**Press release, European Association of Urology**

# *RNA sequencing opens door to accurate, highly specific test for prostate cancer*

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A study on non-coding RNA (Ribonucleic Acid) from prostate cancer patients has identified a series of new prostate cancer markers which can be found in urine. Combining these RNA markers into a single test potentially opens the door for simple, accurate non-invasive testing for prostate cancer.

Current tests for prostate cancer, such as the PSA and PCA3 tests, are not particularly accurate, leading to a high level of missed cancers or false positives. A test with greater specificity and accuracy may make population screening much more viable.

A group of German researchers, led by Professor Friedemann Horn (of the University of Leipzig and the Fraunhofer Institute for Cell Therapy and Immunology IZI, Leipzig) and Professor Manfred Wirth (of the University of Dresden) has taken a systematic approach to identify new biomarkers, which can offer greater prostate cancer specificity.

A particular focus is non-coding RNAs. RNA serves as part of the mechanism which regulates the production of proteins from the genetic material, but until recently most scientists had felt that the great majority of RNA ('non-coding RNA') had no real function, and was simply accumulated 'clutter'. Now, greater understanding of non-coding RNAs indicates that they can regulate a number of physiological and pathological processes, including development and progression of cancer, and so might serve as markers of these processes.

The team took 64 prostate biopsy samples and read 200 million sequences from each sample. They were able to identify more than 2000 genes that showed a significant difference between tumour and control samples. Several of these showed higher specificity and sensitivity than established prostate markers. One of these non-coding RNAs, designated TAPIR (*Tumour-Associated Proliferation-Inducing RNA*), also showed significant promise in halting cancer cell growth, although it is too early to know if this will translate into a clinically-useful target.

These biomarkers were found in urine samples of prostate cancer patients as well, and first measurements show that they allow a precise detection of prostate cancer. Based on these results, the team is working to develop a highly specific and sensitive urine-based test for the early diagnosis of prostate cancer. This test will be based on a combination of several biomarkers, as this will give greater specificity than a single marker.

Commenting, Professor Wirth (EAU Treasurer) said:

"*This is early work, but it is already showing results. This is a new approach to developing diagnostic tests, and comes from applying real basic science to a practical clinical problem. Given that our initial results show a high specificity for prostate cancer in urine tests, the prospects are good that we will be able to translate this into a better test for prostate cancer. We have several good candidate biomarkers, however we are aiming to design a test which utilises a combination of biomarkers. This will give significantly better specificity than existing tests. Our work on RNAs is allowing us to design a completely new kind of prostate cancer test.*"

The program is part of RIBOLUTION (RIBOnucleic acid-based diagnostic soLUTIONs), a consortium funded by the Fraunhofer Future Foundation. In this interdisciplinary consortium, five Fraunhofer institutes and several universities have collaborated to identify new RNA biomarkers and to develop novel diagnostic tests.

**ENDS**

**Notes for Editors**

**PLEASE MENTION THE EUROPEAN ASSOCIATION OF UROLOGY CONGRESS IN ANY STORY RESULTING FROM THIS PRESS RELEASE**

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The 31st European Association of Urology conference takes place in Munich from 11th to 15th March. This is the largest and most important urology congress in Europe, with up to 13,000 expected to attend. Conference website http://eaumunich2016.uroweb.org/

ABSTRACT

Novel long non-protein coding RNAs as biomarkers and potential therapeutic targets for prostate cancer

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INTRODUCTION & OBJECTIVES: Long non-protein coding RNAs (lncRNAs) exhibit tissue- and disease-specific expression patterns and therefore represent promising biomarker candidates. The Fraunhofer RIBOLUTION (RIBOnucleic acid-based diagnostic soLUTIONs) R&D consortium aims at identifying and validating novel biomarkers for various diseases. To address the high clinical need for better biomarkers for early diagnosis of prostate cancer (PCa), we conducted an unbiased transcriptome-wide expression study to identify and charactise novel biomarkers, including lncRNAs, for PCa.

MATERIAL & METHODS: Tumour and matched tumour-free fresh frozen tissue samples were obtained from radical prostatectomies of PCa patients with a follow-up of at least 7 years. Prostate tissues from surgery of benign prostatic hyperplasia or from radical cystoprostatectomies served as controls. RNA was isolated from cryosections that were quality-controlled for tumour cell contents. 64 samples were subjected to strand-specific RNA next-generation sequencing at a depth of 200 million reads per sample. Biomarker candidates were subsequently validated in 256 prostate samples by customized microarrays that covered all differentially expressed transcripts derived from the sequencing study as well as all RNAs annotated in public databases.

RESULTS: We discovered more than 2,000 genes exhibiting a significant differential expression between tumour and control samples (false discovery rate <0.01). Amongst them, several novel lncRNAs exhibited high diagnostic specificity and sensitivity (area under the ROC curve (AUC) >0.9) and outperformed established markers like PCA3 in our study. These RNAs were also detected in urine samples of PCa patients, allowing for a non-invasive measurement of these biomarkers. To study the function of selected transcripts, knock-down experiments by RNA interference were performed in PCa cell lines. Knock-down of an lncRNA that we call TAPIR (tumour-associated proliferation-inducing RNA) yielded a complete proliferation arrest in LNCaP cells, suggesting that this lncRNA may be essential for PCa cell growth. Furthermore, TAPIR was found to be highly elevated in several other cancers, and therefore might represent a generally oncogenic RNA.

CONCLUSIONS: Our study revealed several novel lncRNA biomarkers with a high potential for the development of a precise urine-based and non-invasive test for early PCa diagnosis. The data suggest an oncogenic function for several of these transcripts, rendering them promising therapeutic targets for PCa.