UNIVERSITÄT ZU LÜBECK
Institut für Molekulare Medizin

TECHNISCHE HOCHSCHULE LÜBECK

Identification of urinary biomarkers for bladder cancer diagnosis by performing differential gene expression and pathway analysis on RNA-seq data

Urinary RNA-based biomarkers are the key indicator in urine based diagnostic tests for urinary bladder carcinoma, which is one of the highly sort after diagnostic tool in the recent years due to the non-invasive nature, possibility of early diagnosis and comparative low cost of this Technology. Urine contains organic compounds such as RNAs, proteins, hormones and many more. These compounds are secreted into urine from the urothelial cells in bladder cell lining including potential tumor cells. Apart from those, detached bladder tumor cells could also be found in urine. This makes voided urine a promising source for the research of macromolecules including RNA as potential biomarkers for the identification of bladder carcinoma.

Differential gene expression and pathway analysis were performed on RNA-se data between healthy (C) and first time high-risk (AH) cancer patients and between patients with relapsed high-risk cancer (AHR) and recovered patients who have been cleared for the recurrence of cancer (CR). Results showed that only 13 significantly expressed genes were common in both analyses. Which calculates to only 14% of all differentially expressed genes in AH vs C analysis and only 10% in AHR vs CR analysis. Two different novel biomarker candidate combinations are suggested for the diagnosis of high risk bladder carcinoma. These overlaps of markers seem to make it necessary to search for RNA-based biomarkers that distinguish initial and relapse cancer stages exactly.

Protein coding genes; RIC3 acetylcholine receptor chaperone (RIC3), leukocyte specific transcript 1 (LST1), vascular endothelial growth factor A (VEGFA), sterile alpha motif domain containing 12 (SAMD12), cornulin (CRNN) and MAL (T cell differentiation protein (MAL)) are suggested as urinary biomarker candidates for the diagnosis of initial high risk bladder carcinoma (AH patient group).

Protein coding genes PTPRF interacting protein alpha 1 (PPFIA1), protein phosphatase 1 regulatory subunit 18 (PPP1R18), TBC1 domain family member 3C (TBC1D3C) and flavin containing dimethylaniline monoxygenase 2 (FMO2) are suggested as potential urinary biomarker candidates for the identification of recurrent high risk bladder carcinoma (AHR patient group).

This thesis work focused on suggesting possible biomarker candidates via differential gene expression and pathway analysis. The Scope of this thesis did not include the investigation of urinary ncRNAs and circular RNAs. More urinary RNA based biomarkers could be added to the candidate list by identifying suitable ncRNA and circular RNA biomarker candidates as well. However diagnostic tests depend on the accuracy, specificity and sensitivity. Hence performing Quantitative reverse transcription PCR (RT-qPCR) on the urinary RNA-based marker candidates is also suggested in order to validate the short listed biomarkers.

Author: Manikwadura Dilini Tharindika

Submitted on: 28th April 2022