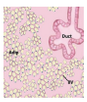
CANCER PREVENTION RESEARCH

HIGHLIGHTS FROM THE LITERATURE

Editors' Selections from Relevant Scientific Publications

Obesity Promotes Breast Epithelium DNA Damage in Women Carrying a Germline Mutation in *BRCA1 or BRCA2*



Obese adipose tissue in the mammary gland (by Arendt et al. via Cancer Research

Bhardwaj et al. investigated whether high body mass index (BMI) increases breast cancer risks for women carrying BRCA 1 or BRCA2 mutations. They examined noncancerous breast tissue from 69 such women and found that BMI and biomarkers of metabolic dysfunction were positively correlated with DNA damage in epithelia. RNA sequencing data revealed that obesity altered breast adipose microenvironment and activated estrogen biosynthesis. Blocking signaling pathways mediated by either estrogen or obesity-associated factors leptin or insulin, reduced DNA damage. Additionally, a high-fat diet increased DNA damage and mammary tumors in Brca1$^{+/-}$mice. These results provide mechanistic insight linking obesity and breast cancer in BRCA mutation carriers, and suggest that reducing risk may involve maintaining a lower body weight, addressing metabolic problems and targeting estrogen.

Bhardwaj P, . . . Brown KA. ***Sci Transl Med****. 2023 Feb 22;15(684):eade1857.*

Helicobacter pylori, Homologous-Recombination Genes, and Gastric Cancer

H. pylori in stomach (by Ed Uthman via Wikimedia Commons

Usui et al. investigated the combined effects of *Helicobacter pylori* infection and germline pathogenic variants in cancer-predisposing genes on gastric cancer. The study analyzed 27 cancer-predisposing genes using samples from two independent Japanese cohorts. The first cohort included 10,426 gastric cancer patients and 38,153 nonmalignant disease controls, while the second cohort had 1433 newly diagnosed gastric cancer patients and 5997 cancer-free controls. This study established an interaction between *H. pylori* infection and pathogenic variants in nine gastric cancer risk genes, including BRCA1, BRCA2, APC, ATM, CDH1, MLH1, MSH2, MSH6, and PALB2. These findings suggest that *H. pylori* elimination may be particularly valuable for individuals carrying a pathogenic variant in these genes.

Usui Y, . . . Momozawa Y. ***N Engl J Med****. 2023 Mar 30;388(13):1181-1190.*

doi: 10.1158/1940-6207.CAPR-16-6-HFL

Lung Adenocarcinoma Promotion by Air Pollutants

Lung and polluted air (by Gerd Altmann via Pixabay)

Insights into how air pollution promotes lung tumor growth could inform the development of emissions controls that better protect public health. Hill et al. have analyzed the relationship between exposure to airborne particulate matter measuring ≤2.5 μm (PM2.5) and carcinogenesis in England, Taiwan, and South Korea, identifying a clear pattern in which higher regional PM2.5 levels correlate with elevated incidence of EGFR-driven lung adenocarcinoma, which is highly prevalent in never-smokers. Subsequent tests in mice showed that PM2.5 exposure caused lung macrophages infiltration and release of interleukin-1β, which favored selection and proliferation of already-mutated cells. These results demonstrate the need to look beyond mutagenesis in defining carcinogenic effects and highlight the importance of air quality regulations in cancer prevention.

Hill W, . . . Swanton C. ***Nature****. 2023 Apr;616 (7955):159-167.*

Inferring Early Genetic Progression in Cancers with Unobtainable Premalignant Disease

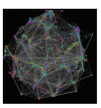


Illustration of an algorithm (by gephi via Flickr)

A solid understanding of the initial stages of tumor development can give clinicians an edge in prevention, diagnosis, and treatment, but premalignant tissue is inaccessible for many cancers. Leshchiner et al. have developed an algorithm called PhylogicNDT that makes it possible to reconstruct this early mutational history based on sequencing data from primary tumors. The authors show that they can recapitulate the decades-long process of tumor formation for the well-studied human papillomavirus-negative (HPV−) head and neck squamous cell carcinoma (HNSCC). More importantly, they demonstrate the same feat with HPV+ HNSCC, for which premalignant tissue is seldom obtainable and the earliest stages are poorly understood, highlighting the potential to uncover informative mutational milestones for otherwise hard-to-study tumor types.

Leshchiner I. . . Rocco JW. ***Nat Cancer****. 2023 Apr 20. doi: 10.1038/s43018-023-00533-y.*

Intercellular Hif1α Reprograms Mammary Progenitors and Myeloid Immune Evasion to Drive High-risk Breast Lesions

Small extracellular vesicles (adapted from an image by SuperManu via Wikimedia Commons)

A recent study by Bertolini et al. investigated the impact of hypoxic small extracellular vesicles (sEVs) derived from breast cancer cells on early stages of breast tumorigenesis and multifocal disease. The researchers found that the hypoxic sEVs disrupted normal mammary epithelia differentiation, expanded stem and luminal progenitor cells, and induced atypical ductal hyperplasia and intraepithelial neoplasia, as well as causing systemic immunosuppression and promoting oncogenic traits like epithelial-mesenchymal transition, angiogenesis and luminal cell invasion. In addition, these sEVs accelerated bilateral breast cancer onset and progression driven by oncogene MMTV-PyMT. The signaling of these sEVs was mediated by the transcription factor HIFα, which is packaged in the hypoxic sEVs. This study identifies a critical potential biomarker and tumorigenic pathway for invasive breast cancers.

Bertolini I, . . . Altieri DC. ***J Clin Invest****. 2023 Apr 17;133(8):e164348.*

Cancer Screening in the United States During the Second Year of the COVID-19 Pandemic

Cancer screening awareness (adapted from Rawpixel)

The COVID-19 pandemic has a significant impact on cancer screening services. Star et al. examined records from the National Health Interview Survey to assess past-year cancer screening rates for eligible individuals in 2019 and 2021. They found that screening rates for breast cancer, cervical cancer, and prostate cancer remained lower than prepandemic levels in the second year of the COVID-19 pandemic, particularly among Asian individuals. While colonoscopy rates were also low, stool testing rates rose, especially among Black and Hispanic populations and those with low socioeconomic status. The findings highlight the role of home-based screening during healthcare system disruptions and the need for healthcare systems to increase efforts to promote cancer screening among eligible populations.

Star J, . . . Jemal A. ***J Clin Oncol****. 2023 Feb 23: JCO2202170.*