This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

The present file describes the advertisement for 9/10 doctoral candidate (DC) positions within MSCA Doctoral Network ColoMARK (MSCA-DN-2021-101072448).

1. ColoMARK

The ColoMARK network integrates 17 teams with multidisciplinary expertise (omics, epidemiology, microbiome, circulating tumour DNA, bioinformatics, statistics & machine learning, assay development, circulating RNAs, circulating tumour cells, tumour profiling, clinics) aiming at the identification and development of novel colorectal cancer (CRC) biomarkers via state-of-the-art liquid biopsy approaches. ColoMARK will provide cross- and interdisciplinary innovative training with special emphasis on transversal competences to 10 doctoral candidates (DCs). They will constitute a next generation of **effective, multi-skilled and proactive future professionals** that comply with the tenets of the Principles for Innovative Doctoral Training, and that achieve enhanced intersectoral employability.

2. Eligibility criteria for all DC positions under MSCA

- The applicants MUST not have resided or carried out their main activity (work, studies, etc.) in the country of the recruiting beneficiary for more than 12 months in the 36 months immediately before the recruitment date (unless as part of a compulsory national service or a procedure for obtaining refugee status under the Geneva Convention).
- Applicants MUST NOT be in possession of a PhD
- Additional eligibility criteria may be described for each position in the descriptions below.

3. Working conditions

DCs will receive a fully funded working contract for three years including health insurance and social benefits.

Salaries will comply with MSCA and local institution regulations. This quantity describes the living allowance for the DCs, including all costs related to the contract, including social security and insurance, where appropriate. A flat rate Mobility allowance will also be included in the contract. Additional allowances (family, long-term and special needs) will be added if applicable. Recruited DCs **must work exclusively for the action**.

4. Requirements and obligations

- The DC must be ***enrolled in the local PhD programmes of the hosting institutions,*** which will contribute greatly to providing specialised education on both core scientific topics, as well as transversal skills.

- In addition, the DC must participate in ***training activities provided by the ColoMARK*** including network-wide training, clinical rotations, workshops, summer/winter schools, or e-training. This reinforces the doctoral candidates´s exposure to a varied choice of training activities outside of the host lab, and will be focused on enhancing the personal, team-wide and network-wide capabilities of the DCs.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

- One of the strongholds of MSCA Doctoral Network actions is the flexibility of DC work amongst the different teams, and this mobility enhances and improves the participant interrelations. Therefore, all ColoMARK DCs will perform ***a minimum 5 months of secondments*** at other ColoMARK teams, including at least 3 weeks in the non-academic sector (according to internal regulations that restrict interactions with for-profit organisations).

- ColoMARK is greatly committed to patient and public involvement in research (PPI). DCs will therefore team up and work alongside patients in order to produce better research and researchers.

5. Framework for recruitment procedure

DC recruitment will take all measures to implement the principles set out in the Commission Recommendation on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers. This means recruitment will follow an ***open, transparent, impartial and equitable*** recruitment procedure, on the basis of:

- scientific skills and the relevance of the research experience
- the impact of the proposed training on the researcher's career
- a fair gender representation by promoting genuine equal access during recruitment. This will include an unbiased assessment of skills and merits during evaluation. Where two applicants are tied with regards to merits, ColoMARK choose the one from the underrepresented sex.

6. Recruitment process

Vacancies will be advertised and published internationally, to guarantee openness of the call. The call for applicants will be **open from 1st to 31st Jan 2023**.

Shall any conflict of interest arise during the procedure, this shall be notified to the ColoMARK project manager at: colomark@gmail.com.

DC recruitment will be a two-stage process. On ***stage 1***, applicants will be evaluated firstly on eligibility, and then according to their CV: academic and professional qualifications, prior research experience and skills, publications, teaching activities, level of independence, knowledge transfer and dissemination output, mobility experience, and letter of motivation describing their purpose and goal in participating in ColoMARK. Career breaks or variations in the order of CVs will not be penalised. The CVs will be evaluated by the supervisor and co-supervisor for each position, and additional input may be provided by other ColoMARK members if required.

The top applicants or those attaining a minimum score will then proceed to ***stage 2***. Applicants will be notified of this decision by February 28th. For this stage, the letters of support will be evaluated together with an interview by a Selection Committee consisting of the two supervisors and additional local team members. Please note that all interviews will be

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

recorded, and that by applying to any of these positions, you accept these conditions. Recordings will be kept privately for use exclusively within the ColoMARK consortium. Interviews will happen during March 2021

Due to the mobility rule, a basic level of written and oral English will be required from the applicants in order to guarantee appropriate communication upon incorporation at the host groups.
Results from the selection process and the list of selected DCs will be published at the latest by 31st May 2023. **The applicants must start their employment under ColoMARK by 15th May 2023**.

7. Application procedure

Aspirants should apply for each DC position according to the specific descriptions provided below. The following information must be included for all applications:

- Academic qualifications, including official certificates with marks and credits (for BSc and MSc)
- Narrative CV (1,000 words max)
- Motivation letter describing their interest in the selected DC project(s)
- Abstract (500 words max) description of MSc thesis (and copy of derived publications, if appropriate)
- 2 letters of support (including e-mail and telephone contact information)

Applications to a maximum of 3 different DC projects within ColoMARK is permitted, but this information should be clearly disclosed in the motivation letters to each of the positions, and ranked in order of preference.

DESCRIPTION OF DC PROJECTS AND POSITIONS

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC1 project title

Study of ctDNA biomarkers in the context of bowel cancer screening programmes.

Recruiting centre

Fundación Instituto de Investigación Sanitaria de Santiago (FIDIS), Santiago de Compostela (Spain).
Supervisors: Dr C. Fernandez (FIDIS), Assoc. Prof. Dr E. Heitzer (Medical University of Graz, Austria).
The DC will be enrolled in a doctoral programme at the University of Santiago de Compostela (USC).

Group description

Dr Ceres Fernandez (she/her) is an emergent PI at IDIS. Her work so far has focused on genetic predisposition to colorectal cancer and the identification of novel biomarkers to offer better prevention strategies for the disease. After obtaining her PhD in 2011, she worked for 3 years as a Marie Curie IEF Fellow under Prof Ian Tomlinson at the Wellcome Centre for Human Genetics (University of Oxford), and later as a postdoctoral senior researcher at the Santiago Biomedical Research Institute (IDIS), where she is currently a PI.
Dr Fernandez has a vast experience in NGS data analysis, genome-wide association studies (GWAS), and transcriptome-wide association studies (TWAS), and is a pioneer in multi-omic wide association approaches in CRC. The work in her lab revolves around 3 major research topics: genetic predisposition to gastrointestinal cancers, biomarker identification for cancer prevention using liquid biopsy and omic strategies, and genetic determinants of adverse drug reactions to chemotherapeutic agents. Her team presently includes one lab technician, one PhD student, and one bioinformatician.
She has published over 35 works in indexed journals, including 15 as main author, 6 in D1 and 9 in Q1, totalling over 1,500 citations. She has an h-index of 20 and an i10 of 25. As a PI, she has obtained funding in several projects funded by the MSCA IEF, Fundació Olga Torres (2018 & 2021), ISCIII-AES (2019 & 2022), MICINN and MSCA Doctoral Networks (2022). She has also participated in more than 10 national and international projects as a team member. She has been a member of COST Actions EuColonGene (BM-1206), TransColonCan (CA-17118), and recently, CA21116 TRANSPAN.

