

Progress on Prostate Cancer Research

April 2020

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Research

Advancements in prostate cancer research provide hope for finding a cure and lead to the discovery of new treatments to minimize the impact of a man's prostate cancer and maximize his quality of life. This regular *Hot SHEET* supplement includes some of the latest research from the Prostate Cancer Foundation (www.pcf.org).

The PCF is the world's leading philanthropic organization funding and accelerating prostate cancer research. Founded in 1993, the PCF has raised more than \$745 million and provided funding to more than 2,000 research programs at nearly 200 cancer centers and universities.

Breaking Down Barriers to Treatment – Literally

In the past few years, several new treatment options have become available to patients with advanced prostate cancer. Radionuclide therapy is a new class of treatments which uses a hybrid “targeting” molecule to bind to a target protein on prostate cancer cells and a radioactive “killing” molecule to destroy the cell. One such target is called Prostate-Specific Membrane Antigen (PSMA). PSMA-targeted radionuclide therapy is being tested in a Phase 3 clinical trial. However, **these therapies do not work in all patients, and more options are needed.**

One barrier to effectively delivering treatment surrounds the tumor itself: the *stroma* (coming from the Greek for “layer” or “bed covering”). The tumor stroma is composed of many non-tumor cells that exist in normal tissues and play a role in wound-healing processes. A team led by PCF-funded UCLA investigators (Dr. Johannes Czernin, Dr. Jeremie Calais, Dr. Christine Mona and Dr. Katharina Lueckerath), are taking an innovative approach to treatment by literally breaking down this “wall.”

A key component of the stroma are *fibroblasts*, a cell type that are commonly recruited into tumors. These “cancer-associated fibroblasts” are highly supportive of tumor growth and metastasis via expression of proteins including *fibroblast activation protein* (FAP). FAP is expressed in the stroma of many tumor types to various degrees, including in 20% of primary prostate cancers. A compound that specifically binds to FAP may be able to identify, target, and ultimately destroy tumors.

Researchers from the University of Heidelberg in Germany have developed small molecule inhibitors of FAP (FAPi-46). These small molecules can be labeled with a diagnostic radioactive molecule that will light up in a PET scan, thus making the FAPi useful for identifying which cancers express FAP. FAPi-46 can also be labeled with a therapeutic radioactive molecule. **When the therapeutic FAPi binds to stroma fibroblasts it may damage stroma function and damage the barrier around the actual tumor cells.** From there, chemotherapy or another radioactive drug aimed at the now-exposed tumor cells could be deployed.

What does this mean for patients? Although this novel approach is still several years away from clinical care, research actively continues. The UCLA team has initiated clinical studies testing radiolabeled FAPi as a PET imaging agent in patients with different cancer types. **The team is also testing FAP-targeted radiotherapy in prostate cancer mouse models.** The toxicity profile in small animals has been favorable.

For more information visit www.pcf.org, email info@pcf.org, or call 1-800-757-2873.