kidney, lung, colorectal, ovarian, and uterine. Liang’s study, which extracted pseudogene expression levels from this data, is part of the TCGA Pan-Cancer Analysis project, an effort to look for patterns across cancer types and genomic dimensions, such as mutations (the genome) and expression levels (the transcriptome).

Liang found that unique sets of pseudogene transcripts were expressed in each form of cancer. In addition, subtypes defined by pseudogene expression levels corresponded closely with subtypes defined by other molecular markers, such as estrogen receptor expression in breast cancer.

In kidney cancer, by joining pseudogene markers with clinical variables, such as disease stage, Liang was able to divide patients into prognostic risk groups. Without pseudogenes, three groups emerge, but adding pseudogenes separates the middle group into two that differ in overall survival. Liang did not investigate the mechanistic roles of pseudogenes, but, he says, “pseudogenes are a novel dimension that we can use to further understand the subtypes.”

“The study included almost 10 times more samples than previous work, which really drives home the validity of the conclusions that pseudogenes can be used as cancer markers,” says Zhang.

Liang hopes to find another large dataset to validate his findings, and also to expand his current analysis across additional types of cancer. “If these patterns are robust, we can consider using pseudogene expression data to build prognostic models that have clinical value,” he says.

**3D Imaging Finds More Breast Cancers**

Adding 3D imaging to traditional digital mammography finds more invasive breast cancers and reduces false positives, a new study finds, although it is not yet known whether the new technology improves breast cancer survival.

Researchers retrospectively reviewed 454,850 mammograms from 13 breast centers. More than a third used 3D imaging, or digital breast tomosynthesis, done at the same time as traditional mammography, whereas the rest used traditional mammography alone.

The invasive cancer detection rate increased from 2.9 per 1,000 traditional mammograms to 4.1 per 1,000 combined 3D mammograms, researchers reported (JAMA 2014;311:2499–507). False positives were 15% less likely using the 3D approach, and there were 16 fewer callbacks for additional imaging per 1,000 screenings.

“Conventional mammography is far from ideal,” says senior author Emily Conant, MD, chief of breast imaging at the University of Pennsylvania’s Perelman School of Medicine in Philadelphia. “3D mammography is an improvement because it addresses two of the major limitations of mammographic screening—there are too many false positives and the sensitivity is not what we’d like, so we miss cancers.”

The FDA approved the Selenia Dimensions digital breast tomosynthesis system (Hologic; Bedford, MA) in 2011 in combination with traditional mammography for breast cancer screening. Using multiple low-dose X-rays taken at different angles, thin “slices” of breast tissue are reconstructed into a 3D image that gives a clearer view of breast tissue.

In an accompanying editorial, Etta Pisano, MD, and Martin Yaffe, PhD, called for more research, noting that it is still uncertain whether tomosynthesis should replace traditional digital mammography (JAMA 2014;311:2488–9).

Conant notes that because the study was not designed to follow women over time, it is not known whether 3D mammography saves lives. It is also unclear which women benefit the most from 3D scans, she says.

“We need research that looks at patient-level data such as breast density, patient age, and the types of cancer detected with 3D mammography that weren’t detected with conventional mammography,” Conant says. “We need to better understand what each woman needs.”

**Improved Survival Ends Nivolumab Trial Early**

A phase III trial testing Bristol-Myers Squibb’s (BMS) immunotherapeutic drug nivolumab to treat advanced melanoma was stopped early after the treatment demonstrated a clear improvement in overall survival (OS) compared with standard chemotherapy.

The control group in the randomized, double-blind study—dubbed CheckMate-066—was invited to switch to nivolumab after an independent data-monitoring committee found evidence of superior OS in patients who took nivolumab, BMS reported. The trial was comparing nivolumab 3 mg/kg every 2 weeks with dacarbazine 1,000 mg/m² every 3 weeks in 418 patients with previously untreated BRAF wild-type unresectable late-stage melanoma. It was conducted primarily in Canada and Europe, where dacarbazine is a standard first-line therapy.

“The outcome of CheckMate-066 is an important milestone in the field of immuno-oncology as it represents the first well-controlled, randomized phase III trial of an investigational PD-1 checkpoint inhibitor to demonstrate an overall survival benefit,” says Michael Giordano, MD, head of oncology development at BMS.

Nivolumab is a monoclonal antibody that targets PD-1, a receptor on activated T-cells that inhibits the immune system from attacking cancer cells. BMS is testing the therapy in melanoma, non–small cell lung cancer, and renal cell carcinoma, for which the drug received fast track designation from the FDA last year.

In March, investigators published results from a 107-patient phase I trial showing that nivolumab led to tumor regression and increased OS in patients with advanced melanoma (J Clin Oncol 2014;32:1020–30). The median OS was 16.8 months, with a median response of 2 years among the 33 patients who experienced tumor regressions.
3D Imaging Finds More Breast Cancers

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