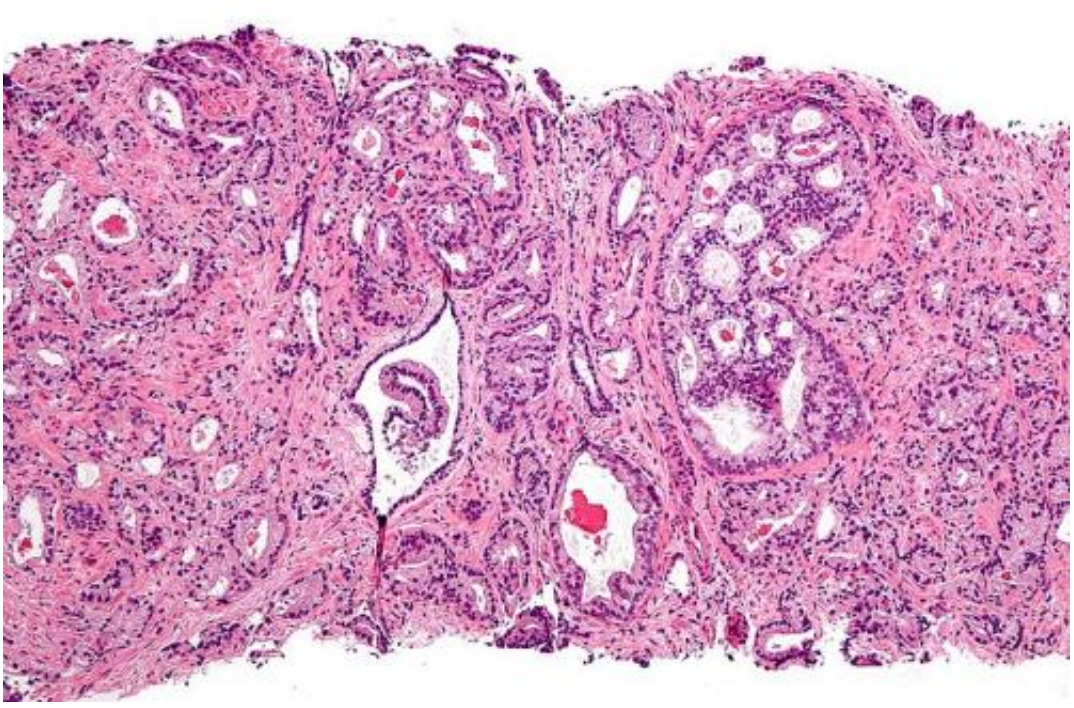
Patient prostate tissue used to create unique model of prostate cancer biology

December 15 2016



Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

For the first time, researchers have been able to grow, in a lab, both normal and primary cancerous prostate cells from a patient, and then implant a million of the cancer cells into a mouse to track how the tumor progresses. The achievement, say researchers at Georgetown University Medical Center who led the research, represents a critical advance in the effort to understand the origin and drivers of this puzzling cancer—the

most common in men. The study was published online today in *Oncotarget*.

"This is a new and much-needed platform for prostate cancer research. By matching normal and cancer cells from a patient, we can now study the differences—what molecules are key to tumor development and growth, and, ultimately, match treatments that might disable this cancer," says the study's senior investigator, associate professor of pathology, Xuefeng Liu, MD, a member of the Center for Cell Reprogramming (CCR) at Georgetown University Medical Center.

The breakthrough was possible because the research team used conditional reprogramming (CR), a laboratory technique, developed and described by Liu, Richard Schlegel, MD, PhD, director of the CCR, and their colleagues at Georgetown in 2011, that makes it possible to continuously grow cells in a laboratory indefinitely. The method uses special "feeder" cells and a chemical inhibitor.

"This is the only system that can grow healthy and cancer cells as if they were just extracted from a patient, and expand them—a million new cells can be grown in a week—as long as needed," he says.

The CR method is being developed for a number of uses, such as living biobanks, personalized and regenerative medicine, and this study, using donated tissue from a 57 year-old man who underwent a radical prostatectomy, demonstrates the first steps needed towards those goals in prostate cancer. Previous studies have proven the utility of CR in a variety of tissue types, including breast, lung, and colon cancer. Liu says many labs around the world are now using this technique, which is called "conditional reprogramming."

"Prostate cancer is highly heterogenetic—it is different person to person, can be slow growing or rapidly aggressive, or both over time. We really

don't understand the basic biology of prostate cancer and that makes it very difficult to find targeted therapies," Liu says. "The use of matched patient-derived cells provides a unique model for studies of early prostate cancer."

In this proof-of-principle study, the researchers showed, using DNA sequencing and karyotyping technologies, that the patient's unique cell characteristics were maintained in both normal and tumor CR laboratory cells. This means nothing genetically changed due to the CR laboratory technique, the researchers say. Investigators also demonstrated the malignant properties of tumor cells compared to the matched normal cells. These are all hallmarks of tumor development, Liu says.

"Now we can compare what is different between the patient's normal and cancerous cells, and what changes when the cancer cells are allowed to morph into an advancing tumor," he says. "We will then use this technique to explore prostate tissues from other cancer patients. Comparisons between what happens within an individual patient's tissue, and then between patients, will give us priceless information about how we can best diagnose this baffling disease and treat it appropriately."

Study co-authors include Olga A. Timofeeva, PhD, Nancy Palechor-Ceron, DMD, Hang Yuan, PhD, Ewa Krawczyk, PhD, Geeta Upadhyay, PhD, Aleksandra Dakic, PhD, Songtao Yu, MD, Shuang Fang, MD, Sujata Choudhury, PhD, Xueping Zhang, PhD, Yun-Ling Zheng, MD, PhD, Chris Albanese, PhD, Richard Schlegel, MD, PhD, Xiaogang Zhong, PhD, Andrew Ju, MD, and Anatoly Dritschilo, MD, from Georgetown University Medical Center; Guanglei Li, Geng Liu, and Yong Hou from Beijing Genome Research Institute, Shenzhen, Guangdong, China; Myeong-Seon Lee from Cheongju University, the Republic of Korea; Han C Dan, from the University of Maryland; and Youngmi Ji and Johng Rhim, MD, from the Uniformed Services University of the Health Sciences, Bethesda, Maryland.

Georgetown University has pending patent applications in US and internationally for conditional cell reprogramming and has been awarded a US patent by the United States Patent Office (9,279,106). This technology has been licensed exclusively to a company for further development and commercialization. Georgetown University and the inventors (Liu and Schlegel) receive payments and potential royalties from Propagenix. Schlegel is also a co-founder in the company that has a license to this technology.

More information: Conditionally reprogrammed normal and primary tumor prostate epithelial cells: a novel patient-derived cell model for studies of human prostate cancer, *Oncotarget* http://www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=view&path%5B%5D=13937&path%5B%5D=44431

Provided by Georgetown University Medical Center