Research brief

A controller for Ebola

A study in *iScience* shows that nitazoxanide, which is licenced to treat parasitic infections such as cryptosporidium, is a promising host-directed therapy for Ebola. Ebola virus normally evades RIG-1 and PKR, human proteins involved in host viral detection. In-vitro experiments showed that nitazoxanide can enhance antiviral sensing through RIG-1, amplifying interferon-1 responses. The investigators then showed that nitazoxanide inhibits growth of Ebola virus in human cells. Genetically edited cells without PKR and RIG-1 were vulnerable to Ebola infection, even when nitazoxanide was added, showing that the drug's effects depend on these two proteins. In-vivo studies of nitazoxanide's effects are planned.

ApoE and hep B

Researchers at the University of Alabama at Birmingham (USA) have shown how human apolipoprotein E (ApoE) is vital to infection and production of hepatitis B virus. With in-vitro and murine studies, the investigators showed that ApoE is likely incorporated into the virus envelope. Neutralisation experiments showed that an ApoE-specific monoclonal antibody could reduce hepatitis B virus infectivity by 90%. Silencing of ApoE by siRNA also hampered infectivity as well as production of virions. In cells with the ApoE gene knocked out, hepatitis B virus production was decreased, but could be restored through ectopic expression of apoE. Taken together, these experiments show the importance of ApoE in hepatitis B virus infection, which could be a target for the development of new antivirals.

Keeping HIV at bay

The effort to find a cure for HIV continues, with researchers at University of Texas Medical Branch at Galveston (USA), showing how a small molecule could prevent reactivation of latent HIV. Using structure-guided drug design, the investigators synthesised several small molecules to manipulate BRD4, a human protein involved in epigenetic regulation of HIV transcription. One of the compounds, ZL0580, suppressed reactivation of HIV in CD4 cells. In ex-vivo experiments, ZL0580 delayed reactivation of HIV and viral rebound in the blood of infected patients after the cessation of traditional antiretroviral therapy. These findings could direct the development of probes or therapeutic agents for epigenetic silencing of HIV.

Taking the heat

Scientists at the University of Bath (UK) have developed a technique to encapsulate vaccine components that could lead to the development of a new thermostable tuberculosis vaccine. Previous work has shown how a process of ensilication—building a silicon cage—can protect model proteins from denaturing through heat. In their new study, published in *Scientific Reports*, the investigators showed for the first time that ensilication can work for a vaccine antigen (ag85b) and adjuvant protein (Sbi). Ensilication maintained their structure and in-vitro function despite heating. The need to keep vaccines cold is one of the major barriers to vaccination because ensuring constant refrigeration is difficult in many poor or isolated places.

The clout of a clot

Patients with haemophilia, who are deficient in blood clotting factors, are at greater risk of pneumonia and sepsis, leading some speculation that coagulation factors might have antibacterial properties. A study published in *Cell Research* on Aug 9, seems to prove the case. In-vitro studies of coagulation factors VII, IX, and X, showed that the light chains of these proteins can break down the lipopolysaccharides of the bacterial outer membrane of *Escherichia coli*. The cells were dead within 4 h. Further experiments in mice showed that the light chains could be effective against extremely drug-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* infections in vivo. The mechanism of action for this effect differs from most other antibiotics, giving hope that they might lead to effective new treatments for resistant organisms.

Looking at Lassa

Structural studies, led by researchers based at The Scripps Research Institute (USA), have shown how antibodies neutralise Lassa virus, and suggest how new, broadly effective vaccines against Lassa might be developed. The Lassa glycoprotein is the essential for attachment to host cells and is the only exposed protein in the virus. The investigators compared antibodies of low, medium, and high affinity for the glycoprotein to identify the most important residues involved in binding. They showed that most antibodies bind to a specific site on the virus and substituting amino acids at this site, the team developed an antibody that can neutralise all strains of Lassa in vitro.

Hijacking the host

New findings have shown how leishmania hijacks the intracellular transport mechanisms of host cells to deliver its virulence factors GP63 and LPG. Leishmania survives inside the vacuole of infected macrophages. The researchers found that GP63 and LPG are concentrated in the host cell's endoplasmic reticulum. Genetic deactivation of host cell molecules involved in intracellular transport blocked the spread of the virulence factors, confirming the hypothesis. The pathway could be a target for new interventions, and might play a role in infection with other organisms such as mycobacteria or legionella.

Sean Cleghorn

For more on **Ebola and nitazoxanide** see *iScience* 2019; published online Aug 8. https://doi.org/10.1016/j.isci.2019.07.003

For more on **apolipoprotein E and hepatitis B virus infection** see *PLoS Pathog* 2019; published online Aug 8. https://doi.org/10.1371/journal.ppat.1007874

For more on **maintaining HIV latency** see *J Clin Invest* 2019; **129:** 3361–73. https://doi.org/10.1172/JCI120633.

For more on **creating a thermostable tuberculosis vaccine** see *Sci Rep* 2019; **9:** 11409. https://doi.org/10.1038/s41598-019-47657-9

For more on the **antibacterial properties of coagulation factors** see *Cell Res* 2019; published online Aug 9. https://doi.org/10.1038/s41422-019-0202-3

For more on the **structure of Lassa virus antibodies** see *Cell* 2019; **178:** 1004–15. https://doi.org/10.1016/j.cell.2019.07.020

For more on **leishmania virulence** see *PLoS Pathog* 2019; published online July 29. https://doi.org/10.1371/journal.ppat.1007982