Discovery and Evaluation of Urothelial Bladder Cancer Protein Biomarker Candidates in Urine

High throughput proteomics measurements enable comparisons of clinical samples from large populations of patients and controls. This represents a formidable opportunity for the discovery of early diagnostic or prognostic biomarkers, i.e. molecular indicators of a pathological state or its probable evolution that are present before the onset of specific clinical symptoms. New challenges lie in the integration of these technologies in the discovery and the evaluation of novel biomarkers, to translate initial findings into manageable lists of candidates for the purpose of designing new clinical assays. The DECanBio project (EU-FP7) aimed at (i) developing reliable analytical protocols and strategies for the generation of robust quantitative proteomics data, (ii) using them for the discovery and evaluation of new candidate biomarkers of bladder cancer in urine.

Among available technologies for biomarkers discovery, two methods emerged with a high potential for integration: the Accurate Mass and retention Time (AMT) tag proteomics method used for global sample profiling [1] and the Selected Reaction Monitoring SRM approach used for targeted candidate evaluation [2]. Importantly, both methods relied on the same sample type and standardized preparation method [3]. Using the AMT tag approach on a 98 patients cohort (cancer vs. healthy controls), among 1180 monitored proteins, statistical analysis yielded a list of 97 candidates. SRM was used to evaluate a selection of 134 candidates originating in part from our AMT results, but also from literature mining, from another 2DE study on the same cohort and from a separate transcriptomics screen on bladder tumors biopsies. This evaluation entailed estimation of differential concentrations of these candidates in 121 urine samples from cancer patients and control patients with a suspicion of bladder cancer that had been cleared by pathological examination. Among the 134 screened candidates, 108 could be accurately monitored in urine, and 71 showed potential for diagnosis or prognosis of bladder cancer incidence or recurrence.

References