the bacteria of their cage-mates, which reduced tumor formation in the AIM2-deficient mice. “Mice lacking AIM2 have a distinct microbiol 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 Subramaniam, 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, generating clues 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.”

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