Computational biology PhD position (f/m/d): Computational drug screening and synthetic lethality drug repurposing to identify novel therapeutic options for prostate cancer

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This is a 3-year PhD position, that is part of a European Doctoral Network (DN) program entitled **"Prostate cancer omics mediated intervention (PROMOTE)"** involving 13 research centres from Germany, Greece, Austria, Portugal, and Spain.

The PhD position is hosted at Delta 4 GmbH, Vienna, Austria.

Delta4 is a Vienna-based TechBio company at the forefront of digital drug discovery and development. Delta4 leverages a proprietary computational analytics platform (Hyper-C), combined with biomedical testing and clinical validation of candidate drugs. Our unique approach integrates iterative big data/in silico and experimental screens, offering the most efficient matching of clinical indications and compound/drug effects. Our R&D process allows a fast track to clinical stage testing; our methodological core is tailored toward precision to increase the probability of success. Our focus is the repositioning of existing drugs for novel indications.

By generating IP for such drug-disease combinations we establish a pipeline of clinically and economically attractive indications. Results of our lead program on the rare chronic kidney disease focal segmental glomerulosclerosis have been published recently (Transl Res. 2023 259:28-34 ; Kidney Int Rep. 2023 9(2):478-481). Previous computational data integration workflows have led to the identification of novel drug combinations in other tumour entities (Oncotarget. 2018 9(91):36379-36391; PLoS One. 2019 14(1):e0210859).

The PROMOTE Consortium / Background

PROMOTE focuses on the multidisciplinary education of doctoral candidates (DCs) in -omics and artificial intelligence (AI) mediated intervention to improve the clinical management of Prostate Cancer (PCa).

PCa is the second most common malignancy, affecting ~1.3 million men every year worldwide. Tragically, there is a treatment paradox, as ~45% of PCa patients experience slow-growing cancer and are unlikely to progress rapidly, while PCa is not curable at an advanced stage. Evidently, clinical management of PCa is not optimal, as patients who do not require treatment are over-treated, while for those where immediate actions are required, efficient treatment is still needed.

To fill the above gaps, PROMOTE was formed to educate DCs in emerging -omics and AI technologies and deliver:

1. novel non-invasive tools (based on biomarker- and AI- models) to guide intervention, and

2. more efficient treatment options for advanced PCa (particularly metastatic) driven by molecular characterisation of the disease phenotypes.

PROMOTE brings together 13 leading centres from different disciplines, including 3 SMEs, 4 university hospitals with clinical laboratories, 2 research institutes, and 4 universities, closely collaborating with a solid scientific background, as demonstrated by multiple publications.

PROMOTE research builds on:

 1. available biobanks and -omics datasets within the PROMOTE consortium, including >3000 urinary proteomics, >1100 imaging datasets paired with biopsy and pathology data, >350 paired RNA and proteomics urinary profiles, >100 tissue proteomics and ~300 phospho-, proteo-genomic and transcriptomics profiles from public repositories

 2. established software and analytical protocols on -omics data integration, AI feature extraction and integration, systems biology, pathway enrichment, drug repurposing and in vitro testing, and

 3. infrastructure to support hosting and training of DCs.

Objectives of the PhD

The overall objective of this PhD-project in PROMOTE is to consolidate omics profiles in the context of prostate cancer to generate network-based molecular models for the disease. Network alignment methods shall be used to identify compounds that show beneficial interference between disease pathobiology and drug mechanism of action. A particular focus will be placed on compounds that affect target molecules involved in synthetic lethal interactions within the context of tumour progression. The potential of identified compounds and compound combinations targeting synthetic lethal interactions will be tested in combinations with researchers from the Medical University of Innsbruck.

Methods

The PhD student will mostly work on data analysis and statistical analysis using R or Python. There will be some interaction with the wet laboratory (in-vitro compounds testing).

Expected Results

- Meta analysis of omics data in the context of prostate cancer
- Generation of a network-based molecular model of prostate cancer
- Identification of compounds interfering with prostate cancer pathobiology
- Identification of drug combinations that address synthetic lethal interactions

Additional Information on the PhD

Supervision

- You will be enrolled in a PhD program at the Medical University of Vienna or Innsbruck
- You will be supervised by Dr Paul Perco, Prof. Klaus Kratochwill, and Prof. Isabel Heidegger-Pircher

Planned secondments

The position includes 2 mandatory stays in partner laboratories to complete training:

1) Mosaiques Diagnostics GmbH: training proteomics data analysis.

2) Medical University Innsbruck: testing of drug combinations derived from the analysis of synthetic lethal interactions.

Required skills and education:

- You hold a master's degree in bioinformatics/computational biology
- Fluent in a scripting language (R or Python) for data wrangling, explorative analysis and data visualization
- A solid understanding of cellular and molecular biology; knowledge of the hallmarks of cancer is a plus (Cell 2000 100:57-70; Cell 2011 144:P646-674)
- Experience with SQL, JSON, XML
- Statistical analysis of large biological datasets (e.g. Omics data)
- Experience with extracting data from key biological databases (NCBI, Ensembl, UniProt, GEO, ArrayExpress)
- Knowledge of key biological ontologies/vocabularies (Medical Subject Headings, Gene Ontology, Anatomical Therapeutic Chemical Classification, …)
- Knowledge of graph theory and key graph measures
- Experience with biological network modelling and visualization (e.g. Cytoscape, igraph, …)

Marie Skłodowska-Curie ITN rules
- You must **NOT** have a doctoral degree at the date of your recruitment.
- You must comply with the **mobility rule**: not have resided or carried out your main activity (work, studies, etc.) in Austria for more than 12 months in the 36 months immediately before the recruitment date.

Benefits

- You will benefit from all Marie Skłodowska-Curie Action scheme advantages.
- You will participate in web seminars (in English) of the collaborative network of the laboratory.
- You will attend yearly meetings organised by the PROMOTE consortium, as well as international and national congresses.
- You will work at a modern office in the beautiful 8th district of Vienna.
- Salary range: 3.200 - 4.000 EUR brutto / month

How to apply

Please submit your candidacy via JOIN (or email to office@delta4.ai) including the following information:

- your CV and motivation letter
- your MSc transcript (diploma, courses, and grades)
- two reference letters or contact details from your previous scientific supervisors