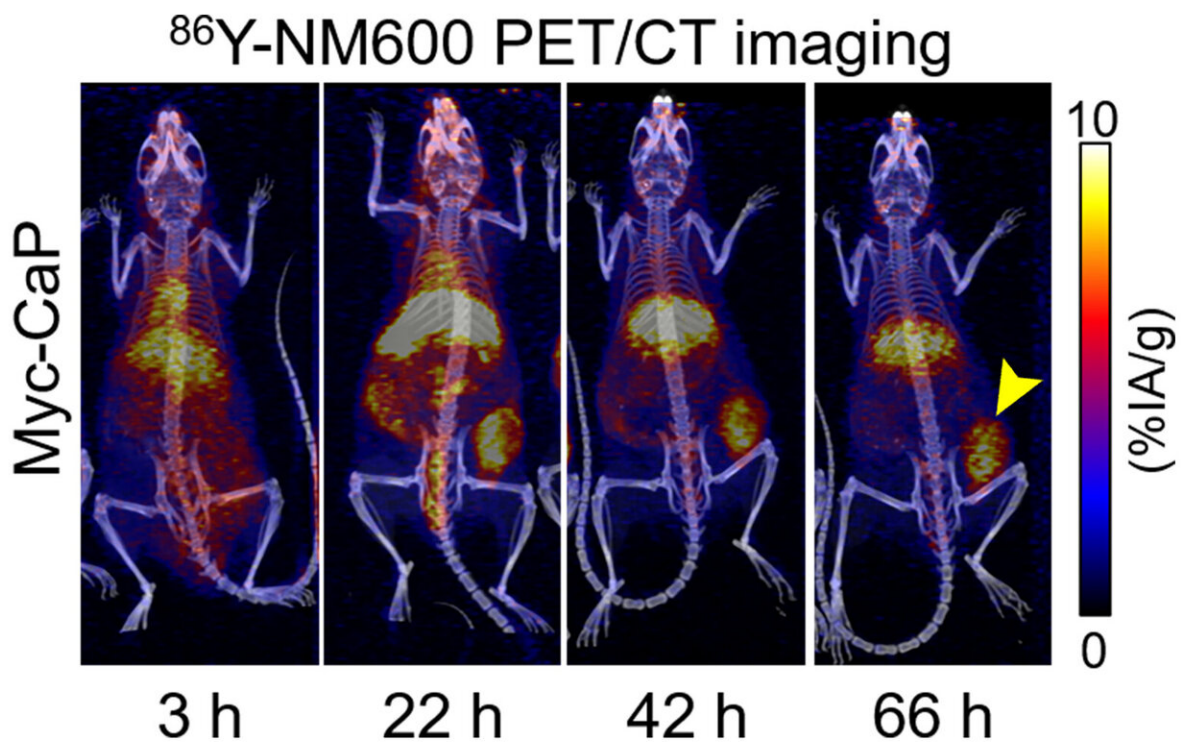


Targeted radionuclide therapy enhances prostate cancer response to immunotherapies

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PET/CT imaging showing uptake and retention of ^{86}Y -NM600 (imaging agent) in immunocompetent mice bearing prostate tumors. PET imaging data was employed to estimate tumor dosimetry and prescribe an immunomodulatory ^{90}Y -NM600 (therapy agent) injected activity. Credit: R Hernandez et al., University of Wisconsin-Madison, WI.

Targeted radionuclide therapy has been found to create a favorable tumor microenvironment in prostate cancer that improves the effectiveness of immunotherapies. The research, presented at the Society of Nuclear Medicine and Molecular Imaging's 2020 Annual Meeting, shows that immunomodulation can be achieved with relatively low radiation dose that does not affect the normal immune system.

Due to a significantly immunosuppressive tumor microenvironment, immunotherapy has had limited success in the treatment of [prostate cancer](#). External beam radiotherapy, which has been shown to remodel the tumor microenvironment of irradiated tumors to make them more immune-susceptible even at low radiation doses, is limited to the localized disease setting.

"Understanding this treatment dynamic, our goal in this study was to demonstrate that systemically delivered targeted radionuclide [therapy](#) provides beneficial immunomodulatory effects that may enhance the response of prostate cancer to immunotherapies," said Reinier Hernandez, Ph.D., assistant professor of medical physics and radiology at the University of Wisconsin-Madison in Madison Wisconsin.

In the study, male mice bearing syngeneic prostate tumor allografts were administered ⁸⁶Y-NM600 and received positron emission tomography/computed tomography (PET/CT) scans at three, 24, 48 and 72 hours after injection. Radiotracer uptake was analyzed in tumors and in healthy tissues, which allowed researchers to estimate the dosimetry for the targeted radionuclide therapy ⁹⁰Y-NM600.

Groups of mice were administered either a high or low dose of ⁹⁰Y-NM600, and tumor growth and survival were monitored for 60 days. A separate group of mice received the same ⁹⁰Y-NM600 doses and were euthanized to analyze the immunological effects ([flow cytometry](#), immunohistochemistry and Luminex cytokine profiling) of the

radionuclide therapy on the tumor microenvironment and [lymphoid tissues](#).

Data from PET/CT imaging revealed that ⁹⁰Y-NM600 immunomodulates the tumor [microenvironment](#) of prostate tumors by modifying tumor-infiltrating lymphocyte populations, upregulating checkpoint molecules, and promoting the release of pro-inflammatory cytokines. ⁹⁰Y-NM600's pro-inflammatory effects on the [tumor microenvironment](#) were found to be elicited at relatively low radiation doses without incurring systemic toxicity.

"Our results provide a rationale for combining targeted radionuclide therapy with immunotherapies, which, so far, have proven ineffective in prostate cancer. Improving immunotherapy in prostate cancer could bring about a potentially curative treatment alternative for advanced-stage patients. We are actively working to advance the immunomodulation concept into Phase I clinical trials," stated Hernandez.

The study also presents a paradigm change in targeted radionuclide therapy, where the maximum tolerable dose may not always be the most beneficial to patients. "A key finding of our work is that immunomodulation is best achieved with a relatively low radiation dose to the tumor which does not affect the normal immune system," Hernandez noted. "As high radiation doses to normal lymphoid organs can negate the benefits of immunomodulation, estimating the radiation doses imparted to the [tumor](#) and normal tissues prospectively by using patient-specific image-based dosimetry techniques is critical. This means that, essentially, a theranostic approach must be implemented."

Provided by Society of Nuclear Medicine and Molecular Imaging

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