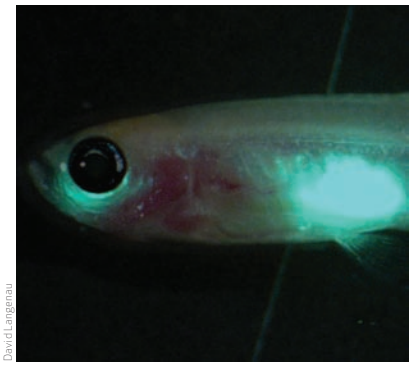

David Langenau

Human cancers grow with similar kinetics and histology when engrafted into *prkdc*$^{-/-}$, *il2rga*$^{-/-}$ zebrafish. Because the fish are transparent, researchers can assess tumor growth as well as responses to treatment.

cells—and raising fish at temperatures conducive to human tumor growth," says Langenau. "It's the first immune-compromised zebrafish model that can robustly engraft and grow human cancers and allows for accurate oral drug dosing similar to what is achieved in the clinic."

Previous studies have shown that human cancers can be engrafted in larval zebrafish prior to development of the adaptive immune system, says Langenau. However, these models sustain tumor growth for only 7 to 10 days, after which immune responses kill off engrafted cells. In addition, larval fish engraft only a small number of cells and are typically raised at lower temperatures than necessary for human tumor growth (<35°C vs. 37°C), so they cannot replicate what happens in humans.

Immune-deficient mouse models are the gold standard for studies involving xenotransplantation, but the animals have inherent limitations, including being expensive to maintain and having fur, which complicates imaging. Using the *prkdc*$^{-/-}$, *il2rga*$^{-/-}$ zebrafish, Langenau's team tested a combination of the PARP inhibitor olaparib (Lynparza; AstraZeneca) plus temozolomide chemotherapy to treat rhabdomyosarcoma and found that it halted tumor growth. They repeated the study in mouse models and got the same results.

Researchers are now trying to add patients with rhabdomyosarcoma to an ongoing phase II trial that's evaluating the drug combination in patients with Ewing sarcoma.

The *prkdc*$^{-/-}$, *il2rga*$^{-/-}$ zebrafish could dramatically lower the cost and scale of large drug studies, notes Cecilia Moens, PhD, of Fred Hutchinson Cancer Research Center in Seattle, WA. Besides being less expensive to maintain compared with immune-compromised mouse models, zebrafish are translucent, allowing researchers to see drug activity in the animals' bodies in real time.

"The ability to image tumor cells while animals are still alive—and monitor how they respond to treatment—is extremely powerful," she says. "In addition, working with adult fish opens up new opportunities for us to visualize tumor–host interactions throughout both the innate and adaptive immune systems."

The findings also have significant implications for the future of personalized therapy, says Langenau. "The dream is to be able to implant a patient's own tumor into zebrafish, treat them with available therapies, and return that information to clinicians to inform clinical care," he says. "It's precision-guided medicine using zebrafish avatars." *–Janet Colwell* ■

For more news on cancer research, visit *Cancer Discovery* online at http://cancerdiscovery.aacrjournals.org/CDNews.

## NOTED

**Merck will buy Peloton Therapeutics for $1.05 billion** up front in a deal that could earn Peloton up to $1.15 billion more in milestone payments. Merck will gain access to Peloton's experimental therapies including PT2977, a HIF2α inhibitor that has shown promise in treating metastatic renal cell carcinoma.

**The FDA approved the first PI3K inhibitor for breast cancer—alpelisib** (Piqray; Novartis). Combined with fulvestrant, the drug treats men and postmenopausal women with HR-positive, HER2-negative, *PIK3CA*-mutated, advanced breast cancer whose disease has worsened after an endocrine-based regimen. In the pivotal phase III SOLAR-1 trial, patients who received the combination had a median progression-free survival of 11 months, compared with 5.7 months for patients who received a placebo plus fulvestrant.

**Many randomized clinical trials for cancer drugs may not use optimal control arms** (JAMA Oncol 2019 May 2 [Epub ahead of print]). Researchers analyzed 98 multiarm trials that led to 96 drug approvals between 2013 and 2018 and found that 16 approvals were based on trials with suboptimal control arms. Of these control groups, 10 used an inferior agent or didn't allow combinations, and four limited the investigator's choice.

**Television ads will be required to include prices for certain prescription drugs** covered by Medicare or Medicaid. The rule, issued by the Centers for Medicare & Medicaid Services, requires commercials to include prices for drugs that cost more than $35 for a month's supply or for a typical course of therapy.

The U.S. District Court in Boston, MA, ruled that **two U.S. scientists should be listed as inventors on six cancer immunotherapy patents.** The court determined that the patents, previously issued to Ono Pharmaceutical and Tasuku Honjo, MD, PhD, of Kyoto University in Japan, should also include Gordon Freeman, PhD, of Dana-Farber Cancer Institute in Boston, MA, and Clive Wood, PhD, of Boehringer Ingelheim. The patents describe the PD-1 pathway, the foundation of the PD-1 inhibitor nivolumab (Opdivo; Bristol-Myers Squibb).