

Novel Diagnostic Approach for Prostate Cancer

Better discrimination from benign lesions

Methods for early detection of cancer should be simple and reliable. In the case of prostate cancer, the S100A9 protein appears to be equal or even superior to prostate specific antigen (PSA) as a diagnostic marker. This is the conclusion of a publication by **Alexander Hermani** of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), jointly with other researchers, in the journal *Clinical Cancer Research*. Compared to the so-called PSA test, which indicates elevated PSA levels also in the case of benign (non-cancerous) conditions, S100A9 is better suited to discriminate cancer from benign prostatic hyperplasia. This is the result of a study involving 75 prostate cancer patients.

In recent times, there has been increasing evidence to suggest that members of the S100 protein family, including S100A9, are associated with specific tumors such as liver, lung, and breast cancers. In the blood of ovarian cancer patients, elevated levels of S100A8 and S100A9 have been detected. Scientists also believe that S100 proteins serve as ligands that can bind to the RAGE receptor. The receptor-ligand complex appears to trigger a cellular signaling cascade that ultimately influences a cell's dividing and traveling behavior.

These data and findings served as a starting basis for the work of **Alexander Hermani** and **Professor Dr. Doris Mayer**, head of the DKFZ research group "Hormones and Signal Transduction". They investigated tissue samples from human prostate tumors in various stages. In collaboration with other Heidelberg colleagues and partners at the University Hospitals in Mannheim, the investigators found out that the two members of the S100 protein family and their potential receptor are produced in precursors of cancer and, in increasing amounts, in advanced tumors of the prostate. In contrast, they detected none or only low levels of these proteins in benign tissue.

In addition, the scientists investigated whether S100A9 is found in the blood. If so, it would qualify as a characteristic marker of prostate cancer. And indeed: Compared to healthy individuals or patients with benign prostate conditions, S100A9 levels in the blood of cancer patients were found to be significantly elevated. Particularly relevant is the higher significance of S100A9 detection: While the PSA test does not facilitate clear discrimination between benign and malignant prostate conditions, the newly tested candidate makes it easier to differentiate between these two diagnostic findings.

The results of the Heidelberg investigators may also prove valuable for prostate cancer prevention and novel treatment concepts. Thus, the complex of S100 ligand and its receptor provides a potential target for special treatment strategies. However, further investigations are necessary to better understand the function of the molecules.

**Alexander Hermani, Jochen Hess, Barbara De Servi, Senad Medunjanin, Rainer Grobholz, Lutz Trojan, Peter Angel, Doris Mayer: "Calcium-binding proteins S100A8 and S100A9 as novel diagnostic markers in human prostate cancer", *Clinical Cancer Research*, 2005 July 15; 11(14):5146-52.*

Background:

According to the "Dachdokumentation Krebs" (general cancer documentation) of the Robert Koch Institute, almost 37,150 men were newly diagnosed with prostate cancer in 2000. Thus, this type of cancer has become the most frequent malignant tumor in men, even more frequent than lung cancer today. As a rule, it is a disease of the elderly man: Almost 90 percent of patients are over 60 years old at the time of diagnosis; the average age at the time of diagnosis is 72 years. An estimated three out of ten men over the age of 70 have a latent prostate carcinoma that does not change any further, does not cause any symptoms and, in most cases, will not cause any problems for the rest of their lives. Only a small portion of these hidden tumors appears to start growing more rapidly at some point.

To diagnose the disease, physicians have so far been using two relatively simple examination methods: tactile examination and a test called PSA count based on a blood sample taken from the patient. However, early detection of prostate cancer has repeatedly been a matter of discussion among scientists and health politicians, since it unclear whether the blood test, in particular, is really of value for the general population or whether it is useful only for a few men, while causing unnecessary anxiety for many others.

Experts around the world are searching for ways to make early detection more effective. Special attention in such a search is devoted to blood tests, since these are usually simple and quick to perform. From a technical point of view, the PSA test for prostate cancer diagnosis is such a technique. The main objection of many experts has been that mass screening programs as required for early cancer detection would also identify many small, not very malignant tumors that may not require treatment and that the affected men might not only receive unnecessary treatment but also be exposed to severe psychological stress.

The task of the Deutsches Krebsforschungszentrum in Heidelberg (German Cancer Research Center, DKFZ) is to systematically investigate the mechanisms of cancer development and to identify cancer risk factors. The results of this basic research are expected to lead to new approaches in the prevention, diagnosis and treatment of cancer. The Center is financed to 90 percent by the Federal Ministry of Education and Research and to 10 percent by the State of Baden-Wuerttemberg. It is a member of the Helmholtz Association of National Research Centers (Helmholtz-Gemeinschaft Deutscher Forschungszentren e.V., HGF).

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