Research brief

Mutant hero proteins?

Blood cells from people with a rare muscle disease have been shown to be resistant to HIV-1 infection. The disease, limb girdle muscular dystrophy, is caused by a genetic mutation in the transportin 3 gene (*TNP03*), which produces a mutated protein and leads to weakness in the limbs and pelvis. The wildtype TNP03 protein is also a key factor in HIV-1 infection, working as a nuclear importer, prompting researchers to do an in vitro study, in which they showed HIV viral integration to be reduced 16-fold in cells of people with the mutated protein versus the wildtype. Further probing of the association might give clues to treatments for both diseases.

Mumps the word

In the past decade, mumps outbreaks in the USA have occurred in close-contact settings, such as colleges, despite most young adults having been vaccinated against the virus. Findings from a new study suggests why—protection against mumps conferred by the measles, mumps, and rubella vaccine might wane over time. The study assessed blood samples from 71 adults aged 18–23 years, most of whom had had the vaccine at least 10 years ago. The findings showed that antibody concentrations against mumps were significantly lower than they were against rubella. 10% of the study participants had no memory B cells against mumps.

HIV signature

Two previous independent studies have shown partial effectiveness of an adenovirus-based HIV-1 vaccine candidate (Ad26/gp140) in non-human primates. To understand better the protection conferred by the vaccine, researchers sequenced RNA from blood samples taken from the macaques immunised and challenged in these trials. They identified a gene expression signature that conferred resistance (to either simian immunodeficiency virus or simian-human immunodeficiency virus) and was related to the B-cell activation in effective immune responses. They detected that the same signature was also associated with the protection seen in the trial of the RV144 vaccine, the only HIV vaccine thus far assessed in human beings. That the signature might be common between animals, and vaccines, suggests that it could be used to better understand the protection conferred by HIV vaccines.

Damming dengue

One reason that there is no treatment for severe haemorrhagic dengue might be that we do not understand why some patients go on to develop this severe form of the disease and others do not. Findings from a new study suggest that an enzyme in human cells called tryptase might play a crucial part by increasing vascular leakage and leading to severe disease. Using in vitro human microvascular endothelial cells, investigators showed that tryptase breaks down endothelial cell tight junctions. Furthermore, they showed that nafamostat mesylate, a tryptase inhibitor, blocked dengue-induced vascular leakage in mice. In two independent human dengue cohorts, tryptase concentrations were associated with dengue haemorrhagic fever severity.

A new sepsis option?

Findings from a study done at Southern Medical University in Guangzhou, China, suggest that, one day, faecal transplantation might be a treatment to help people recover from sepsis. The scientists assessed stool samples from 22 adults with sepsis and 34 otherwise healthy people. 16S rDNA sequencing, metabolic, and metaproteomic analyses showed that the gut microbiota in people with sepsis is severely disrupted. They then transferred faecal samples to mice and induced sepsis, showing that mice given healthy faecal samples had less liver damage than those given samples from patients with sepsis.

Klebber clogs

About half of people infected with hypervirulent, drug-resistant strains of the bacteria *Klebsiella pneumoniae* die. It is encouraging therefore that US researchers have developed a promising candidate conjugate vaccine. The vaccine targets the two most virulent strains, K1 and K2, and contains surface proteins and sugars biologically manufactured within a bioengineered, harmless strain of *Escherichia coli*. Researchers gave the vaccine or placebo to 20 mice and infected them with one of the two virulent strains. In mice given placebo, 80% infected with K1 and 30% infected with K2 died. In those given the vaccine, 20% infected with K1 and none infected with K2 died. Biological synthesis offers an advantage over traditional chemical synthesis, which takes more time and is expensive.

New malaria drug target

An international team of researchers might have discovered a malaria drug target with the ability both to treat the disease and to prevent forward transmission. They did high-throughput screening of 24 000 compounds and identified a selective inhibitor to the *Plasmodium falciparum* protein kinase PfCLK3. The kinase is central to the parasites' RNA splicing mechanism and its inhibition, the study's findings showed, leading to the downregulation of more than 400 essential parasite genes, thus stunting the parasite at its asexual stage and blocking later transmission to mosquito vectors as gametocytes. The inhibitor cleared parasites from infected mice.

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For more on **TNP03 and HIV infection** see *PLoS Pathog* 2019; **15:** e1007958

For more on **mumps vaccination** see *Proc Natl Acad Sci USA* 2019; published online Sept 3. https://www.pnas.org/cgi/doi/10.1073/pnas.1905570116

For more on **HIV vaccines** see *Sci Transl Med* 2019; **11:** eaaw4236

For more on **the role of tryptase in dengue** see *J Clin Invest* 2019; **130:** 128426

For more on **sepsis and the microbiome** see *FASEB J* 2019; published online Aug 28. https://doi.org/10.1096/fj.201900398RR

For more on ***Klebsiella* vaccine** see *Proc Natl Acad Sci USA* 2019; published online Aug 27. https://doi.org/10.1073/pnas.1907833116

For more on **PfCLK3 and malaria** see *Science* 2019; **365:** eaau1682