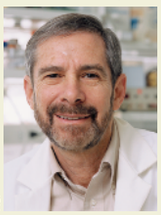
PEOPLE

Paul Workman, PhD, was named chief executive and president of the Institute of Cancer Research (ICR) in November, replacing Alan Ashworth, PhD. Workman was previously the ICR's deputy chief executive and director of the Cancer Research UK Cancer Therapeutics Unit. In addition, he has worked as an academic researcher at the Universities of Cambridge and Glasgow in the UK, and at Stanford University in the United States.

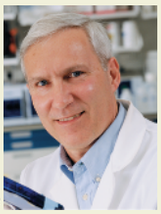
Through the ICR's new Centre for Evolution and Cancer, Workman aims to outpace cancer evolution and drug resistance by discovering drugs that act on currently untargeted cancer proteins; finding and implementing the best drug combinations; and developing drugs that tackle more than one signaling pathway.

President Barack Obama awarded the National Medal of Technology and Innovation, bestowed upon "visionary thinkers whose creativity and intellect have made a lasting impact on the United States and its workforce," to nine scientists and inventors, including two from the NCI, late last fall.



NCI

Douglas R. Lowy, MD



NCI

John T. Schiller, PhD

Douglas R. Lowy, MD, chief of the Laboratory of Cellular Oncology, and **John T. Schiller, PhD,** deputy chief of the Laboratory of Cellular Oncology, were recognized for their research on the human papillomavirus (HPV). Together, they studied the life cycle of HPV and led the initial development of the prophylactic vaccines that laid the groundwork for the subsequent development of the commercial HPV vaccines Cervarix (GlaxoSmithKline) and Gardasil (Merck). The vaccines protect against the HPV types that cause nearly all cervical cancers.

Two Drugs Beat Back Lung Tumors

Two new EGFR-blocking drugs shrink lung tumors that have developed resistance to standard therapy with tyrosine kinase inhibitors (TKI), according to a pair of new studies.

TKIs such as erlotinib (Tarceva; Genentech) are first-line therapies for patients with metastatic non–small cell lung cancer (NSCLC) whose tumors have certain *EGFR* mutations. However, the tumors usually become resistant to these therapies, often due to the T790M mutation. Erlotinib and related drugs obstruct EGFR's ATP-binding pocket, but the T790M mutation prevents the drugs from interacting with the pocket, allowing cancer cells to continue growing.

At the recent 2014 Symposium on Molecular Targets and Cancer Therapeutics in Barcelona, Spain, sponsored by the European Organization for Research and Treatment of Cancer, the NCI, and the American Association for Cancer Research, two research groups presented evidence on the effectiveness of separate investigational drugs that can bind to and inactivate EGFR despite the T790M mutation.

In a phase I/II trial, Jean-Charles Soria, MD, PhD, of the Institut Gustave Roussy in France, and colleagues in Europe, Australia, and the United States tested the EGFR inhibitor rociletinib (CO-1686; Clovis Oncology), which inhibits activated EGFR with or without the T790M resistance mutation. The researchers enrolled 193 patients with NSCLC, who had received three prior therapies on average, in the ongoing trial.

Among the 27 rociletinib-treated patients who received optimal doses of the drug and for whom the team had CT scan results, 18 had a confirmed response to the drug; the median progression-free survival was 10.4 months.

"Sixty-seven percent activity lasting nearly a year is very good," says Soria, who presented the group's findings. In some patients, the drug triggered high blood glucose levels, which were controlled with the diabetes drug metformin.

Several other studies of rociletinib are under way, including a phase III trial comparing it to chemotherapy.

The second group, led by Haruyasu Murakami, MD, PhD, of the Shizuoka Cancer Center in Japan, reported results from a phase I trial of another drug, ASP8273 (Astellas Pharma), that also inhibits mutant EGFR. So far, 31 patients with NSCLC, all of whom received prior therapy with a TKI, have been enrolled in the trial.

The researchers found that tumors shrank in 7 of the 9 patients who had both the EGFR and T790M mutations. Although the drug spurred gastrointestinal symptoms such as diarrhea and nausea, it didn't lead to high blood sugar.

"Although the number of patients is still small, ASP8273 would be expected to have clinical benefits," says Murakami, adding that phase II trials of the drug are being planned.

Two other drugs that are effective against EGFR harboring the T790M mutation, AZD9291 (AstraZeneca) and HM61713 (Hanmi Pharmaceutical), have also shown promise in patients with NSCLC in phase I and phase I/II clinical trials. ■

Pembrolizumab Shows Potential in Breast Cancer

With no approved targeted agents for triple-negative breast cancer (TNBC), women diagnosed with this disease have few treatment options besides chemotherapy. However, the immune checkpoint inhibitor pembrolizumab (Keytruda; Merck) may be effective in some patients, according to a report from the 2014 San Antonio Breast Cancer Symposium (SABCS) in San Antonio, TX, December 9–13.

By binding to the PD-1 receptor and blocking its ligands, PD-L1 and PD-L2, pembrolizumab—approved by the FDA in September for advanced melanoma—prevents tumor cells from using this pathway to escape immune surveillance.

In the phase Ib study presented at SABCS, 18.5% of 27 evaluable patients responded to pembrolizumab, "an encouraging signal that's worthy of