expressed proteins are associated to subpopulations of cells and whether information allows for information regarding cellular phenotype,” says Pontén. “Researchers interested in various genes or cancers can go into the atlas and see how a given protein is expressed across a specific type of cancer.”

The new analysis reveals that almost half of protein-encoding genes implicated in cancer are expressed across all tissues while only a small percentage of our genes are tissue-specific. “Tissue specificity versus widespread expression patterns can help identify diagnostic markers and develop drugs targeting specific cancer types,” says Pontén. “The definition of proteins expressed in all tissue types has bearing on drug targets, since 30% of all FDA-approved drug targets are expressed in all tissues.”

First CDK 4/6 Inhibitor Heads to Market

The first of a novel class of cell cycle-targeting cancer medicines passed muster in early February, when Pfizer’s palbociclib (Ibrance) won accelerated FDA approval. Palbociclib is indicated for use in combination with letrozole as a first-line hormonal therapy in postmenopausal women with locally advanced or metastatic HER2-negative, estrogen receptor (ER)-positive breast cancer. However, the drug still must prove that it prolongs overall survival.

Antiestrogens such as letrozole are the mainstay for treating this type of breast cancer, but tumor resistance is common and additional therapies are sorely needed. Palbociclib represents a new generation of medicines designed to rein in an out-of-control cell cycle.

The Pfizer pill selectively inhibits cyclin-dependent kinases (CDK) 4 and 6, which normally trigger cell growth and division. Two other CDK4/6 inhibitors—one from Novartis (LEE 001) and one from Eli Lilly (LY 2835219)—are also in clinical testing for breast tumors and other cancers.

Palbociclib’s expedited FDA approval and designation as a “breakthrough therapy” were granted based on evidence that it doubled progression-free survival (PFS) in older women with advanced HER2-negative, ER-positive breast cancer. In the phase II PALOMA-1 study, women receiving the palbociclib–letrozole combination had a median PFS of 20.2...
The drug might therefore offer the first effective second-line treatment option for patients with this rare and aggressive form of thymus cancer, whose 5-year survival rate is 30% to 50%.

The findings are exciting because there have been very little data to support any treatment options for patients whose cancers have progressed despite first-line platinum-based therapy; says Gregory Riely, MD, PhD, a medical oncologist at Memorial Sloan Kettering Cancer Center in New York, NY, who specializes in treating thymic tumors. “This is certainly the most active drug we’ve seen for patients who have had prior therapy for thymic carcinoma.”

Several observations suggested that tyrosine kinase pathways—such as those that involve VEGFR, KIT, and PDGFR, which stimulate cell survival, proliferation, and/or angiogenesis—contribute to thymic epithelial cancers. For example, overexpression of these proteins or their ligands is associated with thymic carcinoma or other thymus pathology in humans. Furthermore, several small case studies have suggested that drugs that hinder VEGF, KIT, or PDGF signaling fight thymic epithelial tumors. Giuseppe Giaccone, MD, PhD, associate director for clinical research at Georgetown Lombardi Comprehensive Cancer Center in Washington, DC, and his colleagues therefore speculated that sunitinib, which targets these pathways, might curb the cancer’s growth.

Sunitinib Effective for Rare Thymus Cancer

Sunitinib (Sutent; Pfizer), a tyrosine kinase inhibitor already approved for several cancers, slowed disease progression in a phase II trial of patients with advanced thymic carcinoma who failed the standard first-line chemotherapy. The drug might therefore offer the first effective second-line treatment option for patients with this rare and aggressive form of thymus cancer, whose 5-year survival rate is 30% to 50%.

The open-label trial enrolled two cohorts with a total of 41 patients who had advanced thymic epithelial tumors—25 with thymic carcinoma and 16 with thymoma—whose tumors had progressed after one or more rounds of platinum-based chemotherapy. After a median follow-up of 17 months, 6 of the 23 assessable patients with thymic carcinoma (26%) had partial responses; 15 (65%) achieved stable disease; and 2 (9%) had progressive disease. The thymoma cohort closed early due to insufficient drug activity. The results were published in February (Lancet Oncol 2015;16:177–86).

“The take-home message is that there is a drug that works in thymic carcinoma and it is a relatively well-tolerated, well-known drug,” says Giaccone, the study’s senior author. “This will become standard second-line treatment for patients with thymic carcinoma.”

Giaccone and colleagues attempted to identify somatic variations in genes, including those for sunitinib’s targets, that might identify individuals who would benefit from the drug. No association was found between a specific mutation and response to sunitinib. The researchers also probed the immunological effects of sunitinib administration. They documented an increase in expression of the checkpoint receptors PD-1 and CTLA4—molecular markers of regulatory T-cell activity. The result might reflect what typically would be a healthy attempt to keep inflammation in check, the authors suggest, but in this situation, a sunitinib-incited immune attack presumably shrinks the tumor and is desirable. Perhaps drugs that block checkpoint receptors would prolong sunitinib’s assault on the cancer. To explore that idea, Giaccone’s team recently opened a phase II trial of the PD-1 inhibitor pembrolizumab (Keytruda; Merck) in patients with advanced thymic carcinoma.

TCGA Releases Head and Neck Cancer Data

Researchers have published the most comprehensive genomic analysis of head and neck cancers. Their findings may lead to improved treatments for this type of cancer; current therapies are successful only about half of the time.

More than 90% of head and neck cancers are squamous cell carcinomas, and most are triggered by tobacco or alcohol use or by infection with human papillomavirus (HPV). To clarify how these tumors develop and identify potential new treatment targets, researchers with The Cancer Genome Atlas (TCGA) analyzed squamous cell carcinomas from 528 patients, three times as many as in any comparable study. Instead of relying on one technique, as most genome profiling projects for this type of cancer have done, the team used several methods, including whole-exome sequencing, microarray analysis, and copy-number analysis.

“We think of this [project] as an atlas or encyclopedia” of these tumors, says co-author D. Neil Hayes, MD, of the University of North Carolina Lineberger Comprehensive Cancer Center in Chapel Hill. Hayes and more than 300 colleagues recently reported results for the first 279 patients (Nature 2015;517:576–82).
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