colorectal cancer, but not whether it is required to sustain tumor growth," says the study's senior author Scott Lowe, PhD, chair of the Cancer Biology and Genetics Program at Memorial Sloan Kettering Cancer Center in New York, NY. "Instead of deleting the gene, which is the standard method, we used a genetic trick to silence it and turn it back on, which allowed us to see not only what initiates a cancer but also what maintains it once it's already formed."

The ability to alternately silence and reactivate APC expression solves a long-standing problem of how to suppress gene expression without completely blocking Wnt signaling and damaging normal intestinal cells, says Lowe. He noted that normal cell differentiation began to occur almost immediately following APC restoration, suggesting that only partial inhibition of Wnt signaling is required to induce tumor regression, thus sparing surrounding normal tissue.

Lowe's team was surprised to observe that suppressing APC expression led to rapid regression in tumors with KRAS and p53 mutations, which are found in about half of all colorectal tumors. While it was known that these mutations promote tumor growth in APC-mutated colorectal cancer, it was not known whether they would continue to drive disease progression when APC is active.

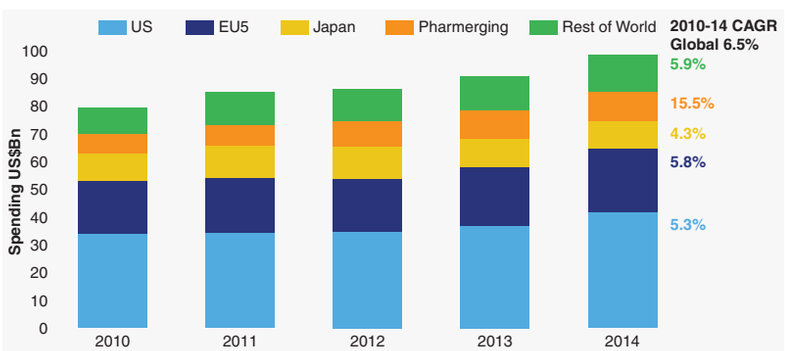
"We thought that KRAS and p53 mutations would at least blunt the ability of APC to regress the tumor," says Lowe. "Instead it appears that by restoring this one gene in tumors with multiple genetic alterations, the tumor cells go through a normal process of differentiation and some even seem capable of returning to normal stem cells."

The findings may help inform efforts to develop drugs that target the Wnt pathway, says Lowe. Recently, small-molecule tankyrase inhibitors have shown promise in cell culture and animal studies for modulating Wnt signaling and potentially suppressing colorectal cancers driven by APC mutations.

"This study might be the best validation to date of the Wnt pathway as a therapeutic target," says Lowe. "What's most exciting is the discovery that, with the right coaxing, it's possible to restore normal functions in a tumor that has multiple genetic changes." ■

BY THE NUMBERS

Global Oncology Drug Spending, 2010–2014



IMS Institute for Healthcare Informatics

According to the IMS Institute for Healthcare Informatics, global spending on oncology drugs hit $100 billion in 2014, an increase of 10.3% over 2013 and an increase in the compound annual growth rate (CAGR) of 6.5% over the previous 5 years. The United States accounts for 42.2% of total spending, followed by the EU5—France, Germany, Italy, Spain, and the United Kingdom. The share of global spending among "pharmerging" countries—21 nations including Brazil, China, India, Mexico, and Russia—grew faster than other segments between 2010 and 2014—15.5%. The full report is available at www.imshealth.com.

NOTED

- A recent study found that **older patients who received stem cells from younger, unrelated donors with higher numbers of CD8 cells had significantly reduced risk of disease relapse** and improved survival compared with those who received stem cells from donors with low numbers of CD8 cells, including older matched siblings (J Clin Oncol 2015 June 8 [Epub ahead of print]).
- **Ventana Medical Systems announced that the FDA approved its ALK assay as a companion diagnostic** to aid in the identification of patients with non–small cell lung cancer likely to benefit from crizotinib (Xalkori; Pfizer).
- In a phase III trial involving 326 patients with relapsed acute lymphoblastic leukemia, **the investigational antibody–drug conjugate inotuzumab–ozogamicin led to complete responses in 80% of patients** compared with 33% of patients treated with standard care, usually chemotherapy. The findings were reported at the 20th Congress of the European Hematology Association in June.
- **The FDA is teaming up with the online network PatientsLikeMe to better understand the side effects of 1,000 different drugs, including anticancer drugs,** as reported by the site's 350,000 members. Because the data are generated by patients, the information provides insights into their experiences over time, including drug tolerance, adherence, and quality of life.
- Noted San Diego developer and **philanthropist Conrad Prebys will donate $100 million to the Sanford Burnham Medical Research Institute in nearby La Jolla, CA.** In recognition of his contribution, the Institute has changed its name to the Sanford Burnham Prebys Medical Discovery Institute.
- **Hawaii's governor signed a bill raising the legal smoking age to 21 statewide,** making Hawaii the first state to do so. The law will also ban the sale, purchase, and use of electronic cigarettes by anyone under 21. The law will take effect on January 1, 2016.

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