Relevant publications

- Fernandez-Rozadilla *et al.* Deciphering colorectal cancer genetics through multi-omic analysis of 100,204 cases and 154,587 controls of European and Asian descent. Nature Genetics. Accepted. Pending publication.
- Bonjoch*, Fernandez-Rozadilla* *et al. BMPR2* as a candidate novel germline predisposition gene for colorectal polyposis. Gastroenterology. Under review
- Hita-Millan, Carracedo, Fernandez-Rozadilla (CA). 2021. Liquid Biopsy Biomarkers for Immunotherapy in Non-Small Cell Lung Carcinoma: Lessons Learned and the Road Ahead. Journal of Personalized Medicine.
- Fernandez-Rozadilla et al. 2021. Exome sequencing of early-onset patients supports genetic heterogeneity in colorectal cancer. Scientific Reports
- Fernandez-Rozadilla et al. 2021. Tumour profiling at the service of cancer therapy Frontiers in Oncology.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Project description & references

Background: Colorectal cancer is one of the most prevalent tumours and an important disease burden. Current prevention strategies largely rely on the implementation of population-wide screening programmes that rely on FIT as a proxy for bowel malignancy. Nevertheless, the sensitivity of FIT testing could be complemented with other molecular tests to optimise detection rates.

Hypothesis: we believe that liquid biopsy strategies could make a relevant contribution for risk biomarker development in the context of screening.

Objectives: The main aim of this project is to assess the usefulness of ctDNA mutation detection for patients undergoing CRC screening. We aim to describe the sensitivity and specificity of these biomarkers to be detected in the circulation as opposed to the primary bowel neoplasia, particularly in the context of pre-malignant lesions (polyps). We will also inspect the usefulness of ctDNA mutation detection for improved screening in combination with heritable genetic risk predictors.

Methodology: Patients will be categorised into risk groups depending on the endoscopic and histological findings, and following the guidelines of the Spanish Gastroenterology Association. DC1 will evaluate the different ctDNA available technologies (NGS-based, ddPCR-based) and identify that with the highest sensitivity/specificity for early stages (pre-malignant polyps and localised tumours). Then, for each of the 150 patients, he/she will obtain the genomic profiles of: a) somatic mutation of the primary growth (including hotspot driver mutations; and b) the circulatory somatic mutation profile. The ctDNA predictivity will also be compared and/or used in conjunction with the a priori genetic polygenic risk score obtained from the genotyping of the 200+ SNPs that influence CRC risk. Models will be created to conjugate the fixed predisposition component together with epidemiological risk factors and dynamic ctDNA values to identify patients that should undergo colonoscopy.

- Heitzer, E., Ulz, P. & Geigl, J. B. Circulating tumor DNA as a liquid biopsy for cancer. Clin Chem 61, 112-123, doi:10.1373/clinchem.2014.222679 (2015).
- Diaz, L. A., Jr. & Bardelli, A. Liquid biopsies: genotyping circulating tumor DNA. J Clin Oncol 32, 579-586, doi:10.1200/JCO.2012.45.2011 (2014).
- Crowley, E., Di Nicolantonio, F., Loupakis, F. & Bardelli, A. Liquid biopsy: monitoring cancer-genetics in the blood. Nat Rev Clin Oncol 10, 472-484, doi:10.1038/nrclinonc.2013.110 (2013).
- Heitzer, E., Haque, I. S., Roberts, C. E. S. & Speicher, M. R. Current and future perspectives of liquid biopsies in genomics-driven oncology. Nat Rev Genet 20, 71-88, doi:10.1038/s41576-018-0071-5 (2019).
- Newman, A. M. et al. An ultrasensitive method for quantitating circulating tumor DNA with broad patient coverage. Nat Med 20, 548-554, doi:10.1038/nm.3519 (2014).
- Siravegna, G. & Bardelli, A. Blood circulating tumor DNA for non-invasive genotyping of colon cancer patients. Molecular oncology 10, 475-480, doi:10.1016/j.molonc.2015.12.005 (2016).

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Academic qualifications requested

BSc in biomedical sciences* (or similar, depending on country) + MSc in bioinformatics OR BSc in computer science* + MSc in genomics*.

Skills requested

Proven bioinformatic understanding of NGS data analysis, particularly DNA variant calling
Working abilities on Linux environment and programming skills on R, bash or python

Skills valued

Previous experience with ctDNA data analysis
Lab experience working with ctDNA
Knowledge/work on cancer genetics/genomics
Previous experience with prediction models, including polygenic risk scores
Previous experience on biomarker development

Application procedure

Applicants should follow the application procedure and submit the files as a single pdf here: **FIDIS Job Opportunities (position 001/2023).**

*similar (in content) degrees may be considered (depending on description), as the titles may vary depending on country of origin

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC2 project title

A multi-omics and pathway centric investigation of the relationship between lifestyle factors & CRC risk

Recruiting centre

International Agency for Research on Cancer (IARC), Lyon (France).
Supervisors: Dr V. Viallon (IARC), Dr D. Hughes (University College Dublin, Ireland).
The DC will be enrolled in a doctoral programme at the University Claude Bernard, Lyon.

Group description

Dr. Vivian Viallon obtained a PhD in Mathematics in 2006 at Université Pierre et Marie Curie (Paris 6) under the supervision of Dr Paul Deheuvels. He was then recruited as an Assistant Professor of Statistics at the Department of Biostatistics of Hopital Cochin / Université Paris Descartes (Paris 5), before joining the Electrical Engineering and Computer Science Department of University of California, Berkeley, in 2009. In 2010, he was recruited as an Associate Professor of Statistics at University Claude Bernard (Lyon), and he joined the IARC as a Scientist in 2007. Over the years, he developed expertise in causal inference methods, survival analysis, high-dimensional statistics and machine learning methods, as well as their application for the analysis of omics data in cancer epidemiology.
He has published over 100 works in indexed journals, including 29 as main author, totalling over 2,800 citations. He has an h-index of 20 and an i10 of 25.
Dr. Vivian Viallon is now leading the Biostatistics and Data Integration Team (BDI) within the Nutrition and Metabolism Branch (NME) at IARC. BDI aims to develop and apply modern statistical tools to investigate lifestyle, metabolic and genetic factors involved in cancer development in diverse populations, with the aim of contributing to primary prevention of cancer. These objectives are achieved through access to world-leading epidemiological resources, such as the EPIC study and the UK Biobank, and collaborations with international consortia.

Relevant publications

N. Ballout, C. Garcia, V. Viallon. Sparse estimation for case-control studies with multiple subtypes of cases. Biostatistics, 22(4):738-755 (2021).
E. Ollier, V. Viallon. Regression modelling on stratified data with the lasso. Biometrika, 104(1): 83-96 (2017).

