

Award-winning agent developed for prostate cancer diagnosis and treatment

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Prostate-specific membrane antigen (PSMA) is a surface protein that is normally present on healthy prostate cells, but is found at much higher levels on prostate cancer cells. It is barely found in the rest of the body. "Therefore, PSMA is an ideal target for diagnostic purposes as well as targeted therapies against prostate cancer," says biotechnologist Dr. Matthias Eder of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ).

Eder's group has developed a small molecule (PSMA-617) that is capable of specifically attaching to PSMA and can be labeled with various radioactive substances, called radionuclides.

When chemically bound to gallium-68, a weakly radioactive diagnostic radionuclide, PSMA-617 can be used to visualize even the smallest assemblies of [prostate cancer](#) cells in PET ([positron emission tomography](#)) scans. "In this way, physicians are able to detect small secondary tumors in other organs or closely monitor response to therapy. Diagnostic approaches that have been used in the clinic so far have not come close to this sensitivity," says Eder.

Alternatively, the researchers can also bind a therapeutic radionuclide called lutetium-177 to PSMA-617. This radiopharmaceutical is taken up by tumor cells that carry the PSMA target molecule and then destroys these cells from the inside. This might be a promising treatment option, particularly in cases of hormone-resistant prostate carcinoma, which is very difficult to treat.

At Heidelberg University Hospital, a team led by nuclear medicine specialist Prof. Dr. Uwe Haberkorn has already used radioactively labeled PSMA-617 to treat individual patients with advanced prostate cancer. The physicians made use of the therapeutic nuclides lutetium-177 and actinium-225. After treatment with the lutetium-labeled radiopharmaceutical, levels of the prostate cancer marker PSA fell sharply in 70 percent of cases; after treatment with the actinium-labeled radiopharmaceutical, this effect was observed in all patients.

In addition, PET/CT images confirmed that metastases had shrunk or were no longer detectable. "The results were so promising that we plan to go ahead with a clinical trial as soon as possible to examine whether PSMA-617 is superior to other therapy methods," says Haberkorn.

"Other agents that target PSMA and can be coupled with strong or weak radiation emitters are already being developed," explains Prof. Dr. Klaus Kopka, a chemist and departmental head at the DKFZ. "However, only a few of these agents have turned out to be ideal. Most of them are too unstable, accumulate insufficiently in cancer cells and wash out too slowly from healthy organs. By contrast, PSMA-617 accumulates in large quantities in tumors and metastases and is stored well in [cancer cells](#). As a result, prostate cancer can be irradiated from the inside, so to speak."

More information: Martina Benešová, Martin Schäfer, Ulrike Bauder-Wüst, Ali Afshar-Oromieh, Clemens Kratochwil, Walter Mier, Uwe Haberkorn, Klaus Kopka, and Matthias Eder: Preclinical Evaluation of a Tailor-Made DOTA-Conjugated PSMA Inhibitor with Optimized Linker Moiety for Imaging and Endoradiotherapy of Prostate Cancer. *J Nucl Med* 2015; [DOI: 10.2967/jnumed.114.147413](https://doi.org/10.2967/jnumed.114.147413)

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