Circulating miRNAs as non-invasive markers for diagnosis and staging in prostate cancer (P-892)

Key facts
- Circulating miRNA
- Screening of 667 miRNA in serum samples of prostate cancer patients
- miRNA-375 and miRNA-141 upregulated
- marker for diagnosis and staging in prostate cancer

Background
Circulating miRNAs have recently been indicated as practicable and promising biomarkers for non-invasive diagnosis in various tumor entities. However, cell-free miRNAs have not been found to correlate with clinico-pathological variables in epithelial carcinomas. In order to develop a marker for prostate cancer we screened 667 miRNAs in serum samples from patients with metastatic (n=7) and localized prostate cancer (n=14).

The Technology
Various miRNAs were highly abundant in the sera of patients with metastatic disease, and five upregulated miRNAs (miRNA-375, miRNA-9*, miRNA-141, miRNA-200b and miRNA-516a-3p) were selected for further validation. In the first validation study (n=45), selected miRNAs were analyzed in a prospectively collected serum set taken from different prostate cancer risk groups. Most of the selected miRNAs were significantly correlated with adverse risk factors when different clinico-pathological variables were analyzed. Circulating miRNA-375 and miRNA-141 turned out to be the most pronounced markers for high risk tumors. Their levels also correlated with high Gleason score or lymph-node positive status in a second independent validation study (n=71). In addition, the expression levels of miRNA-375 and miRNA-141 were monitored in 72 prostate tissue samples (36 tumor vs. 36 benign). Both miRNAs were highly expressed in all samples and significantly up-regulated in the tumors compared to normal tissues. Overall, our observations suggest that miRNA-375 and miRNA-141 expression is enhanced in prostate cancer specimens and their release into the blood is further associated with advanced cancer disease.

Development Stage
Circulating miRNAs are suitable noninvasive biomarkers for tumor progression in the future. However, the prognostic relevance of particular markers like miRNA-375 and miRNA-141 has to be further corroborated. To this end, large-scale clinical studies for the detection of miRNA levels in serial samples after surgery or treatment are required.

Advantages
Circulating miRNAs are correlated with clinico-pathological endpoints. High levels of circulating miRNA-375 and miRNA-141 were detected in patients with high-risk prostate cancer. In prostate tumor tissue miRNA-375 and miRNA-141 are upregulated in comparison to normal and benign tissue.

Applications and Commercial Opportunity
Kit and diagnostic marker using circulating miRNAs as non-invasive markers for diagnosis and staging in prostate cancer.

Inventors
The invention was jointly conceived by Jan Christoph Brase, Holger Sültmann, Ruprecht Kuner, Maria Fälth, Marc Johannes of Deutsches Krebsforschungszentrum Heidelberg (DKFZ) as well as Thorsten Schiømm, Thomas Steuber and Alexander Haese of Martini Klinik Hamburg as well as Tim Beissbarth of University of Göttingen.
Further Information
No other public information is currently available, but further information (speaking with the inventor) is available under a signed Confidential Disclosure Agreement (CDA).

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Intellectual Property
A priority patent application “Circulating miRNAs as non-invasive markers for diagnosis and staging in prostate cancer” EP 09 174 455.7 was filed October 29, 2009 and a subsequent international PCT application has been published under WO2011/051471.

References:

Figure a: Clustering of 45 serum samples based on the expression levels of five circulating miRNAs. Expression levels are color coded in a heatmap. Gleason scores: black, ≥8 or M+; dark gray, Gleason 7; light gray, Gleason 6; NM (lymph-node status or metastases): black, N1 or M+; light gray, N0; white, NX; M (metastases): black, M+; light gray, MX.

Figure b: miRNA-375 and miRNA-141 expression in prostate tissue samples. Ct values in prostate tumor (n = 36) and normal tissues (n = 36). Statistically significant differences were determined using the Wilcoxon test.