Bioinformatics Research Internships: Novel genes in prostate cancer

The Department of Urology of the Erasmus MC Rotterdam is offering student projects in the field of bioinformatics for Bachelor and Master students. Our research questions focus on discovery of novel genes for prostate cancer (PCa) by integration of several established high throughput technologies.

Prostate cancer is one of the most common cancers in men, mostly occurring above the age of 50 with its incidence rate increasing with age. Despite its wide spread in males, PCa tumors often remain unnoticed and until metastasis occur. Therefore, testing for the presence of prostate specific antigen (PSA test) is often performed. However, since PSA is not prostate cancer specific and does not offer prognostic value, many patients with benign tumors undergo unnecessary treatment, as they cannot be distinguished from aggressive forms. At the same time, modern medicine is unable to predict the occurrence of metastasis and resistant disease.
Hence, our goal is to investigate novel genes and transcripts in prostate cancer that can address the need for highly specific biomarkers and help in prognosis of tumor development.

Currently, we have three defined projects available for internships and/or graduation projects (thesis):

1. Discovery of novel prostate cancer-associated genes

RNA- and DNA-sequencing of PCa patients offers a large source of clinical information that enables us to search for aberrations within PCa on both genomic and transcriptomic level.
From Affymetrix exon arrays and RNA-Seq analyses, we discovered novel unannotated prostate cancer specific transcripts that might be related to aggressive tumor types. We would like to extend this search for novel genes using RNA-Seq data and perform assembly of the reads into the mature mRNA. Analysis steps include sequence alignment, assembly of novel transcripts and subsequent abundance estimation. Furthermore, PCa specific alternative splicing and promoter use are also of interest. In order to do so, a fully functional pipeline should be developed which can involve already existing tools, such as aligners (bowtie, BWA, GSNAP etc.). The resulting genes might play a crucial role in development and progression of prostate cancer and are therefore potential biomarkers for PCa.

2. Discovery of novel fusion events in PCa

Fusion genes are hybrid genes that are formed during chromosomal rearrangements and can occur between loci on the same chromosome (intrachromosomal) as well as on different chromosomes (interchromosomal). A well known example in PCa is the TMPRSS2-ERG fusion gene which has been researched extensively during the past years. However, gene fusions are not necessarily limited to two genes. In addition, the transcripts resulting from a gene fusion might play a role as tumor promoters

(gain of function) or tumor cells might lose tumor suppressing factors due to inactivating rearrangements.
In order to find these novel fusion genes, the student will develop a pipeline to analyze 100x coverage whole genome DNA-Seq data obtained from PCa patients and combine the results with data coming from RNA-Seq experiments. At this, we hope to discover novel fusion genes and expressed fusion transcripts that subsequently can be validated in the wetlab.

3. Coexpression analysis of potential prostate cancer biomarkers

As mentioned above, we have found novel prostate cancer specific transcripts using Affymetrix Exon Array and RNA-Seq data. To continue this research, we intend to perform an extensive coexpression analysis to reveal corregulated transcription factors that might be responsible for the gene regulation of the novel transcripts. The student will optimize the new algorithm for coexpression and develop a pipeline for coexpression analysis of transcripts, resulting in a coexpression network for our novel gene candidates. This pipeline should be organized in modules to easily boost the pipelines capabilities, enabling us to perform further research towards coregulation and potential binding partners on DNA level (ChIP-Seq).

The research group

The group headed by Prof. Dr. Guido Jenster consists of about 20 scientists including postdocs, PhD students, technicians, bioinformaticians and BSc and MSc students.

The research is focused on genes and pathways responsible for prostate cancer initiation and progression. In addition, model systems and biomarkers for this disease are being developed. The latest technologies including in RNA-Seq and DNA-Seq are implemented to optimally identify and validate genes and markers of interest.

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