Bioinformatic analysis of tumor genomes in the absence of paired normal tissue samples

Summary

The goal of the project is to examine, assess, and develop further the methods to analyse tumor genomes at the level of exomes, full genomes, and transcriptomes and quantify the extent of useful information that can be gained from samples where paired normal tissue is not available. As there exists a large body of tumor samples, particularly FFPE samples, where detailed clinical information is available, including long term patient outcomes, but often normal tissue control is missing, this project will address the need to bring the genomic information contained in these samples into use for clinical and translational research. The project is implemented in collaboration with the North-Estonian Medical Center and initial focus is on lung cancer.

Research field:	Biomedicine and health technology
Supervisor:	Prof. Dr. Olli-Pekka Smolander
Availability:	This position is available.
Offered by:	School of Science
	Department of Chemistry and Biotechnology
Application deadline:	Applications are accepted between June 01, 2022 00:00 and June 30, 2022 23:59 (Europe/Zurich)

Description

Lung Cancer is the leading cause of cancer-related death world-wide; The survival of lung cancer patients at 5 years after diagnosis is only 10% to 20% in most countries. In 2020, 2.21 million new lung cancer cases and 1.80 million deaths were reported globally. About 20% of cases are being diagnosed at an early stage when the disease is still curable by surgery. However, 30-55% of patients initially treated with radical surgery develop recurrence despite curative resection and among those median recurrence free survival is 11.5 months. Despite significant advances in surgery from pulmonectomy to minimally invasive surgery, and in radiotherapy from 3D conformal to intensity modulated radiotherapy, lung cancer remains one of the deadliest cancers in developed countries. Sequencing studies in lung cancer have reported prognostic signatures, but no signatures have been validated in independent studies and their accuracy of survival estimation remains limited.

The aim of the study is to investigate potential prognostic markers in a cohort of patients and to correlate these markers with clinical outcome (recurrence free survival and overall survival), In addition, we also aim to characterize frequency of ALK alterations in Estonian population.

The cohort in the study are patients who initially diagnosed local disease and had received treatment with curative intent. Approximately half of the patients had lung cancer recurrence diagnosed later. Total number of patients for which the whole exome sequencing data has been already obtained is 200.

In summary:

- To evaluate the prognostic role of different clinical and laboratory markers in recurrence free and overall survival in lung cancer patients
- To investigate gene alterations to identify a prognostic genomic signature and to evaluate the role of cancer related immune and neurotrophic factors in clinical outcome

To analyze changes associated with the lung cancer recurrence and metastatic behaviour, the aim is to use between-group analysis, existing mutation databases (e.g., gnomAD, ExAC and COSMIC) to filter out normal population level variation and known clinically related variation in the case of novel variants, and the national genomic resources

from the Estonian genome centre to provide panel of normal genomes. The role of known clinically related mutations will be examined similarly using the existing databases. The effect of genomic alterations can be further investigated using RNAseq and single cell methodologies with corresponding data analysis approaches. In connection with this project, also copy number variations and fusion gene events will be analysed in the sample cohorts.

Responsibilities and (foreseen) tasks

- Compile an analysis framework for existing cohort of samples
- Set up variant filtering and analysis environment to separately analyse different clinically relevant sample groups
- Incorporate the existing information on Estonian population genomics to the analysis workflow
- Analyse the effects of known clinically relevant genomic alterations to the lung cancer recurrence
- Investigate the role of novel genomic alterations to lung cancer recurrence over several patient groups

Applicants should fulfil the following requirements:

- a master's degree in biosciences (preferably in connection with bioinformatics, computational biology, or biostatistics)
- a clearly expressed interest in the topic of the position
- excellent command of English
- strong and demonstrable communication, writing and analytical skills
- capacity to work both as an independent researcher and as part of an international team
- capacity and willingness to provide assistance in organizational tasks relevant to the project

The following experience is beneficial:

- Linux command line use
- Programming in Python and/or use of R environment
- Working knowledge of HPC computing
- Variant annotation databases and tools, particularly ANNOVAR
- Analysis of genomic and/or transcriptomic data
- Previous experience on cancer biology

The candidate should submit a motivation letter expressing interest in the topic and a transcript of records from an applicable higher education degree.

We offer:

- 4-year PhD position in a large and international technical university within a research group with demonstrated ability to carry out high quality research in biosciences field
- The chance to do impactful research in one of the most important health and medicine related contexts globally
- Opportunities for conference visits, research stays and networking globally with leading universities and research centers in the field of cancer biology, genomics, and personalized medicine

About the department

The department of Chemistry and Biotechnology was created in the School of Science of Tallinn University of Technology in 2017 when the former Institute of Chemistry and the Institute of Gene Technology from the Faculty of Mathematics and Natural Sciences and the Institute of Food Science from the Faculty of Chemistry and Materials Technology merged. Recent scientific discoveries in chemistry, molecular biology and food technology have opened completely new perspectives in fields as medicine, industry, agriculture, and the environment.

The institute is the main provider of studies in the Bachelor's programs in Applied Chemistry, Food and Gene Technology and the Master's programs in Applied Chemistry and Biotechnology and Food Technology and Development. The majority of students majoring in applied chemistry and gene technology and some students of food technology do their dissertations in the research groups of the institute. The institute also offers doctoral studies in all the above areas and is a home for more than 20 research groups.

In addition, the institute teaches a number of special subjects to students from other schools: General Chemistry, Chemistry, Environmental and Ecology, Fundamentals of Science-Based Health Behavior, and Fundamentals of Life. Institute also participates in the international Bioceb Master's program (European Master in Biological and Chemical Engineering for a Sustainable Bioeconomy, www.bioceb.eu), which hosts international students in the spring semester and teaches three subjects.

Additional information

For further information, please contact Prof. Olli-Pekka Smolander or visit
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