PEOPLE

Glenn Dranoff, MD, a professor of medicine at Dana-Farber Cancer Institute and Harvard Medical School in Boston, MA, has been named the founding editor-in-chief of *Cancer Immunology Research.* Published by the American Association for Cancer Research, the journal will launch online at the organization's annual meeting in April, followed by monthly print issues beginning in June.

The leader of the Dana-Farber/Harvard Cancer Center Program in Cancer Immunology, Dranoff has devoted his research efforts to understanding tumor immunity and to the development of cancer vaccines.

Karen E. Knudsen, PhD, began a 5-year term as editor-in-chief of *Molecular Cancer Research* this month. She succeeds Michael B. Kastan, MD, PhD, executive director of the Duke Cancer Institute in Durham, NC.

Knudsen is a professor in the departments of cancer biology, urology, and radiation oncology at Philadelphia's Thomas Jefferson University and deputy director for basic science at the affiliated Kimmel Cancer Center. In addition to authoring book chapters and dozens of peer-reviewed articles, she has held several leadership roles on scientific publications, including *Cancer Research.*

Center for Scientific Review

Richard Nakamura, PhD, has been chosen as the new director of the NIH's Center for Scientific Review (CSR). He will lead 450 scientists and administrative staff, overseeing their efforts to manage 80,000 NIH grant applications a year, the majority of which are reviewed by CSR peer review groups. The CSR holds 1,600 review meetings a year.

Prior to joining the CSR in 2011, Nakamura spent 32 years at the National Institute of Mental Health, serving as both its scientific and deputy director.

CDK Inhibitor Triples PFS in Breast Cancer

Women with estrogen receptor (ER)–positive breast cancer who took an investigational drug targeting cyclin-dependent kinases 4 and 6 (CDK4/6) in combination with the aromatase inhibitor letrozole experienced a "dramatic and clinically meaningful effect," researchers reported on December 5 at the 2012 Cancer Therapy and Research Center (CTRC) and American Association for Cancer Research (AACR) San Antonio Breast Cancer Symposium in Texas. Based on the positive results, these researchers expect to launch a phase III trial of the agent in 2013.

In the current phase II study, patients who took Pfizer's CDK4/6 inhibitor PD-0332991 with letrozole (Femara; Novartis) achieved a progression-free survival (PFS) period of 26.1 months compared with 7.5 months for patients who were treated with letrozole alone. "This was a welcome result," commented Norman Sharpless, MD, deputy director of the Lineberger Comprehensive Cancer Center at the University of North Carolina (UNC) at Chapel Hill, who was not associated with the study. "A tripling of PFS in this disease is a great finding."

CDKs, which participate in cell proliferation, tend to be overactive in cancer.

Richard Finn, MD, associate professor of medicine at the Jonsson Comprehensive Cancer Center at the University of California, Los Angeles, and the study's principal investigator, explained that the primary function of CDK4/6 is to phosphorylate the retinoblastoma (RB) protein, which ordinarily blocks early events in the cell cycle. Phosphorylation inactivates RB so that cells can continue to divide. In some cancers, however, CDK4/6 hypherphosphorylates RB, which can lead to uncontrolled cell growth.

By inhibiting CDK4/6, Pfizer's experimental drug prevents RB hyperphosphorylation. Moreover, Finn added, it has minimal side effects.

According to Finn, preclinical studies indicate that only ER-positive breast cancer cells had robust responses to PD-0332991. "ER positivity appears to be a marker for an intact RB pathway," he said.

That's noteworthy, UNC's Sharpless added, given that RB loss occurs in roughly 10% of all cancers. "The drug won't work in patients who lack the RB pathway," he noted, "so that gives us a good negative biomarker for who won't respond to treatment. What we need now is a better positive biomarker to identify those who might respond best in breast cancer and other cancer types." ■

Surveillance Network Aids Prostate Research

Up to 50% of men diagnosed with prostate cancer have a form of the disease that grows so slowly that it's unlikely to ever threaten their health if left untreated. Unfortunately, physicians currently have no precise way to determine which patients can forego treatment.

"We need to find out whether a tumor is a wolf in sheep's clothing or if it's really a sheep," says Stuart Holden, MD, director of Cedars-Sinai's Louis Warschaw Prostate Cancer Center in Los Angeles, CA, and medical director for the Prostate Cancer Foundation, a philanthropic organization that funds research on the disease.

Thanks to a $5-million grant from the foundation, researchers from Johns Hopkins Medicine in Baltimore, MD, and colleagues at Cedars-Sinai have launched the National Proactive Surveillance Network (NPSN), a repository of patient information that will advance understanding of who needs treatment. Patients at the 2 institutions who are diagnosed with early-stage, low-volume prostate cancer will be invited to join the program; other institutions will be added to the network in mid- to late 2013.

Patients pursuing proactive surveillance defer treatments such as surgery and radiation therapy. Instead, they are closely monitored with physical exams and medical tests every 6 months and a prostate biopsy every year. If cancer progresses, they may opt for treatment. This strategy is also called active surveillance, expectant management, or watchful waiting.

Participants regularly complete detailed lifestyle and nutrition questionnaires, and their blood and urine samples and biopsy tissue are banked

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in the repository, says H. Ballentine Carter, MD, director of Adult Urology at Johns Hopkins. Prostatectomy tissue is collected from participants who decide to have surgery.