Project description & references

Background: Colorectal cancer (CRC) is one of the most prevalent tumours and an important disease burden. Current prevention strategies largely rely on the implementation of population-wide screening programmes (BSCP), that rely on FIT as a proxy for bowel malignancy. Nevertheless, BCSP has low adherence and the sensitivity of FIT testing could be complemented with other molecular tests to optimise detection rates.
Hypothesis: We believe that metabolomics data together with lifestyle and other omics data available in large prospective studies can help identify biomarkers predictive of CRC risk development, which could be relevant in the context of BCSP.
Objectives: To use available metabolomics and other multi-omics data, together with detailed anthropometric and lifestyle data from 1,120 matched case-control pairs nested within the EPIC cohort and other datasets available from ColoMARK to understand CRC development

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

from the perspective of metabolic perturbations from its earliest stages.

Methodology: DC2 will develop and apply supervised and unsupervised machine learning methods for the construction of omics and multi-omics signatures associated with CRC risk. Multi-omics signatures of CRC risk derived in different subgroups of individuals characterised by specific lifestyle patterns will lead to the identification of candidate metabolites and genes that might underpin the impact of lifestyle on colorectal cancer development. The corresponding biological pathways will be explored making use of state-of-the art bioinformatics network-based tools to combine our results with prior knowledge from the literature and biochemical databases.

- M. Breeur, P. Ferrari, …, V. Viallon. Pan-cancer analysis of pre-diagnostic blood metabolite concentrations in the European Prospective Investigation into Cancer and Nutrition. BMC Medicine, 20:351 (2022).
- Chaudary et al. MOGONET integrates multi-omics data using graph convolutional networks allowing patient classification and biomarker identification. Nature Communications 12(1):3445 (2021).
- N. Assi, M. Gunter, ..., V. Viallon, P. Ferrari. Metabolic signature of healthy lifestyle and its relation with risk of hepatocellular carcinoma in a large European cohort. American Journal of Clinical Nutrition 108:117-126 (2018).

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills

Academic qualifications requested

An MSc with appropriate training in statistics, biostatistics, machine learning, or related fields.

Skills requested

Strong background in R and/or Python.

Skills valued

Experience with cancer epidemiology, with the analysis and/or pre-processing of omics data.

Application procedure

Applicants should follow the application procedure and send the files to nmb@iarc.fr and indicate “Application for ColoMARK PhD position” in the subject line.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC3 project title

Exploring the role of the microbiome, gut barrier dysfunction, host genetics, and metabolic interactions in the development of colorectal cancer

Recruiting centre

University College Dublin (UCD), Dublin (Ireland)
Supervisors: Dr D. Hughes (UCD), Sander Tuit (GenomeScan, Netherlands)
The DC will be enrolled onto UCD's structured PhD programme within the School of Biomolecular & Biomedical Science (SBBS). This includes some taught elements and transferrable skills training providing an excellent foundation for a research career. https://www.ucd.ie/graduatestudies/researchprogrammes/structuredphd/

Group description

Dr David Hughes is highly experienced in cancer molecular epidemiology analyses. His current research examines how nutritional, genetic, metabolic, microbial and lifestyle factors may affect the initiation and progression of cancer, with a focus on colorectal cancer (CRC). Investigative approaches include observational and experimental studies in large European cancer cohorts. He is a PI in the EPIC study (http://epic.iarc.fr/) and a member of its colorectal and liver cancer Working Group, a governing council member of the International Society for Selenium Research, and a working group member of the International HundredK+ Cohort Consortium (IHCC, https://ihccglobal.org). He is co-director of the Cancer Biology & Therapeutics (CBT) cluster within the Conway Institute at UCD (where the student will be located, http://www.cbtlab.ie/). Within CBT, Dr Hughes's group consists of 1 postdoctoral scientist, 1 PhD student, 1 Research Assistant, and several undergraduate and master student projects. Embedded within UCD, the Conway Institute (https://www.ucd.ie/conway/) is an interdisciplinary research centre exploring mechanisms of health and disease towards the development of preventative strategies and novel diagnostic & therapeutic solutions. The CBT lab enables the student to work in collaborative environments and be supported and mentored by postdoctoral and senior postgraduate researchers. The student will be enrolled into the SBBS school, supported by a Doctoral Studies Panel (DSP) that will include two other experienced UCD academics.

Dr Hughes currently leads prospective cohort and case-control studies of the influence of bacterial antigens, gut barrier integrity, microbial profiles, and nutritional status of micronutrient minerals on risk of cancer at various organ sites. Current projects are funded by the Health Research Board (HRB) of Ireland, UCD Ad Astra Fellowship, and IHCC. He has been a member of EU COST Actions TransColonCan (CA-17118), and recently, CA21116 TRANSPAN. He has published 85 articles in indexed journals, totalling over 5300 citations, with a h-index of 29.
See for example microbiome research: https://www.youtube.com/watch?v=wELpozH0DQI, and nutrient research: https://www.ncl.ac.uk/healthier-lives/news/past-events/

Relevant publications

- Karavasiloglou N, Hughes DJ, et al, & Jenab M. Pre-diagnostic serum calcium concentrations and risk of colorectal cancer development in two large European prospective cohorts. *Am J Clin Nutr* 2022 *(in press).*
- Butt J, et al, & Hughes DJ. Association of Pre-diagnostic Antibody Responses to

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Escherichia coli and Bacteroides fragilis Toxin Proteins with Colorectal Cancer in a European Cohort. *Gut Microbes* 2021, 13(1): 1-14.
- Genua F, Raghunathan V, Jenab M, Gallagher WM, & Hughes DJ. The role of Gut Barrier Dysfunction and Microbiome Dysbiosis in Colorectal Cancer development. *Front Oncol* 2021 Apr 15;11:626349.
- Rothwell JA et al. Metabolic Signatures of Healthy Lifestyle Patterns and Colorectal Cancer Risk in a European Cohort. *Clin Gastroenterol Hepatol* 2020 Dec 3:S1542-3565(20)31635-9.
- Butt J, et al, & Hughes DJ. Antibody responses to Helicobacter pylori and risk of developing colorectal cancer in a European cohort. *Cancer Epidemiol Biomark Prev* 2020, July 1; 29(7): 1475-1481.
- Scott AJ, et al. The International Cancer Microbiome Consortium Consensus Statement on the Role of the Human Microbiome in Carcinogenesis. *Gut* 2019 Sep;68(9):1624-1632.
- Murphy N, et al. Lifestyle and Dietary Environmental Factors in Colorectal Cancer Susceptibility. *Mol Aspects Med*2019 Jun 28. 69:2-9.

Project description & references

Background: Accumulating research suggests that a disturbance in the gut microbiome can influence development of colorectal neoplasia from early lesions to tumours (1).
Hypothesis: Gut microbiome involvement in colorectal carcinogenesis may occur through inflammatory-induced weakening of the protective gut mucosal barrier by obesity, dietary/lifestyle, and microbiome metabolic factors that lead to exposure of the gut epithelium to pathogenic bacteria and their toxins (2-4).
Objective: To apply circulating (liquid biopsy) measures of gut barrier dysfunction and bacterial translocation into the circulation as biomarkers of colorectal carcinogenesis and disease progression. Blood-based detection of bacteria and gut-barrier health may allow novel screening strategies for CRC cancer prevention, diagnosis, and management.
Methodology: Measures of gut barrier dysfunction will be assessed by protein ELISA assays, while bacterial translocation and metabolic activity will be ascertained by bacterial antigen immunotyping, plasma metabolomics, and circulating bacterial DNA sequencing. The contribution of host genetics related to immune/microbiome and microbial metabolite interactions will be assessed using existing GWAS data. This will be conducted in patient case-control cohorts of colorectal adenomas and cancer, available in UCD and through ColoMARK partners. Additionally, the project will include data analysis integration with the metabolomics data, together with detailed anthropometric and lifestyle data, from 1,120 matched case-control pairs nested within the EPIC cohort in DC2. Analytic approaches will include multivariable logistic regression and mediation analyses. Thus, this PhD will involve laboratory assays such as ELISA assays, qPCR, and metagenomic sequencing, but there will be a major focus on biostatistical and bioinformatic approaches. Together, this will help shed light on the involvement of microbial translocation and microbially derived metabolic perturbations on adenoma progression and CRC development.

