

New biomarkers improve prostate cancer diagnostics

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IPA has developed the means to simultaneously measure RNA molecules specifically and precisely from tiny samples of many specimens at once. Fully-automated facility for validation of biomarkers. Credit: Fraunhofer IZI

New biomarkers will improve diagnostics of endemic diseases in future, such as prostate cancer. Their mission: to recognize the tumor earlier and classify it more precisely – thereby helping avoid unnecessary operations.

Does the patient have cancer of the [prostate gland](#), commonly called prostate cancer? A question like this is difficult for physicians to answer. Up to now, they have been dependent on clues provided by the prostate-specific antigen PSA. If the prostate gland is attacked by cancer, it releases more of this protein into the bloodstream. However, this test has a weakness: it is very imprecise. If it yields an elevated value, patients have to undergo a biopsy. This involves the practitioner taking several tissue samples using a biopsy needle and having them examined by a pathologist. This entails certain risks, just like any intervention. It can lead to infections in rare cases.

If the physicians detect malignant tumor tissue in the biopsy, they usually have to remove the prostate. However, besides the aggressive form of prostate cancer, there is also a type that only grows very slowly and may not need to be operated on. It has been difficult to differentiate it from the aggressively growing tumors until now, though. The result: physicians operate on the majority of the 70,000 people in Germany who are diagnosed with prostate cancer every year. "Some of these interventions could potentially be avoided if we were to have a biomarker that revealed what kind of cancer is involved," says Prof. Friedemann Horn, Professor of Molecular Immunology at the University of Leipzig and department head of the Fraunhofer Institute for Cell Therapy and Immunology IZI in Leipzig. The term 'biomarker' denotes a measurement value that shows whether a person or an organ is healthy or diseased – these could be metabolic products, specific proteins, or nucleic acids, for instance.

Biomarkers provide insight

Researchers are hoping now to locate biomarkers like this through the RIBOLUTION Project, which is short for "Integrated Platform for Identification and Validation of Innovative RNA-based Biomarkers for Personalized Medicine" (www.ribolution.de). The project is being

supported by the Fraunhofer Future Foundation. The Fraunhofer Institutes for Applied Information Technology FIT, Interfacial Engineering and Biotechnology IGB, Manufacturing Engineering and Automation IPA, Toxicology and Experimental Medicine ITEM, and Cell Therapy and Immunology IZI are participating in addition to several universities. The project involves not just prostate cancer – researchers also hope to improve the diagnoses of other [endemic diseases](#) like rheumatism and chronic obstructive lung disease, which is characterized by coughing, production of sputum and difficulty in breathing. The research will concentrate on the search for ribonucleic acids, RNAs for short, that can indicate the biological state of cells and tissues very accurately.

However, how do the scientists know which biomarkers are early indicators of prostate cancer, or which RNA differentiates slow-growing tumors from aggressive ones? To find these kinds of biomarkers, the scientists compare healthy and tumorous tissue. Physicians at the University Hospital Dresden led by Prof. Manfred Wirth have been storing specimens of these in liquid nitrogen for fifteen years and documenting the course of the disease in patients even after they are released. Before the researchers could investigate these samples in detail, however, they had to prepare them: they cleaved every single tissue sample into 150 ultra-thin sections – each only a few thousandths of a millimeter thick – and classified them anew. "In the meantime, we now have more than 100,000 tissue sections that are unambiguously classified. There has never been a biological database of this quality before now," says Horn.

Researchers have sequenced the complete genome for 64 of these specimens – that is, analyzed and quantified any RNA present in the samples. They have obtained a very large quantity of data for their efforts: 300,000 RNAs have been decoded, with the information adding up to 50 terabytes – that represents about 100,000 CDs. The scientists

have compared the data and have already found 4,000 RNAs out of the 300,000 that could turn out to be biomarkers. They will check these again against a larger group of patients and trim the selection down further. "We are excited about the initial results of this validation process," reports Horn. He sees a good chance that several of the biomarkers discovered can improve the diagnoses of prostate cancer.

"Interest from the medical technology industry is gigantic," says Horn. If the results of RIBOLUTION are confirmed, then a corresponding biomarker assay, i.e. a biomarker test kit, could be on the market in few years – and physicians as well as patients could simply and quickly obtain information about the state of [prostate cancer](#). The market is big: over 100,000 assays would be needed just in Germany annually.

Provided by Fraunhofer-Gesellschaft

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