the bacteria of their cage-mates, which reduced tumor formation in the AIM2-deficient mice. "Mice lacking AIM2 have a distinct microbial ecology," says lead author Si Ming Man, PhD, raising the possibility that modifying gut microbiota might prevent colon cancer.

Experts praised the work of both teams. "The two papers are very significant and will give us a basis to explore the role of the human AIM2 protein in development of epithelial cancers," says Divaker Choubey, PhD, of Ohio's University of Cincinnati College of Medicine.

That both groups demonstrated that the role of AIM2 in preventing colon cancer is important, says Naeha Subramanian, PhD, of the Institute for Systems Biology in Seattle, WA. "Two groups published at the same time, and their conclusions are concordant." ■

New Insight into Mucinous Ovarian Cancer

Historically, ovarian cancer has been treated as one disease. However, molecular studies indicate four main tumor subtypes that show distinct treatment responses: serous, clear-cell, endometrioid, and mucinous ovarian carcinoma.

To find germline variants that might flag individual susceptibility—and new therapeutic targets—for these tumor types, researchers turned to genome-wide association studies (GWAS). One recent study describes three new genetic loci specifically associated with the risk for mucinous ovarian carcinoma (MOC; Nat Genet 2015;47:888–97).

"Once you find genetic loci that affect the risk, it's like giving clues to Sherlock Holmes for where to look next, and what aspects of the biology to study," says Andrew Berchuck, MD, director of gynecologic oncology at Duke University School of Medicine in Durham, NC, and senior author of the study. "These variants could shed some light on the pathogenesis of this disease."

Many clinical trials currently focus on therapeutically targeting germline mutations, such as *BRCA1* and *BRCA2*, known high-risk factors for high-grade serous ovarian cancer (HGSOC), the most common subtype. However, only 3% of women diagnosed with ovarian cancer have primary, invasive MOC, leaving a dearth of data to analyze.

In this study, researchers compared genotypes from 1,644 women with MOC to those of 21,693 unaffected controls and discovered three new risk loci. One variant, near the *HOXD9* gene, is in a region of the genome that predisposes women to the HGSOC subtype; the other two lie near the *INFL3* and *PAX8* genes, both implicated in the development of colorectal cancer.

With this information, researchers can follow dysfunctional cell pathways that may point toward the cancer's origins. Previous studies have shown that *HOXD9* belongs to a family of transcription factors that control cell differentiation. The precise functions of *INFL3* and *PAX8* aren't known, but data suggest that their expression may help maintain a malignant state.

"This study is really a starting point to try to understand the biology of mucinous ovarian cancer, particularly if they can identify the biological relevance for these genes," says Elizabeth Swisher, MD, a professor of obstetrics and gynecology at the University of Washington and medical director of the Breast and Ovarian Cancer Prevention Program at the Seattle Cancer Care Alliance.

One caveat with GWAS: Each locus may have many single-nucleotide variants that could be responsible for the risk association, notes Berchuck. Although researchers can test the correlation between each variant and the level of gene expression, such laboratory-based simulations aren't definitive evidence of causality. In the future, gene-editing methods may allow researchers to mimic the variants, to more accurately assess the biologic effects.

"This is just the start," says Simon Gayther, PhD, a professor of preventive medicine at the University of Southern California's Keck School of Medicine in Los Angeles and corresponding author of the study. "The more we do these studies focusing on MOC, the more it will become clear that this cancer has its own biology, its own genetic susceptibility, its own prevention approaches, and therapies that need to be developed." ■

NOTED

- Thanks to a fundraising frenzy, **the Oregon Health and Science University's Knight Cancer Institute will receive $1 billion for cancer research.** In 2013, Phil Knight, the CEO and cofounder of Nike, pledged to give $500 million to the center on the condition that it raise $500 million more within 2 years.
- After being canceled last year due to design flaws and trouble recruiting participants, **the NIH National Children's Study (NCS) may be resurrected, although in a different form.** Appropriations committees in both the U.S. House and Senate approved spending bills for the 2016 fiscal year that include $165 million to form the National Children's Study Alternative.
- **Proton Partners International Limited began work to build the United Kingdom's first proton beam cancer treatment center,** which will be located in Newport. The company plans to build two other centers in the UK—one in Northumberland and the other in London.
- The American Society of Human Genetics issued a position statement saying that **genetic testing should be limited to a single-gene analysis or targeted gene panels** in children and adolescents (Am J Hum Genet 2015;97: 6–21). It also says that testing for adult-onset conditions should be avoided unless a childhood treatment exists, and that secondary findings should be disclosed only when there is "clear clinical utility."
- The U.S. Court of Appeals for the Federal Circuit ruled that **Sandoz must wait 6 months to market Zarxio,** its version of the biologic drug Neupogen (filgrastim; Amgen), following FDA approval. That means that an injunction imposed on the marketing of Zarxio will remain in effect until September 2.
- **The European Commission approved the PD-1 inhibitor pembrolizumab** (Keytruda; Merck) for patients with advanced melanoma. **It also approved the PD-1 inhibitor nivolumab** (Opdivo; Bristol-Myers Squibb) for patients with locally advanced or metastatic squamous non–small cell lung cancer who have already received chemotherapy.

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