- Scott AJ, et al. The International Cancer Microbiome Consortium Consensus Statement on the Role of the Human Microbiome in Carcinogenesis. *Gut* 2019 Sep;68(9):1624-1632.
- Genua F, Raghunathan V, Jenab M, Gallagher WM, & Hughes DJ. The role of Gut Barrier Dysfunction and Microbiome Dysbiosis in Colorectal Cancer development. *Front Oncol*

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

2021, 11:626349.

- Butt J, et al, & Hughes DJ. Association of Pre-diagnostic Antibody Responses to Escherichia coli and Bacteroides fragilis Toxin Proteins with Colorectal Cancer in a European Cohort. *Gut Microbes* 2021, 13(1): 1-14.
- Butt J, et al, & Hughes DJ. Prospective evaluation of antibody response to Streptococcus gallolyticus and risk of colorectal cancer. *Int J Cancer* 2018, 143(2): 245-252.

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills.

Academic qualifications requested

Applicants must have, or expect to have, reached a minimum of an upper second-class (2.1) degree or your institute's equivalent in a relevant honours Bachelor's + a Master's degree

Relevant degree studies include Statistics, Bioinformatics, Mathematics, Computer Science, Microbiology, Biology, Genetics, Nutrition, Biochemistry, Biotechnology, Biomedical Science, Immunology, Public Health, Epidemiology

Excellent written and oral communication skills and a high level of competence in the English language are essential (see http://www.ucd.ie/registry/admissions/elr.html).

Skills requested

The successful candidate should have interests in both laboratory experiments and biostatistical and bioinformatic techniques, and microbial, nutrition, and genetics/genomics research in cancer.
Preferred fields of study and training include Biostatistics, Bioinformatics, Epidemiology, Microbiology, Nutrition, and Genetics.
A knowledge and / or enthusiasm for bioinformatic and statistical analysis of molecular data (such as ELISA protein concentrations, blood serotyping, genetic variation analyses, next generation metagenomic sequencing, and metabolomics) is essential.
The candidate must either have experience of, or be willing to learn the biostatistical and bioinformatic methodologies for the analyses required in this project.
A commitment to research integrity is essential.

Skills valued

Experience in basic biostatistical analysis methodologies is highly valued.
Good verbal communication & writing skills are essential.
Highly desirable skills include working abilities on database management and conducting data analysis using statistical software, e.g., R, SPSS, STATA, SAS, MATLAB, and/or experience of Linux and programming skills on R, bash or python.
Experience with several techniques including ELISA, qPCR, and DNA sequencing.
Experience in metagenomic and/or genomic sequence analysis.
Experience in Metabolomics and/or Mass spectrometry.
Experience with cell free DNA laboratory experiments.
Knowledge/work on cancer epidemiology (or relevant aspects of microbiome, nutrients,

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

metabolites or genetics/genomics).
Previous experience on biomarker development.
Experience in reviewing scientific literature.

Excellent organisational skills.

Application procedure

Applicants should follow the application procedure and submit the files via email to david.hughes@ucd.ie as a single .pdf document.

Before applying, we kindly advise you to carefully read the description for DC positions within MSCA Doctoral Network ColoMARK (MSCA-DN-2021-101072448). There, you will find all the relevant information and the list of the documents to attach to your application. Notice: if you do not meet eligibility criteria, you will not be considered for the position.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC5 project title

Retention of subtyping from tissues to liquid biopsies

Recruiting centre

GenomeScan B.V., (GenomeScan), Leiden (the Netherlands).
Supervisors: Dr S. Tuit (GenomeScan), Dr C. Fernandez (FIDIS, Spain) and Assoc Prof T. van Wezel (Leiden University Medical Centre, Netherlands).
The DC will be enrolled into a PhD programme at Leiden University Medical Center (LUMC).

Group description

GenomeScan is a young enterprise that originated from the long and intensive collaboration between the Leiden University Medical Center (LUMC) and ServiceXS B.V. Today, the company has extensive technical expertise and access to the latest Next Generation Sequencing (NGS) technologies. Those technologies include the NovaSeq6000 platform (Illumina), Sequel II (PacBio) and the newest single cell technologies from 10XGenomics (Chromium). This infrastructure is coupled with established protocols for DNA sequencing (SNP/variants calling, haplotyping, methylation and hydroxy-methylation, WES, WGS) and RNA sequencing (mRNA, smallRNA, long non-coding RNA, miRNA discovery).
Sander Tuit will act as supervisor on the project, project manager R&D at GenomeScan. He conducted his PhD work in computational tumour immunology at the University of Bonn. Thereafter, he worked as researcher at the Leiden University Medical Center, analysing multi omics data to unravel targets for T-cell therapy of cancer and predictive biomarkers for response to GvHD treatment utilising mesenchymal stromal cells. In 2021 he joined GenomeScan as project manager R&D, where he manages (inter-)nationally funded research and innovation projects. He has expertise in next generation sequencing technologies and analysis.

Project description & references

Background: Classical tissue biopsy approaches have proven to be pivotal for our fundamental as well as clinical understanding of colorectal cancer. However, such studies are hindered by several issues, including tumour heterogeneity, limiting representative biopsy sampling. The collection of study samples in this context is complex and generally requires invasive procedures (surgery, endoscopy), which preclude multiple sampling. As a result, progress is still to be made when it comes to effective prediction, diagnosis and treatment of colorectal cancer.
Hypothesis: The emergence of liquid biopsy approaches has reinvigorated tumour biomarkers research due to easier access, less invasiveness and allowing for serial sampling. This ultimately could contribute to a more accurate reflection of active disease (4-6), while posing much less of a burden for the patient.
Objective: To facilitate the transition from the classical, colorectal tissue biopsies approaches, to liquid biopsy approaches in the clinical setting, we will inspect consensus molecular subgroup (CMS) subtyping retention in liquid biopsies as a tool for tumour characterization.
Methodology: To this extent, the candidate will largely focus on the bioinformatic characterization of the primary/metastatic CMS, originating from tissue biopsy NGS data, and correlate this with matched liquid biopsy NGS data. In addition, we aim to generate a systems biology methodology that allows for liquid biopsy-based early diagnosis and/or subtyping of CRC patients. Lastly, the candidate will be heavily involved in collaborative projects that

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

ultimately aim to push consortium-wide data integration.

