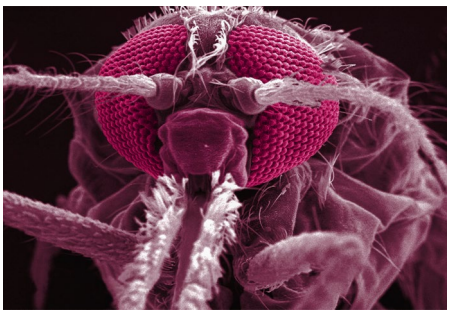
VACCINES

Anti-mosquito immunity

Lancet https://doi.org/10.1016/S0140-6736(20)31048-5 (2020)



Credit: Phanie/Alamy Stock Photo

A vaccine against mosquito salivary proteins is safe in humans and shows promise as a preventative strategy against mosquito-borne diseases.

Mosquito-borne diseases, both emerging and established, pose a substantial burden of disease, and a broad immunization strategy for all would be a real game-changer in global health. Animals that have immunity to mosquito salivary proteins have greater protection against the diseases carried in the mosquito saliva.

Manning et al. carry out a placebo-controlled, double-blind, phase 1 trial of a vector-based vaccine made of *Anopheles gambiae* salivary proteins in 49 healthy adult participants. They find that when combined with other adjuvants, the vaccine is safe, and that participants develop an immune response after vaccination, which suggests promise for this approach in providing protection against mosquito-borne disease. *HS*

https://doi.org/10.1038/s41591-020-0990-5

GENE THERAPY

Targeting porphyria

N. Engl. J. Med. **382**, 2289–2301 (2020)

A phase 3 trial of givosiran, an RNA-interference therapy, for acute intermittent porphyria resulted in a reduced rate of porphyria attacks.

Acute hepatic porphyria is a set of rare diseases in which porphyrins build up, which results in neurotoxic effects. Intermittent hepatic poryphyria is the most common form and is caused by upregulation of hepatic delta-aminolevulinic acid synthase 1, which results in attacks that include symptoms such as abdominal pain, muscle weakness and neuropathy. Treatment options are limited; however, givosiran has shown promise.

In a double-blind, placebo-controlled, phase 3 trial of 94 patients with acute hepatic porphyria, those receiving givosiran had a significantly lower rate of attacks, in addition to improvements in other disease-associated symptoms. *HS*

https://doi.org/10.1038/s41591-020-0987-0

MICROBIOME

Personalized drug-metabolism assessment

Cell **181**, 1661–1679 (2020)

People's gut micobiomes can now be cultured and their metabolic potential can be assessed to identify personal drug-metabolism potential.

The gut microbiome is a diverse organ that is unique to each person and is known to have the ability to metabolize drugs, which alters the effects of therapies. The ability to characterize the effects of a person's microbiome has the potential to anticipate further the treatments to which that person might respond.

Javdan, Lopez et al. develop an in vitro culturing system for whole individual gut microbiomes — the ability to culture these communities has been a hurdle in characterization of the gut microbiome — along with a high-throughput microbiome-derived metabolism screen. They apply their approach to the microbiomes of 21 people and screen 575 drugs with one person's microbiome and 23 selected drugs with all microbiomes. *HS*

https://doi.org/10.1038/s41591-020-0989-y

REGENERATIVE MEDICINE

CNS barrier–forming organoids

Science https://doi.org/10.1126/science.aaz5626 (2020)

Organized human choroid-plexus organoids that secrete cerebral spinal fluid (CSF) can be generated from human pluripotent stem cells and mimic the CNS barrier so that molecules that permeate it (including therapies) can be identified.

The choroid plexus is an epithelial layer that forms the blood–CSF barrier. The CSF is secreted by the choroid plexus and contains hormones, other signaling molecules and nutrients, although the functions of the molecules within it are far from understood. Among other question about this barrier are those about the functional heterogeneity and permeability of the choroid plexus.

To study the choroid plexus and CSF further, Pellegrini et al. modify the protocol for deriving cerebral organoids. Their choroid-plexus organoids are molecularly similar to the choroid plexus in vivo and, notably, organize into distinct compartments and secrete CSF, which will allow further study of the important blood–CSF barrier. *HS*

https://doi.org/10.1038/s41591-020-0991-4

AGING

Senolytic CAR T cells

Nature https://doi.org/10.1038/s41586-020-2403-9 (2020)

Chimeric antigen receptor (CAR) T cells that target an antigen produced by senescent cells are potential therapies in diseases of aging and chronic tissue damage, such as diabetes and fibrosis.

Senescence is a mechanism of tumor suppression in which cell division is halted; however, it also has a role in pathogenesis and in many diseases of aging. Agents that target senescent cells (senolytics) are able to alleviate the pathologies linked to these cells.

Amor et al. identify an antigen (uPAR) specific to senescent human cells and are able to show in vivo in mice that CAR T cells directed against this antigen alleviate pathogenesis with two different pathologies linked to senescence. *HS*

https://doi.org/10.1038/s41591-020-0988-z

Hannah Stower