MicroRNAs have diagnostic and prognostic potential in urinary bladder cancer

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German researchers have identified four biomarkers that correctly determine malignancy of urinary bladder cancers and contribute to the accurate prediction of patient outcomes. Their results are published in the September issue of The Journal of Molecular Diagnostics.

Current prognosticators of bladder cancer, such as tumor grade, stage, size, and number of foci, have limited usefulness for clinicians since they do not accurately reflect clinical outcomes. Therefore, investigators have been searching for new biomarkers with better diagnostic and prognostic capabilities. Focusing on the role of microRNAs (miRNAs), small non-coding RNAs, researchers have identified four miRNAs that together perfectly discriminated between nonmalignant and malignant tissue, including one alone that classified 81% of the samples correctly. Levels of two miRNAs correlated with overall survival time.

Urinary bladder cancer is the fourth most common cancer in the West. According to the National Cancer Institute, it is estimated that in the United States 72,570 individuals will be diagnosed with and 15,210 will die of cancer of the urinary bladder in 2013. At presentation, in 75% of patients the cancers are confined to the mucosa or submucosa (known as non-muscle invasive bladder cancer, NMIBC), whereas in 25% of cases the cancers have already invaded nearby muscle (muscle-invasive bladder cancer, MIBC).

In a series of experiments, investigators analyzed bladder tissue from patients with NMIBC, MIBC, and nonmalignant bladders. After
screening 723 miRNAs by microarray, they selected a subset of 15
distinctively deregulated miRNAs for further validation by real-time
quantitative PCR. Seven miRNAs were found to be up-regulated, and
eight were down-regulated in malignant bladder tissue samples compared
to healthy tissue. Four miRNAs were expressed differently in bladder
cancers that invaded muscle compared to those that did not. With one
exception, no correlation was found between tumor stage and miRNA
levels.

When all 15 of the selected miRNAs were considered together, they
correctly classified 100% of tissues as either normal or malignant.
Further analysis identified four miRNAs that led to 100% correct
classification, and one miRNA (miR-130b) that by itself had an 81% accuracy rate. "These results underline the great potential of miRNAs to
serve as diagnostic markers, as previously noted for other urological
tumors," says lead investigator Klaus Jung, MD, the Department of
Urology at the University Hospital Charité, Berlin and the Berlin
Institute for Urologic Research.

The investigators found that tumor grading could not be correlated with
overall survival. Yet, they were able to find two miRNAs that
significantly correlated with survival: miR-141 and miR-205. miR-141
showed a trend (P=0.08) of being able to stratify patients with muscle-
invasive tumors into two groups with different overall survival times.
"This finding could be of clinical importance, but these results must be
interpreted cautiously," says Dr. Jung. "However, previously published
studies underline the possible prognostic potential of miRNAs to predict
progression and disease-specific or overall survival in bladder cancer
patients."

miRNAs are small non-coding RNAs that contain between 19 and 24
nucleotides. miRNAs regulate gene expression by degrading messenger
RNAs or impairing their translation. In recent years there has been a
growing interest in miRNAs as potential diagnostic and/or prognostic biomarkers in cancers and other diseases.


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