- www.genomescan.nl
- Yiu and Yiu. Biomarkers in Colorectal Cancer. Anticancer Res. 2016 Mar;36(3):1093-102.
- Lech *et al.* Colorectal Cancer Tumour Markers And Biomarkers: Recent Therapeutic Advances. World J Gastroenterol. 2016 Feb 7;22(5):1745-55.
- Siravegna *et al.* Integrating Liquid Biopsies Into The Management Of Cancer. Nat Rev Clin Oncol. 2017 Sep;14(9):531-548.
- Shen *et al.* Sensitive Tumour Detection And Classification Using Plasma Cell-free DNA Methylomes. Nature. 2018 Nov; 563, 579–583.
- Crowley *et al.* Liquid Biopsy: Monitoring Cancer-Genetics In The Blood. Nat Rev Clin Oncol. 2013 Aug;10(8):472-84.
- Guinney *et al.* The Consensus Molecular Subtypes Of Colorectal Cancer. Nat Med. 2015 Oct; 21, 1350–1356.

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills.
Enthusiastic about pursuing a research project within a commercial organisation.

Academic qualifications requested

MSc in Bioinformatics/System Biology, or Biomedical sciences/Molecular Biology (or similar, depending on the country).

Skills requested

Proven understanding of Bioinformatic/System Biology approaches.
Proficiency in R and/or Python programming.
Knowledge on cancer genetics/genomics.

Skills valued

Previous experience with NGS data analysis.
Previous experience on biomarker development.

Application procedure

Candidates are invited to submit all application documents in English to Manager Human Resources Mrs. Vivienne Heemskerk (hr@genomescan.nl).
Please ensure that you qualify before applying, as ineligible candidates cannot be considered.
For further info on the position, please contact Project Manager R&D Sander Tuit (s.tuit@genomescan.nl).

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC6 project title

Development of dynamic chemistry labelling assays to quantify circulating small non-coding RNAs directly from body fluids for the early detection of Colorectal Cancer.

Recruiting centre

DESTINA Genomica SL (DESTINA), Granada (Spain)
This DC position is an industry-focused research position at DESTINA.
Supervisors: Dr S. Pernagallo (DESTINA) and Dr B. Pardini (Italian Institute for Genomic Medicine, IIGM), Prof JJ Diaz Mochon (University of Granada, UGR).
The DC will be enrolled in a doctoral programme at UGR.

Group description

DESTINA is a Spanish biotech company focused on the application and validation of its patented state-of-the-art nucleic acid detection technologies (1). DESTINA has created a unique and reliable chemistry for highly specific detection of nucleic acids. It can be used to identify any known target nucleic acid sequence, and in particular can directly detect small RNAs, without the multiple steps required by current methods (2).
DESTINA is located at the Business Innovation Centre (BIC) of the Technological Park of Health Sciences (PTS) of Granada, Spain. Its R&D labs are equipped with the latest generation of instrumentation for chemistry, biochemistry and molecular biology. DESTINA owns an automated synthesiser for the preparation of DESTINA probes plus Quanterix SR-X Simoa, Luminex 200 and MAGPIX and a Merck SMCxPro Reader for the analytical analysis of liquid biopsies.
Dr S Pernagallo (Operations Director at DESTINA) will act as supervisor for this DC position. Dr S Pernagallo has a distinguished academic and industrial career between Italy, UK and Spain. He is a highly experienced scientist with a proven background in development and validation of novel game-changing solutions for Nucleic Acid Testing (NAT). Author in more than 40 publications and book chapters covering the fields of nanotechnology, analytical chemistry and biomaterials. He is coordinator of national and EU projects with highly multidisciplinary and multicultural teams and supervisor for Master and PhD students.

Project description & references

Background: Small non-coding RNAs (sncRNAs) are important regulators of various biological processes. They are present in biological fluids with different expression levels under pathological conditions. sncRNAs are rapidly emerging as important biomarkers for clinical diagnosis and prognosis of various human diseases including Colorectal Cancer (CRC).
Hypothesis: Profiling of sncRNAs is one of the most active areas of research in the field of liquid biopsy. DESTINA offers a new way to interrogate sequences of sncRNAs through its unique Dynamic Chemistry Labelling (DCL) technology (2-6).
Objectives: The objectives of the present project is to develop novel DESTINA reagents and protocols to interrogate and quantify a panel of sncRNAs, both miRNAs and ctRNAs, in either singleplex or multiplex manner, for the early detection of CRC. The new set of reagents will be used to implement DCL on some of the major diagnostic platforms. Optimal diagnostic platform will be selected by depending on what limit of quantification is required for accurate and reliable direct testing of sncRNAs.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Methodology: The PhD candidate will perform the design and solid-phase synthesis of functionalized PNA oligomers (DESTINA probes) as well as novel tagged SMART-Bases (2-6). DESTINA probes will be designed in order to capture complementary RNA target molecules identified as biomarkers for early diagnosis of CRC. SMART-Bases will be biotinylated in order to perform the DCL on bead-based reading platforms such as Luminex MAGPIX, Quanterix SR-X and Merck SMCxPro (7-12). For the merging of DESTINA's new reagents with the bead-based platforms. DESTINA probes will be coupled with magnetic beads so as to generate new assay kits capable of making an absolute quantification of target sncRNAs directly from body fluids. Protocols for the new kits will be implemented initially by interrogating synthetic RNA mimic oligomers. The analytical performance of the assay kits will be compared with goal standard and SOPs will be produced.
Concluding, novel reagents, kits and assays will be employed to interrogate sncRNAs with early diagnostic value. The project includes assay optimization and validation with clinical samples provided by other ColoMARK members

1. www.destinagenomics.com
2. DNA analysis by dynamic chemistry [2010]. FR Bowler, JJ Diaz-Mochon, MD Swift, M Bradley. Angewandte Chemie 122 (10), 1853-1856.
3. Novel biochip platform for nucleic acid analysis [2012]. S Pernagallo, et al. Sensors 12 (6), 8100- 8111.
4. PCR-free and chemistry-based technology for miR-21 rapid detection directly from tumour cells [2019]. A Delgado-Gonzalez, et al. Talanta 200, 51-56.
5. New Platform for the Direct Profiling of microRNAs in Biofluids [2019]. S Detassis, et al. Analytical chemistry 91 (9), 5874-5880.
6. miR-122 direct detection in human serum by time-gated fluorescence imaging [2019]. E GarciaFernandez, et al. Chemical Communications 55 (99), 14958-14961.
7. Open a New Window on the World of Circulating microRNAs by Merging ChemiRNA Tech with Luminex Platform [2022]. Antonio Marín-Romero, et al. Sensors & Diagnostics, 1, 1243 – 1251.
8. Amplification-free profiling of microRNA-122 biomarker in DILI patient serums, using the luminex MAGPIX system [2020]. Antonio Marin-Romero, et al. Talanta, 219, 121265.
9. Direct Detection of miR-122 in Hepatotoxicity Using Dynamic Chemical Labeling Overcomes Stability and isomiR Challenges [2020]. B López-Longarela, et al. Analytical Chemistry 92 (4), 3388-3395.
10. A PCR-free technology to detect and quantify microRNAs directly from human plasma [2018]. A Marín-Romero, et al. Analyst 143 (23), 5676-5682.
11. Polymerase-free measurement of microRNA-122 with single base specificity using single molecule arrays: Detection of drug-induced liver injury [2017]. DM Rissin, et al. PloS one 12 (7), e0179669.
12. Novel bead-based platform for direct detection of unlabelled nucleic acids through Single Nucleobase Labelling [2016]. S Venkateswaran, et al. Talanta 161, 489-496.

