Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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To determine the pathology that may contribute to progression and fatality of COVID-19 pneumonia, the authors performed postmortem needle-core biopsies of lung, liver, and heart from four patients who died from the disease. All patients had elevated white blood cell counts. Histologically, the lungs showed injury to the alveolar epithelial cells, hyaline membrane formation, and hyperplasia of type II pneumocytes, all components of diffuse alveolar damage. Consolidation by fibroblastic proliferation with extracellular matrix and fibrin forming clusters in airspaces was also evident. Bacterial pneumonia was found in some patients. Changes in the liver and heart were observed but likely were secondary or related to underlying diseases.

Wen et al. sought to validate zyxin (ZYX) as a biomarker of aggressive human glioblastoma multiforme (GBM). Using multiple cohorts of glioma patients, the group showed that ZYX expression correlated with tumor progression and poor prognosis, and they went on to demonstrate its role in invasion and growth. They showed that stathmin 1 (STMN1) was a potential target for ZYX, with ZYX regulating STMN1 protein levels. This axis was shown to be more complex than a simple direct interaction due to the
location in the cell of each protein, and the authors believe that other mediators may yet need to be identified. STMN1 itself was shown to promote invasion of GBM cells as well as rescue the invasion repression caused by ZYX loss. Identifying biomarkers that speak to aggressive phenotypes of disease is often key to early detection and can lead to potential therapeutic targets.

A novel pathway for lipopolysaccharide-induced pulmonary fibrosis development

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Metabolic reprogramming is a wide field, having been shown to play a critical role in many diseases. Hu et al. sought to investigate a gap in the knowledge base and investigate the role lipopolysaccharide (LPS) plays in lung fibrosis. They found that LPS promotes collagen synthesis through aerobic glycolysis via activation of the PI3K-Akt-mTOR pathway, leading to expression of 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase3 (PFKFB3). Furthermore, inhibiting any element along the pathway was sufficient to reverse the phenomena. A mouse model of LPS-induced pulmonary fibrosis was used to show that PFKFB3 expression and aerobic glycolysis were also detected in vivo. The PI3K-Akt-mTOR/PFKFB3 pathway is thus a potential therapeutic target in cases of LPS-induced pulmonary fibrosis.

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A new standard of care for a defined group of colon cancer patients?

In an exploratory clinical trial (ClinicalTrials.gov: NCT03026140), 40 patients with mismatch repair (MMR)-deficient (dMMR) and 20 with MMR-proficient (pMMR) colorectal cancer were given adjuvant immunotherapy (one dose of ipilimumab and two doses of nivolumab, with or without celecoxib, or two doses of nivolumab). Treatment was well tolerated, and all patients underwent radical resections without delays. Of the patients who received ipilimumab + nivolumab (20 dMMR and 15 pMMR tumors), 35 were evaluable. All 20 of the dMMR patients in that group showed pathological complete response, with 19 showing <10% residual tumor and 12 pathological complete responses. In pMMR tumors, 4 of 15 showed pathological responses. Of the pMMR patients who responded, CD8^+PD-1^+ T-cell infiltration was predictive; if validated in a larger cohort, this might help in selecting patients with pMMR tumors for future neoadjuvant immunotherapy studies. The authors propose that neoadjuvant immunotherapy may have potential as the standard of care for this defined group of colon cancer patients.

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Automated diagnosis of hematopoietic diseases*

Tsai et al. sought to develop a high-throughput, highly multiplexed, single-cell assay that would combine the work of the hematopathologist and cell surface expression analysis by empowering mass cytometers to “see” like pathologists. A test group of 71 diverse clinical samples was used to test their protocols, and it was shown that the assay could determine a robust and distinct pattern of morphometric markers for the identifiable cell types. Lamin-B1 could be used to highlight acute leukemias, lamin-A/C could distinguish between normal and neoplastic T-cells, and VAMP-7 recapitulates light-cytometric side scatter. It was also shown that the assay could outperform flow cytometry and comparable expert microscopy when recalibrated for myelomonocytic blast enumeration, reducing the need for years of specialized training. The authors propose that their system, incorporating traditional surface markers with machine learning, provides the scope for automated diagnosis of complex hematopoietic diseases.

Nature Medicine, 2020;26:408–417; https://doi.org/10.1038/s41591-020-0783-x

Identification of novel drivers of lung cancer metastasis to the brain

Patient mortality from lung adenocarcinoma (LUAD) is frequently due to brain metastases (BM-LUAD). Shih et al., seeking to identify potential genomic drivers that promote this metastasis to the brain, performed whole-exome sequencing of 73 cases of BM-LUAD. Using LUAD as the control, the group showed that three candidate genes were apparent, including MYC (12% versus 6%), YAP1 (7% versus 0.8%) and MMP13 (10% versus 0.6%), and significantly more frequent deletions in CDKN2A/B (27% versus 13%). After validating their findings using an independent cohort, they functionally assessed the candidates in patient-derived xenograft models, validating overexpression of each increased incidence of brain metastasis. Their findings show that somatic alterations contribute to brain metastases and validate the concept of using genomic sequencing to identify these candidate genes. These genes then become potential therapeutic targets for prevention and treatment of BM-LUAD.

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