Case study - Screening for Biomarkers

Identification of protein biomarkers for a prognosis of recurrence in bladder cancer

Bladder cancer is the fourth most common type of cancer in men and the ninth most common cancer in women. 70% to 80% of newly diagnosed bladder cancer cases are a low-stage, low-grade nonmuscle-invasive disease. Standard treatment is a transurethral resection of bladder tumour (TURBT), by which the tumour material is available for subsequent analyses. About 50% to 70% of the tumours will recur and 10% to 30% will progress to become a muscle-invasive disease. Therefore, the guidelines for bladder cancer recommend surveillance cystoscopy and urine cytology for nonmuscle-invasive disease every three months for the initial one to two years, repeated at longer intervals over the next two years, and annually thereafter. The predicted lifetime costs for bladder cancer patients are between US$ 99,000 and US$ 121,000. Five-year net cost of bladder cancer in the USA is approximately one billion dollars. As important is the patient's psychic well being: patients live in a state of continuous uncertainty and are confronted with the possibility of a recurrence every three months.

We analysed the protein profiles of nonmuscle-invasive bladder tumours with complex antibody microarrays. The sample set comprised tumours with a local recurrence and tumours without recurrence five years after diagnosis. We identified 100 proteins with highly significant (adjusted p-value < 0.003) differential abundance between these two groups. From this, a multivariate classifier was constructed that is based on the expression variation of 20 proteins and facilitates the prediction of recurrence with a sensitivity of 80% at a specificity of 100%. The overall accuracy of the classification is well within a clinically relevant window of quality. The assay - performed after the initial diagnosis on the then routinely available tissue by clinically established immuno-based protocols - will permit to choose among different treatment modalities and to adjust the rigidity of surveillance via cystoscopy. This will dramatically reduce surveillance costs and improve patients' well being and outcome substantially.

Srinivasan H., Allory Y., Sill M., Vordos D., Alhamdani M.S., Radvanyi F., Hoheisel J.D. and Schröder C. (2014) Prediction of recurrence of non muscle-invasive bladder cancer by means of a protein signature identified by antibody microarray analyses. *Proteomics* 14(11):1333-42. doi: 10.1002/pmic.201300320