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Academic qualifications requested

MSc in Chemistry, Biochemistry or Pharmaceutical Chemistry and Technology (or similar, depending on the country).

Skills requested

Comprehensive organic and solid-phase synthesis and coupling reactions. Knowledge on molecular biology techniques (qPCR, NGS, Microarrays). Basic knowledge on RNA biology especially on sncRNAs and interest in liquid biopsy.
English language proficiency is required.

Skills valued

Organic chemistry laboratory experiments. Previous experience with design and synthesis of small molecules, peptides and/or ideally peptide nucleic acids (PNAs). Knowledge/work with RNA analysis, molecular biology techniques and nucleic acid testing (NAT).

Application procedure

Before applying, we kindly advise you to carefully read the description for DC positions within MSCA Doctoral Network ColoMARK (MSCA-DN-2021-101072448): there, you will find all the relevant information and the list of the documents to attach to your application. Applicants who were educated in non-English speaking countries, must document their proficiency in English when applying for this DC program. The application must be submitted to spain@destinagenomics.com. For further info on the position, please contact Dr. Salvatore Pernagallo (salvatore@destinagenomics.com).
Notice: if you do not meet eligibility criteria, you will not be considered for the position.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC7 project title

Circulating non-coding RNAs as a source of biomarkers for colorectal cancer prognosis and monitoring.

Recruiting centre

Fundació Clinic per a la Recerca Biomèdica (FCRB)/IDIBAPS, Barcelona (Spain).
Supervisor: Dr. Meritxell Gironella (FCRB/IDIBAPS-CIBER). Co-supervisor: Dr. Salvatore Pernagallo (DESTINA S.L.).
The DC will be enrolled in a doctoral programme at the University of Barcelona (UB), Barcelona, Spain.

Group description

The project is to be developed in the Gastrointestinal and Pancreatic Oncology Research Team at IDIBAPS-Hospital Clinic of Barcelona under the direct supervision of Dr. Meritxell Gironella. Fundació Clínic per a la Recerca Biomèdica (FCRB)/IDIBAPS is a fully equipped Public Research Center in Barcelona (Spain) dedicated to biomedical translational research through the close collaboration between basic and clinical researchers, and it holds the 'HR Excellence in Research' logo awarded by the European Commission since 2015.
Dr Meritxell Gironella is a Molecular Biology Researcher who leads the research line about 'Small non-coding RNA and digestive cancers' within the Gastrointestinal and Pancreatic Oncology Team. She also belongs to Spanish Biomedical Research Network Consortium named CIBER, concretely to the CIBEREHD area which brings together some of the most competent Spanish research groups in the fields of Gastroenterology, Hepatology and Gastrointestinal Oncology, including both universities and hospitals and other technological or research centers. She has over 24 years of experience in biomedical research. For the last decade, her efforts have been mainly focused on the study of circulating microRNAs as new biomarkers for colorectal or pancreatic cancer, as well as on the functional study of these molecules in these tumors. She has led 14 public and private projects as PI and has published numerous scientific articles (65; 95% Q1 journals). She has also supervised multiple students at various levels, such as 8 PhD, 4 MSc and 3 BSc theses. Furthermore, she has participated in several COST actions of European Scientific Cooperation such as EuPancreas (BM1204), Transcoloncan (CA17118) and, recently, Transpan (CA21116).

Relevant publications

- Duran-Sanchon S et al., Fecal MicroRNA-Based Algorithm Increases Effectiveness of Fecal Immunochemical Test-based Screening for Colorectal Cancer. Clin Gastroenterol Hepatol. 2021. doi: 10.1016/j.cgh.2020.02.043.
- Fernandez-Castañer E et al., MicroRNAs Deregulated in Intraductal Papillary Mucinous Neoplasm Converge on Actin Cytoskeleton-Related Pathways That Are Maintained in Pancreatic Ductal Adenocarcinoma. Cancers. 2021. doi: 10.3390/cancers13102369.
- Vila-Navarro E et al., MiR-93 is related to poor prognosis in pancreatic cancer and promotes tumor progression by modulating targets involved in microtubule dynamics. Oncogenesis. 2020. doi: 10.1038/s41389-020-0227-y.
- Duran-Sanchon S et al. Identification and validation of microRNA profiles in fecal samples for detection of colorectal cancer. Gastroenterology. 2020. doi: 10.3390/biom10010016.
- Marcuello M et al. Analysis of a 6-miRNA signature in serum from colorectal cancer screening participants as non-invasive biomarkers for advanced adenoma and colorectal cancer

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

detection. Cancers. 2019. doi: 10.3390/cancers11101542.

Project description

Background: Colorectal cancer (CRC) is the third most common cancer worldwide and the second leading cause of cancer-related death. Although many improvements have been made in the last years, there is still a need to identify and develop novel, clinically useful biomarkers that can improve disease outcome. Small non-coding RNAs (sncRNAs) show altered expression patterns and play important regulatory roles in colorectal cancer development and progression. The fact that they can be detected in different body fluids in a stable manner makes them promising new non-invasive biomarkers.

Hypothesis: We believe that detection of sncRNAs in liquid biopsies could make a relevant contribution for biomarker development to improve CRC management.

Objectives & Methodology: The main aim of this project is to identify and validate novel sncRNA-based CRC biomarkers with prognostic value via liquid biopsy approaches by comparing different state-of-the-art technologies. To achieve that aim we will firstly select sncRNA candidates from next-generation sequencing followed by clinical performance assessment by RT-qPCR on liquid biopsies from CRC patients. The best set of sncRNA biomarkers will be also assessed with a different technology developed by another ColoMARK member and performance comparison will be carried out. Relevant results will be validated in independent cohorts from the ColoMARK consortium.

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills.

Academic qualifications requested

BSc + MSc in biomedical sciences* (or similar in content, depending on country of origin).

Skills requested

Previous molecular biology lab experience
Proficient in microsoft office and statistical analysis applied to biomedical sciences (including logistic regression and survival analysis)
Ability to work with high level of autonomy
English writing and oral communication skills
Teamwork ability
Previous working mobility experience

Skills valued

Previous lab experience with clinical samples and use of databases
Previous experience in RNA extraction, RT-qPCR and/or microRNA analysis
Knowledge on cancer biology
Knowledge on non-coding RNA molecular biology
Knowledge in bioinformatic analysis
Previous experience on biomarker development
Previous experience in delivering public presentations
Responsibility, having initiative and creativity will also be considered

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Application procedure

Applicants should follow the application procedure and submit the files in English in a single .pdf document to mgirone@recerca.clinic.cat AND fcrbrrhh@recerca.clinic.cat indicating "Application for DC7COLOMARK" in the e-mail subject line.

Before applying, we kindly advise you to carefully read the description for DC positions within MSCA Doctoral Network ColoMARK (MSCA-DN-2021-101072448): there, you will find all the relevant information and the list of the documents to attach to your application.

Notice: Please ensure that you qualify before applying, as ineligible candidates cannot be considered.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC8 project title

Diagnostic Leukapheresis and intraoperative samples to enhance CTC detection in early CRC

Recruitment centre

Heinrich-Heine University Medical Center, Düsseldorf (UDUS); Düsseldorf (Germany).
Supervisors: Dr Rui Neves (UDUS) and Assoc. Prof. T. van Wezel from the Leiden University Medical Centre (LUMC).
The DC will be enrolled in a PhD programme at UDUS.

Group description

The project is to be developed in the group of Experimental Surgical Oncology from the Department of General, Visceral and Pediatric Surgery at the Heinrich-Heine University Medical Center Düsseldorf (Germany). The group is led by Prof. Dr med. Nikolas H. Stoecklein and the project will be directly supervised by Dr rer. nat. Rui Neves, a senior associate researcher. One main focus of the group's research activities is the genetic heterogeneity of tumours and disseminated metastasis-precursor cells, and its relevance for disease progression and therapy resistance. Prof. Stoecklein has >15 years research experience in minimal residual cancer and liquid biopsy and he pioneered Diagnostic Leukapheresis (DLA) for enhanced CTC detection. Dr. Neves joined the group in 2013 and since then he developed multiple workflows/methods to detect, isolate and analyse CTCs at single cell level and led the so far larger proficiency test for CTC detection technologies (within CANCER-ID project).

Relevant publications

- Fischer JC, ..., Stoecklein NH. Diagnostic leukapheresis enables reliable detection of circulating tumor cells of nonmetastatic cancer patients. Proc Natl Acad Sci U S A. 2013 Oct 8;110(41):16580-5.
- Pixberg CF, ..., Stoecklein NH, Neves RPL. Analysis of DNA methylation in single circulating tumor cells. Oncogene. 2017 Jun 8;36(23):3223-3231.
- Neves RPL, ..., Stoecklein NH. CANCER-ID Consortium. Proficiency Testing to Assess Technical Performance for CTC-Processing and Detection Methods in CANCER-ID. Clin Chem. 2021 Mar 31;67(4):631-641.
- Fehm TN, ..., Neves RPL, ..., Stoecklein NH. Diagnostic leukapheresis for CTC analysis in breast cancer patients: CTC frequency, clinical experiences and recommendations for standardized reporting. Cytometry A. 2018 Dec;93(12):1213-1219.
- Neves RP, ..., Stoecklein NH. Genomic high-resolution profiling of single CKpos/CD45neg flow-sorting purified circulating tumor cells from patients with metastatic breast cancer. Clin Chem. 2014 Oct;60(10):1290-7.

Project description & references

Background: In localised CRC, the detection of CTCs could help to identify patients at risk for metastasis and could help to stratify them to adjuvant therapies.
Hypothesis: Beyond enumeration, the greater potential for CTC-based liquid biopsies lies in their subsequent molecular characterization to provide predictive information for molecular therapies. On the other hand, the analysis of CTCs can provide information on the mechanisms of tumour dissemination. However, the infrequent and unreliable detection of CTCs, poses a limitation for diagnostic applications in localised CRC. To increase CTC-detection, we have developed diagnostic leukapheresis (DLA) that enables the screening of litres of blood, and

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

we have implemented a program for collection of blood samples during surgical intervention for tumour removal.

Objectives & methodology: With this project we aim specifically:

1) To test the value of Diagnostic Leukapheresis (DLA) and intraoperative samples (from the tumour-draining vein and central venous line) in localised CRC for CTC-detection and identification of patients at risk for metastatic disease. 2) To check the utility of DLA and intraoperatively collected CTCs for clinically relevant diagnostic tests (KRAS mutation testing, EGFR expression etc.). 3) To take advantage of the increased CTC yields in DLA products and intraoperative blood samples for comprehensive molecular analysis to dissect the biology of the potential precursor cells of metastatic relapse. 4) To test the value of DLA and intraoperative blood samples for detection of other circulating biomarkers (ctDNA, ctmiRNAs, microbiome and metabolomics). 5) Explore correlation between circulating tumour biomarkers (CTCs, ctDNA) and the integrity status of the gut-blood barrier.

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills

Academic qualifications requested

BSc + MSc in Biomedical sciences/Molecular Biology/Biotechnology* (or similar, depending on country)

Skills requested

Basic knowledge on (cancer) genomics
Basic knowledge on molecular biology techniques

Skills valued

Experience with molecular biology techniques (e.g. NGS Library Preparation)
Experience with Linux environment and programming skills (e.g. on R, python, bash)
Experience on analysis of NGS data
Experience in technologies for CTC enrichment or molecular analysis
Experience with cell culture/biology techniques (e.g. flow cytometry, fluorescence microscopy)

Application procedure

Applicants should follow the application procedure (above in the document) and submit the application documents via email to: rui.neves@med.uni-duesseldorf.de

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC9 project title

Prognostic value of TP53 in exosomes from liquid biopsy studies.

Recruiting centre

Leiden University Medical Center (LUMC), Leiden (Netherlands).
Supervisors: Assoc. Prof. Dr. T. van Wezel (LUMC) and Dr M. Gironella (FCRB, Spain) The project will be performed in close collaboration with DC5, supervised by Sander Tuit, R&D project manager at GenomeScan.
The DC will be enrolled in a doctoral programme at LUMC.

Group description

Dr. Tom van Wezel is a Clinical Scientist at the department of pathology, LUMC. He has supervised >10 PhD students and trained five Clinical Scientist Molecular Pathology. His translational research is focused on molecular pathology of cancer to i) improve the tumour diagnostics; ii) discover therapeutic targets; and iii) resolve the underlying genetic cause of cancer. This is exemplified by recent studies on lung cancer describing the routing to detect both diagnostic and therapeutic targets using NGS (1). Via mutational signatures in cancer, genetically unexplained cancers could be resolved and their characteristics described. For example, for NTHL1 mutation carriers' mutational signatures, cancer risk and family characteristics were described (2, 3). Combinations of somatic and mosaic mutation signatures resolved genetically unexplained suspected cancer syndrome and patients (4,5, 6).

Project description & references

Background: TP53 is the most frequently mutated gene in cancer and both germline and somatic mutations in the TP53 gene play an important role during tumorigenesis and TP53 mutations are a prognostic indicator in cancer. This has been demonstrated in prostate cancer, both in tissues and in liquid biopsies.
Hypothesis: TP53 is a complex gene with different isoforms. Besides the canonical TP53, there are also the alternatively spliced p53 isoforms, p53β and p53γ. Together, all these variant codes for a multiprotein complex for which the functions are not fully understood. The composite P53 complex has functions in DNA repair, growth arrest and apoptosis. In several families with inherited cancer, mutations in the TP53β isoform have been shown to have an effect on TP53 functioning and possibly predispose to various cancer types including CRC. Interestingly, the TP53 isoforms p53β has been shown to be present in exosomes as well.
Objectives: We will study TP53 in ctDNA and exosomes in relation to prognosis in CRC, with a focus on TP53β.
Methodology: A variety of techniques will be used, including RNA and protein expression analysis and NGS based ctDNA detection techniques. The most optimal exosome detection methods will be compared and investigated for our studies.

