinical stages, that may serve in early diagnosis of this malignancy. These findings in the OSCC group will be compared with two other groups of oral potentially malignant disorders: oral leukoplakia and oral lichen planus and with a healthy control group. This project would be particularly suited to dental science graduates with an interest in oral medicine.

ESR2 - Identification of novel molecular biomarkers predictive of benefit to neo-adjuvant chemotherapy in OAC

Supervisor(s): Dr Richard Turkington & Prof. Richard Kennedy (r.turkington@qub.ac.uk or r.kennedy@qub.ac.uk)

Host Institution: The Queen's University, Belfast, UNITED KINGDOM

The ability to predict which patients are more likely to respond to neo-adjuvant therapy in operable OAC has the potential to markedly increase the success of radical approaches in this poor prognosis disease. Through the integration of whole genome sequencing and gene expression data on a large cohort of OAC patients we will develop and validate a novel predictive biomarker to neo-adjuvant chemotherapy. We will also seek to comprehend the underlying biology governing response to chemotherapy revealed by the identification of a biomarker-selected population of patients.

ESR3 - Modulation of salivary inflammatory markers and proteomic analysis in patients undergoing radiotherapy for OSCC & cancer of the head and neck.

Supervisor: Prof. Jose Bagan (Jose.V.Bagan@uv.es)

Host Institution: University of Valencia, Valencia, SPAIN

The objective of this research is to analyze alterations in the salivary inflammatory biomarkers in groups of patients with OSCC and with head and neck cancer (HNC) undergoing radiotherapy, at different times of the irradiation, compared with their baseline and with healthy control groups. This project would be particularly suited to dental science graduates with an interest in oral medicine.

ESR4 - A pathways-based approach to identify determinants of drug resistance in OAC

Supervisor(s): Dr Richard Turkington & Prof. Richard Kennedy (r.turkington@qub.ac.uk or r.kennedy@qub.ac.uk)

Host Institution: The Queen's University, Belfast, UNITED KINGDOM

The presence of drug resistance, either intrinsic or acquired, is the primary reason for treatment failure in OAC. Through the analysis of a large gene expression dataset we will identify determinants of drug

resistance in OAC in order to design innovative therapeutic strategies to increase the efficacy of current chemotherapy. By applying high throughput compound screens to existing and novel OAC models we will identify therapies which can overcome resistance to chemotherapy and so improve survival outcomes in OAC.

ESR5 - Inflammatory caspases as biomarkers for OAC? Determining the role of inflammatory caspases in OAC development and resistance

Supervisor(s): Profs. Emma Creagh & James Murray (ecreagh@tcd.ie or jmurray6@tcd.ie)

Host Institution: Trinity College Dublin, Dublin, IRELAND

This project is based upon previous data generated by our group, which identifies the expression of inflammatory caspases in certain colon cancer cells as specific markers of colorectal cancer. The project will examine whether distinct caspase expression profiles are also observed in oesophageal adenocarcinoma cells, and will examine the functional impact of inflammatory caspase expression during OAC, in terms of cancer development and treatment resistance.

ESR6 - Mcl-1 inhibitors for the treatment of OSCC

Supervisor(s): Profs. Giuseppe Campiani & Stefania Butini (campiani@unisi.it or butini3@unisi.it)

Host Institution: University of Siena, Siena, ITALY

The candidate will be involved in the rational design and synthesis of Mcl-1 inhibitors with the ability to sensitise OSCC cells to apoptosis, and characterized by appropriate pharmacokinetic properties. Accordingly a solid background and expertise in synthetic organic chemistry and medicinal chemistry are highly desirable**.**

ESR7 - HAMLET derivatives as a pre-operative therapy in oesophageal cancer

Supervisor(s): Profs. Ken Mok & Vincent Kelly (mok1@tcd.ie or kellyvp@tcd.ie)

Host Institution: Trinity College Dublin, Dublin, IRELAND

The milk protein alpha-lactalbumin when bound to oleic acid (a.k.a. HAMLET) is highly effective at selectively targeting cancer cells. In this project you will examine the ability and mechanism of HAMLET to stop the proliferation of oesophageal adeocarcinoma cells using state-of-the-art techniques including CRISPR, next-generation sequencing, NMR metabolomics using the Trinity Biomedical Sciences Institute's s 800 MHz NMR, and Oxygraph high-resolution respirometry; the latter being carried out in OROBOROS INSTRUMENTS, Austria.

ESR8 - Development of novel autophagy modulators to improve sensitivity of OSCC to chemotherapy

Supervisor(s): Prof. Giuseppe Campiani & Stefania Butini (campiani@unisi.it or butini3@unisi.it)

Host Institution: University of Siena, Siena, ITALY

We will carry out bioinformatic screening to identify and develop new targets for modulating autophagy

in OSCC. The candidate will be involved in the rational design and synthesis of novel compounds against the most promising targets. Accordingly a solid background and expertise in synthetic organic chemistry and medicinal chemistry are highly desirable.

ESR9 - Pre-clinical evaluation of targeting autophagy for the treatment of OSCC

Supervisor(s): Profs. Daniela Zisterer & Jeff O'Sullivan (dzistrer@tcd.ie or josulli@tcd.ie)

Host Institution: Trinity College Dublin, Dublin, IRELAND

This project will investigate the expression of key autophagic regulatory proteins in OSCC patient samples and correlate expression with existing clinicopathologic factors and overall patient survival. The project will determine whether combining existing OSCC chemotherapy strategies with autophagy inhibition represents an enhanced treatment strategy for patients.

ESR10 - Metabolic profiles in normal, dysplastic and cancerous oral cells

Supervisor(s): Prof. Erich Gnaiger (erich.gnaiger@oroboros.at)

Host Institution: OROBOROS INSTRUMENTS, Innsbruck, AUSTRIA

The objective is to complete a research training programme on high-resolution respirometry with the OROBOROS Oxygraph-2k and O2k-MultiSensor modules to measure real-time bioenergetics and metabolism. The expected results comprise a comparison of oxygen consumption, extracellular acidification and metabolic flux in different cell types under normoxic and hypoxic conditions and in correlation with chemotherapy sensitivity and the identification of differential novel drug targets in the cancer cells.

ESR11 - Mitochondrial function linked to metabolic differences in normal, dysplastic and cancerous oral cells

Supervisor(s): Prof. Richard Porter (rkporter@tcd.ie)

Host Institution: Trinity College Dublin, Dublin, IRELAND

This project will examine the relationship between mitochondrial abundance, morphology, and bioenergetics/metabolism associated with (a) normal, dysplastic and oral cancer cells, and (b) how these factors are affected by invasiveness, migration, anoikis resistance and hypoxia in oral cancer cells.

Partner companies and Institutions: