Scientists determined that there were two patterns of genomic alterations. Although hypoxic tumors often carried single-nucleotide variants in certain genes, these changes tended to be cancer type-specific. On the other hand, multiple tumor types shared copy-number alterations for cancer driver genes. Hypoxic tumors gained copies of MYC in 11 cancer types, for instance, and they lost PTEN in seven. The team also detected effects on miRNAs—84% of them correlated with tumor hypoxia in at least one cancer type. Along with miRNA alterations, hypoxic prostate tumors, for which the researchers had the most data, tended to exhibit genomic instability, TP53 mutations, loss of one PTEN allele, a particularly aggressive pathology, and shorter telomeres.

The study is “a triumph of big data,” says J. Martin Brown, PhD, of Stanford University in California, who wasn’t connected to the research. “This will be a gold mine of information” for further investigation of hypoxic tumors, he says. Adrian Harris, MD, PhD, of Oxford University in the UK, agrees. “It’s an important resource. This pulls together a vast amount of data on 8,000 cancers and describes in much greater depth than previously the hypoxic transcriptome.”

Although several hypoxia-targeting drugs have reached clinical trials, none has been approved. The trials did not sort patients by levels of tumor hypoxia, in part because researchers don’t agree on which biomarkers are most reliable. William Wilson, PhD, of the University of Auckland in New Zealand, who wasn’t connected to the study, says the work “is a step in the right direction toward identifying the appropriate biomarkers, but ultimately for selecting therapy we need to be able to distinguish between gene expression changes driven by hypoxia itself versus mutations that phenocopy those changes.”

However, Bristow says that combining mRNA signatures for hypoxia with measures of genomic instability could reveal which patients are most likely to respond in clinical trials. “Genetic instability and hypoxia track together,” he says. –Mitch Leslie

Hypoxic Tumors Share Genomic Instability

A comprehensive genomic analysis of 19 cancer types demonstrates that hypoxic tumors tend to show genomic instability and share other molecular alterations (Nat Genet 2019;51:308–18). The results also suggest a combination of biomarkers that could identify patients most likely to benefit from clinical trials of hypoxia-targeting drugs.

Tissue hypoxia is relatively common in tumors, which can become more aggressive and metastasize as they adapt to the low-oxygen environment. “Characterizing what makes hypoxic tumors unique is of fundamental importance for understanding tumor biology,” says study co-author Paul Boutros, PhD, of the University of California, Los Angeles.

In a previous study, Boutros, Robert Bristow, MD, PhD, of the University of Manchester in the UK, and colleagues found that patients with hypoxic prostate tumors with genomic instability were more likely to relapse (Lancet 2014;15:1521–32). Whether that pattern holds true across tumor types was unclear, however.

In the new study, a team led by Bristow and Boutros used mRNA abundance data from The Cancer Genome Atlas and the Canadian Prostate Cancer Genome Network to gauge hypoxia levels in 8,006 tumors spanning 19 cancer types. The most hypoxic malignancies were squamous cell tumors of the head and neck, cervix, and lung; the least hypoxic were adenosquamous of the prostate and thyroid. However, the team found a large variation in hypoxia levels among tumors in each type.

The results showed that increased hypoxia correlated with higher genomic instability in multiple tumor types. The scientists determined that there were

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The FDA approved cabozantinib (Cabometyx; Exelixis) for patients with hepatocellular carcinoma who received prior sorafenib (Nexavar; Bayer/Onyx). Approval was based on a phase III trial in which patients treated with the tyrosine kinase inhibitor (TKI) had a median overall survival of 10.2 months and a median progression-free survival of 5.2 months, compared with 8 months and 1.9 months, respectively, in patients who received a placebo.

The FDA approved 23andMe’s direct-to-consumer genetic test for a hereditary colorectal cancer syndrome. The MUTYH-Associated Polyposis Genetic Health Risk report tests for two MUTYH variants that can increase the risk of developing colorectal cancer by 43% to 100%. The FDA previously approved 23andMe’s test for three BRCA1/2 mutations.

Patients with comorbidities are less likely to participate in clinical trials [JAMA Oncol 2019 Jan 10 [Epub ahead of print]]. Researchers analyzed survey data from 5,499 patients with cancer and found that 37.2% of those with comorbid conditions discussed clinical trials with their clinicians, 15.7% were offered slots, and 7.8% participated, compared with 44.1%, 21.7%, and 11.3% of those without multiple health problems.

The U.S. House of Representatives Committee on Oversight and Reform announced it will investigate the drug-pricing methods of pharmaceutical companies. The committee requested information from 12 companies about 18 drugs, including Celgene’s immunomodulatory agent lenalidomide (Revlimid), AbbVie’s Johnson & Johnson’s Bruton TKI brutinib (Imbruvica), and Novartis’s TKI imatinib (Gleevec).

Scientists characterized new subtypes of B-cell acute lymphoblastic leukemia (B-ALL; Nat Genet 2019;51:296–307). Researchers performed an integrated genomic analysis on 1,988 cases of pediatric and adult B-ALL and identified 23 subtypes of the disease, including eight new subtypes. Two of the new subtypes have PAX5 alterations and account for 10% of previously uncategorized cases of the disease; a third, defined by a rearrangement of BCL2 with MYC or BCL6, is associated with poor outcomes in patients.