- Cohen, D, et al. (2020). Optimizing Mutation and Fusion Detection in NSCLC by Sequential DNA and RNA Sequencing. Journal of Thoracic Oncology 15, 1000-1014.
- Grolleman, JE, et al. (2019). Mutational Signature Analysis Reveals NTHL1 Deficiency to Cause a Multi-tumor Phenotype. Cancer Cell 35, 256-266 e255.
- Elsayed, FA, et al. (2020). Monoallelic NTHL1 Loss of Function Variants and Risk of Polyposis and Colorectal Cancer. Gastroenterology 159, 2241-2243 e2246.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

- Terlouw, D, et al. (2020a). Recurrent APC Splice Variant c.835-8A > G in Patients with Unexplained Colorectal Polyposis Fulfilling the Colibactin Mutational Signature. Gastroenterology 159, 1612.
- Jansen, AM, et al. (2017). Distinct Patterns of Somatic Mosaicism in the APC Gene in Neoplasms from Patients With Unexplained Adenomatous Polyposis. Gastroenterology 152, 546-549 e543.
- Jansen, AM, et al. (2016b). Combined mismatch repair and POLE/POLD1 defects explain unresolved suspected Lynch syndrome cancers. Eur J Hum Genet 24, 1089-1092.

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills

Academic qualifications requested

MSc in Biomedical sciences or Molecular Biology (or similar, depending on country)

Skills requested

Knowledge on (cancer) genetics/genomics
Knowledge on molecular biology techniques
Lab experience working with DNA or RNA

Application procedure

Applicants should follow the application procedure (above in the document) and submit the application documents via email to: t.van_wezel@lumc.nl

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

DC10 project title

Single-cell RNA sequencing of circulating tumour cells (CTCs) in CRC patients to identify novel biomarkers of disease monitoring and progression

Recruiting centre

Fundación Instituto de Investigación Sanitaria de Santiago (FIDIS), Santiago de Compostela (Spain).
Supervisors: Dr C. Fernandez (FIDIS) and Dr. Vivian Viallon (IARC, France).
The DC will be enrolled in a PhD programme at the University of Santiago de Compostela (USC).

Group description

Dr Ceres Fernandez (she/her) is an emergent PI at IDIS. Her work so far has focused on genetic predisposition to colorectal cancer and the identification of novel biomarkers to offer better prevention strategies for the disease. After obtaining her PhD in 2011, she worked for 3 years as a Marie Curie IEF Fellow under Prof Ian Tomlinson at the Wellcome Centre for Human Genetics (University of Oxford), and later as a postdoctoral senior researcher at the Santiago Biomedical Research Institute (IDIS), where she is currently a PI.
Dr Fernandez has a vast experience on NGS data analysis, GWAS and TWAS, and is a pioneer in multi-omic wide association approaches in CRC. The work in her lab revolves around 3 major research topics: genetic predisposition to gastrointestinal cancers, biomarker identification for cancer prevention using liquid biopsy and omic strategies, and genetic determinants of adverse drug reactions to chemotherapeutic agents. Her team presently includes one lab technician, one PhD student, and one bioinformatician.
She has published over 35 works in indexed journals, including 15 as main author, 6 in D1 and 9 in Q1, totalling over 1,500 citations. She has an h-index of 20 and an i10 of 25. As a PI, she has obtained funding in several projects funded by the MSCA IEF, Fundació Olga Torres (2018 & 2021), ISCIII-AES (2019 & 2022), MICINN and MSCA Doctoral Networks (2022). She has also participated in more than 10 national and international projects as a team member. She has been a member of COST Actions EuColonGene (BM-1206), TransColonCan (CA-17118), and recently, CA21116 TRANSPAN.

Relevant publications

- Fernandez-Rozadilla et al. Deciphering colorectal cancer genetics through multi-omic analysis of 100,204 cases and 154,587 controls of European and Asian descent. Nature Genetics. Accepted. Pending publication.
- Bonjoch*, Fernandez-Rozadilla* et al. BMPR2 as a candidate novel germline predisposition gene for colorectal polyposis. Gastroenterology. Under review
- Hita-Millan, Carracedo, Fernandez-Rozadilla (CA). 2021. Liquid Biopsy Biomarkers for Immunotherapy in Non-Small Cell Lung Carcinoma: Lessons Learned and the Road Ahead. Journal of Personalized Medicine.
- Fernandez-Rozadilla et al. 2021. Exome sequencing of early-onset patients supports genetic heterogeneity in colorectal cancer. Scientific Reports
- Fernandez-Rozadilla et al. 2021. Tumour profiling at the service of cancer therapy Frontiers in Oncology.

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Project description & references

Background: Colorectal cancer is one of the most prevalent tumours and an important disease burden. Mortality rates are especially relevant in CRC, with later metastatic stages responding poorly to conventional treatments.

Hypothesis: secondary tumours (metastases) are the main cause for CRC-related deaths. In order for these to develop, tumour cells must travel from the primary location to the distant organs through the circulation. The properties of these circulating tumour cells (CTCs) could therefore harbour important information on the CRC metastatic process and provide relevant clues on how to monitor and stop the disease.

Objectives: The main aim of this project is to utilise circulating tumour cells (CTCs and their transcriptomic landscape over the course of the disease and treatment to identify novel biomarkers that can help us guide therapeutic strategies.

Methodology: CRC patients will be recruited and single CTCs isolated to perform single-cell RNA sequencing. DC10 will perform a comparison of CTC isolation procedures and techniques to obtain SOPs for the isolation of CTCs for downstream transcriptomic analyses. The dynamic CTC transcriptomic data will be mined to identify biomarkers that can help predict disease outcome and guide therapeutic strategies. The CTC results will be compared with those obtained from primary tumour analyses and other complementary biomarkers, to create optimal models. Then, results will be validated in additional ColoMARK datasets.

- Behjati S, Haniffa M. Genetics: taking single-cell transcriptomics to the bedside. Nat Rev Clin Oncol 2017
- Castro-Giner F, Scheidmann MC, Aceto N. Beyond Enumeration: Functional and Computational Analysis of Circulating Tumor Cells to Investigate Cancer Metastasis. Front Med (Lausanne). 2018
- Cristofanilli M, et al. Circulating tumor cells, disease progression, and survival in metastatic breast cancer. N Engl J Med. 2004
- Cohen SJ, et al. Relationship of circulating tumor cells to tumor response, progression-free survival, and overall survival in patients with metastatic colorectal cancer. J Clin Oncol. 2008
- Crowley E, et al. Liquid biopsy: monitoring cancer-genetics in the blood. Nat Rev Clin Oncol. 2013
- Lianidou E, Pantel K. Liquid Biopsies. Genes Chromosomes Cancer. 2018.

Additional eligibility criteria

Applicants must fulfil the requested list of academic qualifications and skills

Academic qualifications requested

BSc in biomedical sciences* (or similar, depending on country) + MSc on bioinformatics OR BSc in computer science* + MSc in genomics*.

Skills requested

Proven bioinformatic understanding of NGS data analysis, particularly transcriptomics
Working abilities on Linux environment and programming skills on R, bash or python

This project has received funding from the European Union´s Horizon Europe research and innovation programme under the Marie Skłodowska-Curie Doctoral Network grant agreement No. 101072448

Skills valued

Previous experience with RNAseq data analysis
Lab experience working with CTCs
Knowledge/work on cancer genetics/genomics
Previous experience with prediction models, including predictors
Previous experience on biomarker development

Application procedure

Applicants should follow the application procedure and submit the files as a single pdf here: **FIDIS Job Opportunities (position 002/2023).**

*similar (in content) degrees may be considered (depending on description), as the titles may vary depending on country of origin.