Investigators will analyze the samples and correlate their findings with the clinical data. Such work might lead to the discovery of genetic signatures of aggressive disease, for example, or allow researchers to examine the activity of circulating tumor cells at different disease stages.

Since 1995, Johns Hopkins urologists and oncologists have gathered clinical data on more than 1,000 patients pursuing proactive surveillance for prostate cancer, the largest prospective cohort in the country, notes Carter. Many of those patients will enroll in NPSN. Holden says the Cedars-Sinai team aims to further enrich the data by enrolling about 100 more patients annually.

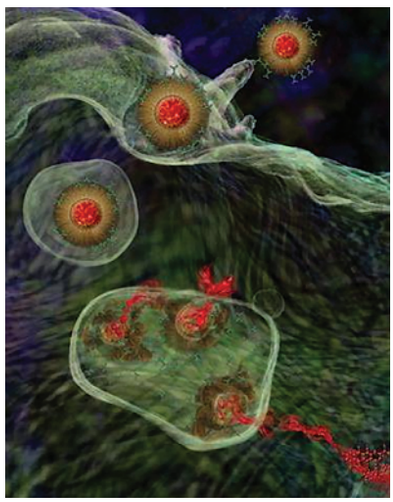
"If we can figure out who has disease that really needs to be treated," he adds, "we will have solved a huge problem." ■

"Minicells" Safely Deliver Targeted Drugs

A new form of targeted drug delivery via "minicells" proved generally tolerable in its first trial in humans. The minicells are derived from mutated bacteria that divide at the poles, producing a nonliving sphere with no nucleus that can be loaded with chemotherapeutic drugs and coated with antibodies that target specific tumor cells.

The 400-nm-wide spheres are large enough to be contained by normal blood vessels but small enough to slip out of the leaky vessels found inside tumors, says Benjamin Solomon, MBBS, PhD, the trial's principal investigator and a medical oncologist at the Peter MacCallum Cancer Centre in Melbourne, Australia. Once inside the tumor, targeted antibodies bind to receptors on the tumor cell. When the minicell is ingested by the tumor cell, it breaks down and the drug is released.

Twenty-eight patients with end-stage solid tumors participated in the phase I multicenter trial, reported on November 9 at the 2012 Symposium on Molecular Targets and Cancer Therapeutics, hosted in Dublin by the European Organisation for Research and Treatment of Cancer, the National Cancer Institute, and the American Association for Cancer Research.



"Minicells" derived from mutated bacteria are nonliving spheres that can be loaded with chemotherapeutic drugs and coated with antibodies that target specific tumor cells.

The patients received 5 weekly infusions of minicells filled with paclitaxel and coated with antibodies targeting the epidermal growth factor receptor (EGFR) protein found on the surface of many tumor cells.

Ten of the patients showed stable disease after 6 weeks, and some continued on minicell therapy for months, with 1 patient receiving 45 doses in 15 months. Side effects included short-lived fevers and, in some cases, chills, typically an hour after dosing. At the highest dose, some patients showed signs of liver function changes.

Minicell developers Himanshu Brahmbhatt, PhD, and Jennifer MacDiarmid, PhD, of EnGeneIC, in Sydney, Australia, hope to reduce side effects by minimizing the presence of endotoxins in the minicell membranes.

The team plans a phase I/II trial to test minicells in patients with gliomas, again targeting EGFR but delivering doxorubicin. Dogs with brain cancer showed promising results with this treatment, notes Solomon.

"The success of the phase I trial allows us to begin to look at efficacy," says Solomon. "But the real potential is packaging drugs that are impossible to give systemically." For instance, the team is exploring the possibility of using minicells to deliver siRNA to silence drug-resistant genes. ■

NOTED

- Harold Varmus, MD, director of the National Cancer Institute (NCI), said that the **NCI will expand its "zone of likelihood" for applications for grant funding from those scoring in the seventh percentile and better to the ninth percentile and better for fiscal year 2013.** Grants scoring below the ninth percentile can be funded after an additional review. NCI aims to support about 1,100 new grants in FY 2013, which is in line with previous years.
- **India plans to build a National Cancer Institute facility that will be the nation's largest cancer center** at an All India Institute of Medical Sciences campus outside New Delhi.
- **Sanofi cut the price of Zaltrap (ziv-aflibercept) in half after criticism of the drug's cost-effectiveness** in *The New York Times* by 3 Memorial Sloan-Kettering Cancer Center physicians. The move "represents a success in moving toward value-based systems of care," commented Debra Patt, MD, MPH, in *Community Oncology*.
- **The U.S. Food and Drug Administration granted priority review for marketing approval of trastuzumab emtansine** (T-DM1; Genentech) in the treatment of people with HER2-positive, unresectable locally advanced or metastatic breast cancer who have received prior treatment with trastuzumab (Herceptin; Genentech) and a taxane chemotherapy.
- **The NCI gave the University of Michigan Comprehensive Cancer Center a $28.4-million, 5-year grant** and renewed its designation as a Comprehensive Cancer Center. The University said that it has received the most NCI funding among U.S. academic medical centers, with the Cancer Center receiving a total of $79 million in 2011. After submitting a 1,937-page grant renewal to the NCI, the Cancer Center underwent a 2-day site visit by reviewers in fall 2011.
- Beginning as early as spring 2013, **the NIH "will begin to hold processing of non-competing continuation awards if publications arising from grant awards are not in compliance with the public access policy,"** wrote Sally Rockey, PhD, deputy director for extramural research, in an entry on her blog.

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