HUMAN GENETICS

The genetic architecture of multiple sclerosis

Science **365**, eaav7188 (2019)

Pasieka / Science Photo Library / Getty.

A large-scale meta-analysis of multiple sclerosis (MS) genetic data identifies over 200 variants that are significantly associated with MS susceptibility.

MS is a debilitating autoimmune disease that affects the central nervous system. Previous studies have identified a number of genetic variants related to the disease; however, most of the genetic risk remains unknown.

Investigators from the International Multiple Sclerosis Genetics Consortium analyzed genome-wide data from over 47,000 individuals with MS and 68,000 controls. They found a large number of new genetic loci associated with MS, including the first variant identified on the X chromosome and an enrichment of MS genes in both the innate and adaptive immune systems in the periphery, as well as in microglia. *KG*

https://doi.org/10.1038/s41591-019-0656-3

CLINICAL ONCOLOGY

PARP inhibitors for all ovarian cancers

New Engl. J. Med. https://doi.org/10.1056/nejmoa1910962 (2019)

The PARP inhibitor niraparib demonstrates clinical benefit in patients with ovarian cancer, regardless of the functional status of the DNA repair machinery.

Mutations in the *BRCA* gene compromise the capacity of tumors to correct DNA breaks through a process known as homologous recombination and have been linked to the efficacy of PARP inhibitors in patients with ovarian cancer. It is not known, however, whether these agents are also effective in tumors with other repair deficiencies or in unselected patients.

Antonio González-Martín and his collaborators find in the PRIMA/ENGOT-OV26/GOG-3012 phase 3 clinical trial that niraparib extends progression-free survival in newly diagnosed patients with advanced ovarian cancer. This benefit is observed in patients whose tumors have HRD due to *BRCA* mutations and to other mechanisms, and also in patients without evidence of HRD. *JC*

https://doi.org/10.1038/s41591-019-0655-4

CARDIOVASCULAR DISEASE

Prevention with a polypill

N. Engl. J. Med. **381**, 1114–1123 (2019)

A randomized controlled trial shows that a polypill containing four inexpensive medications is effective in lowering cardiovascular disease risk in an underserved population—a group of primarily minority and low-income individuals.

The clinical benefits of polypills—pills containing combinations of fixed doses of drugs known to be beneficial for preventing or treating a disease or a set of related diseases—are well established. But whether an inexpensive polypill might be beneficial in groups with low socioeconomic status, which pose challenges to conventional treatment options, hasn't yet been tested.

Thomas J. Wang and colleagues find that a polypill costing $26 per month leads to greater reductions in two important risk factors for cardiovascular disease—systolic blood pressure and low-density lipoprotein (LDL) cholesterol—after 12 months of treatment, as compared to usual care. *MB*

https://doi.org/10.1038/s41591-019-0658-1

NONCOMMUNICABLE DISEASES

A disease transition in sub-Saharan Africa

Lancet Glob. Health **7**, e1375–e1387 (2019)

Between 1990 and 2017, there was a 67% increase in the all-age disability-adjusted life years (DALYs) attributable to non-communicable disease (NCDs) in sub-Saharan Africa.

The disease burden in sub-Saharan Africa is largely attributable to infectious diseases. However, there is an increase in the prevalence of NCDs in low- and middle-income countries as they develop, known as the epidemiological transition, and the prevalence of this transition in the region is not known.

Heba Gouda and colleagues analyzed data from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2017 to identify the DALYs attributable to NCDs in this region. The results show that the rise in NCDs in this region is substantial and poses a major challenge to healthcare systems. *HS*

https://doi.org/10.1038/s41591-019-0659-0

NEURO-ONCOLOGY

Synaptic input drives brain tumor progression

Venkataramani, V. et al. *Nature* **573**, 532–538 (2019).
Venkatesh, H. S. et al. *Nature* **573**, 539–545 (2019).
Zeng, Q. et al. *Nature* **573**, 526–531 (2019).

Neurons form excitatory synapses with brain tumor cells, and this direct neural circuit input promotes tumor growth.

Gliomas, a type of brain tumor, depend upon neuronal activity for growth. Although indirect interactions between neurons and brain tumor cells have been previously described, it was unclear whether direct synaptic electrochemical signaling contributed to tumor progression.

In two separate studies, Michelle Monje and colleagues, and Thomas Kuner, Frank Winkler and colleagues provide evidence for the formation of functional synapses between neurons and glioma cells in xenograft mouse models as well as in human glioma tissue. In a third study, Douglas Hanahan and colleagues show that glutamate secreted by neurons mediates the colonization of brain metastases in a mouse model and that such glutamatergic signaling is active in human brain metastases. *SS*

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