CANCER PREVENTION RESEARCH

HIGHLIGHTS FROM THE LITERATURE

Editors' Selections from Relevant Scientific Publications

Bacterial genotoxin accelerates transient infection-driven murine colon tumorigenesis

Transient bacterial infection leads to colon tumorigenesis (art work from Cancer Discovery)

New research links the enteropathogenic and enterohemorrhagic strains of Escherichia coli bacteria responsible for hundreds of millions of cases of diarrheal disease annually to heightened cancer risk. Liu *et al.* have identified a genotoxin produced by the murine counterpart of these pathogens, *Citrobacter rodentium*, that can fuel onset of colon cancer. This protein, UshA, inflicted considerable genomic damage on murine colon epithelial cells even after transient exposure, and *C. rodentium* infection led to accelerated tumorigenesis in a cancer-prone mouse model. UshA is also produced by human-infecting *E. coli*, and this mechanism could pose a critical link between high prevalence of diarrheal disease and climbing colon cancer rates in sub-Saharan Africa.

Liu Y, . . . Wan F. ***Cancer Discov.*** *2022 Jan;12(1):236-249.*

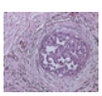
Transition to invasive breast cancer is associated with progressive changes in the structure and composition of tumor stroma

Illustration of breast tumor and tumor microenvironment (adapted from an image by Adrián Blanco-Gómez for Cancer Research)

This HTAN Breast PreCancer Atlas study of ductal carcinoma in situ (DCIS) used a multiplex ion beam imaging by time of flight and a 37-plex antibody staining panel to analyze tumor microenvironment (TME) in 79 patient-matched surgical samples. Risom *et al.* found four TME states that were defined based on the location and function of myoepithelium, fibroblasts, and immune cells. Critically, disruption of the myoepithelial was more advanced in DCIS patients that did *not* develop invasive breast cancer, suggesting this process could be protective against disease recurrence. This study improves understanding of the drivers of breast cancer relapse and emphasizes the crucial role of TME in disease progression.

Risom T, . . . Angelo M. ***Cell.*** *2022 Jan 20;185(2):299-310.e18.*

The breast pre-cancer atlas illustrates the molecular and micro-environmental diversity of ductal carcinoma in situ



Ductal carcinoma in situ (by Kauczuk via Wikimedia Commons)

This histological, molecular, and immunological profiling study explored the diverse, interconnected immune landscapes in 39 premalignant lesions from patients with ductal carcinoma in situ. Nachmanson *et al.* used multiple microdissected regions to analyze phenotype and subtype heterogeneity, B- and T-lymphocyte spatial analysis, mutational profiling, driver mutations, and immunological status. The authors successfully isolated regions within the same sample to characterize different histological features and infer phylogenetic relationships. This study provided richness to the breast pre-cancer atlas and contributed to better models for outcomes and progress risk.

Nachmanson D, . . .Harismendy O. ***NPJ Breast Cancer****. 2022 Jan 13;8(1):6.*

doi: 10.1158/1940-6207.CAPR-15-4-HFL

Pathology of tumors associated with pathogenic germline variants in 9 breast cancer susceptibility genes

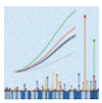
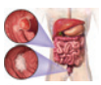


Illustration of gene variants and cancer cumulative risk (adapted from figures by Michael J. Hall for Cancer Prevention Research)

A pair of recent clinical studies identified nine genes that, when disrupted by truncating or missense mutations, can meaningfully increase breast cancer risk. The researchers of the Breast Cancer Association Consortium have now conducted a follow-up investigation of nearly 90,000 participants from one of these trials, BRIDGES, to determine which tumor types are associated with these mutations. This analysis revealed distinctive patterns in terms of age of onset and histological type—for example, triple-negative tumors were notably overrepresented in women with *BRCA1* or *BARD1* mutations. These results could thus enable more accurate risk prediction based on genetic test results and inform the development of improved screening guidelines.

Breast Cancer Association Consortium, . . . Easton DF. ***JAMA Oncol.*** *2022 Jan 27:e216744.44.*

Associations of body mass index at different ages with early-onset colorectal cancer



Colorectal cancer (by Dcoetzee via Wikimedia Commons)

People who were obese in early adulthood have an increased risk of early-onset colorectal cancer later in life. Obesity has long been known as a risk factor for many cancers, but weight loss prior to diagnosis can confound the association. Li et al. analyzed the medical records of 6602 colorectal cancer patients enrolled in a German screening study and compared them to 7950 matched controls. They found that people who had been obese at age 20 or 30 were 2.6 times and 2 times, respectively, more likely to develop colorectal cancer before age 55 as those of normal weight at those ages. The authors say that body mass history, not just current weight, should be considered when assessing a person's risk of colorectal cancer.

Li H, . . . Brenner H. ***Gastroenterology.*** *2021 Dec 13:S0016-5085(21)04074-9.*

Impact of the COVID-19 pandemic on diagnosis of new cancers: A national multicenter study of the Veterans Affairs Healthcare System

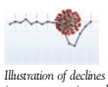


Illustration of declines in cancer screening and diagnosis due to the Covid-19 pandemic (SARS-Cov-2 image is by Ikets via Wikimedia Commons)

Cancer screenings and diagnosis procedures – and the number of new cancers diagnosed – declined significantly due to the Covid-19 pandemic. Restrictions on elective medical procedures resulted in the widespread cancellation of appointments and decreased many people's access to care. Englum et al. reviewed the medical records of more than 9 million veterans who visited 1244 Veterans' Affairs facilities across the United States between 2016 and 2020. They found that these facilities performed 45% fewer colonoscopies in 2020 than the average from previous years, as well as fewer CT scans, biopsies, and cystoscopies. The number of new cancer diagnoses dropped by 13% to 23%, which the authors say necessitates a recovery plan to ensure that health centers can catch up with the backlog and meet the needs of patients whose healthcare access was disrupted.

Englum BR. . . Lal BK. ***Cancer****. 2022 Mar 1;128(5):1048-1056.*