Notable advances 2018

This past year included numerous research studies that broke the mold and elucidated new biology and drug targets. Here are some of the exciting papers from 2018 that moved biomedicine forward.

AGING

Meningeal lymphatics in aging and Alzheimer's disease

Nature **560**,185–191 (2018).

The mechanisms that lead to aging and age-related disease are largely unknown. Recently, lymphatic vessels have been rediscovered in the meninges of the brain, forcing a rethinking of how waste is disposed from the central nervous system.

Researchers in the United States show in mice that meningeal lymphatics have a role in homeostasis of the brain by draining it of macromolecules, such as amyloid beta peptides. Furthermore, they find that impairment of meningeal lymphatics during aging results in decreased cognitive function in mice. Also, using mouse models of Alzheimer's disease, they discover that impaired meningeal lymphatics contribute to aggravation of this disease.

The study suggests that increasing meningeal lymphatic function is a promising target in prevention of age-associated neurological disease. *HS*

https://doi.org/10.1038/s41591-018-0281-6

INFECTIOUS DISEASE

Monitoring yellow fever

Science **361**, 894–899 (2018).

Yellow fever is a severe mosquito-borne virus of the *Flaviridiae* family. It may be transmitted both through a cycle involving nonhuman primates and mosquitoes (known as sylvatic transmission) and a cycle involving humans and mosquitos in urban areas. Brazil has recently had its largest recorded yellow fever outbreak in decades, and new surveillance is required to track transmission route, as urban transmission could be particularly devastating.

In a collaboration between many international scientists, epidemiological, spatial and genomic approaches are combined to characterize yellow fever transmission in the recent outbreak in Brazil. Their results indicate that sylvatic transmission occurred initially, followed by spillover to human areas.

The authors' approach provides a framework for monitoring future epidemics to strategize intervention approaches. *HS*

https://doi.org/10.1038/s41591-018-0280-7

BIOMARKERS

A blood-based biomarker for checkpoint inhibition

Nat. Med. **24**, 1441–1448 (2018).

Immune checkpoint inhibitors (ICIs) have been shown to be more effective in individuals with elevated levels of the protein known as programmed death-ligand 1 (PD-L1) or high levels of mutations in their tumors. However, it is difficult to obtain tissue for analysis of these factors from potential recipients of this therapy.

Scientists from the United States and China developed a blood-based assay to measure mutation levels in tumors and performed retrospective analysis of two large randomized clinical trials. They showed that the levels of tumor mutations in patients with non-small-cell lung cancer who did not respond to first-line treatment could predict which of these patients responded to the ICI atezolizumab (an anti-PD-L1 drug).

The study shows that a high level of tumor mutation is a clinically actionable biomarker for ICI in this type of cancer. *HS*

https://doi.org/10.1038/s41591-018-0282-5

MICROBIOME

Environmental shaping of the microbiome

Nature **555**, 210–215 (2018).
Nature **555**, 623–628 (2018).

There is an increasing understanding that the gut microbiome has a role in physiology and disease, although the relative contributions of the environment and genetics to its composition are unknown.

In one study, an international group of researchers analyzed the host genotypes and gut microbiomes of over 1,000 individuals who share a relatively similar environment. They found that host genetics has a minor role in determining microbiome composition and that diet, drugs and other anthropometric measures strongly influence interperson variability.

In another experiment, researchers based in Germany analyzed the effects of over 1,000 nonantibiotic drugs on the gut microbiome. Their analysis revealed that over 20% of these drugs inhibit the growth of bacterial species in the gut microbiome. Thus nonantibiotic drugs could play a role in antibiotic resistance by applying relevant selective pressure on bacteria and are also involved in shaping the gut microbiome.

Both studies reveal the large role of the environment in forming the gut microbiome. *HS*

https://doi.org/10.1038/s41591-018-0286-1

GENE THERAPY

Gene therapy for beta thalassemia

N. Engl. J. Med. **378**, 1479–1493 (2018).

In the most severe form of beta thalassemia, transfusion-dependent beta thalassemia, affected individuals are dependent on blood transfusion, which is challenging owing to limited donors and complications associated with transfusion. Gene therapy has previously been shown to hold promise in an individual with beta thalassemia.

A team of researchers from Chicago report the interim result from two phase 1/2 clinical studies in which patients' own $CD34^+$ cells were isolated and transduced with a lentiviral vector to deliver the beta globin gene. The cells were then reinjected into the patients.

In their study of 22 patients, the team found that this gene therapy approach reduced or eliminated the need for further transfusions, and there were no adverse events. *HS*

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