DISEASE WATCH | IN THE NEWS

It's all in the genes

A gene that influences our susceptibility to influenza A infection was recently reported in *Nature*. Genetic screening had previously shown that interferon-induced transmembrane 3 (*IFITM3*) restricts infection and thereby mediates resistance to influenza A virus, dengue virus and West Nile virus. Now, Kelam and colleagues find that mice lacking *Ifitm3* are more susceptible to mouse-adapted influenza A virus than wild-type mice and show signs of severe illness owing to a lack of virus restriction and consequent uncontrolled viral replication in the lungs. Consistent with this, the authors found that a significant proportion of individuals hospitalized with pandemic H1N1/09 or seasonal influenza virus infection carried a minor *IFITM3* allele that encodes a truncated protein with a reduced ability to restrict influenza A virus infection *in vitro*. These findings add to our growing appreciation of host genetics during viral infection and should help individuals to make more informed decisions about treatment and vaccination based on whether they carry the allele. ***Nature*/BBC News**

CORBIS

Don't mess with the microbiota

Disturbing the gut microbiota through the use of antibiotics could lead to the development of asthma, according to two studies. Commensal gut bacteria are known to influence the development of the immune system early in life, and their manipulation is thought to be linked to immune dysfunction, including allergies. Writing in *EMBO Reports*, Finlay and colleagues reveal a crucial link between exposure to antibiotics early in life and the development of asthma. They observed that neonatal mice treated with vancomycin had an altered microbial composition in the gut and reduced microbial diversity. Moreover, the neonatal, but not the adult, vancomycin-treated mice were more susceptible to developing experimentally induced asthma and showed enhanced disease severity.

In a related study, published in *Nature Medicine*, Artis and colleagues also report that antibiotic treatment makes mice susceptible to experimentally induced asthma. The authors investigated the molecular mechanism underlying this link and found that signals from commensal bacteria not only limit the levels of serum immunoglobulin E (IgE), which keeps the number of circulating basophils in check, but also directly regulate the development of basophils from precursors. ***EMBO Rep.*/*Nature Med.***

HIV forced out

A drug that can force HIV out of its latent state has been identified, offering new hope for the treatment and eradication of the virus. Previous work had indicated that suberoylanilide hydroxamic acid (SAHA; also known as vorinostat) — a histone deacetylase inhibitor that is used to treat certain types of cancer, mainly lymphoma — may be able to induce the expression of latent HIV in infected cells. When Margolis and colleagues tested the effects of the drug on six individuals with HIV, they found that a single dose stimulated HIV transcription in infected $CD4^+$ T cells. Moreover, they did not observe any side effects. Further work is now needed to test the effects of SAHA on a larger group of patients.

Forcing HIV out of latency should make the infected cells more visible to other cells of the immune system, leading to their elimination. In a separate study, Siliciano and colleagues investigated what happens to infected $CD4^+$ T cells after reversal of HIV latency by SAHA *in vitro*. Surprisingly, the infected cells were not killed by cytototoxic T cells from the same individual. Instead, the authors found that cytotoxic T cells have to be pre-exposed to HIV-derived antigen to kill the autologous infected $CD4^+$ T cells. **Nature News/*Immunity***

Deadly evolutionary changes

The evolutionary dynamics of *Staphylococcus aureus* infection has recently been analysed, providing important insights into the progression of disease caused by this bacterium. *S. aureus* is normally a commensal organism, being carried asymptomatically by 27% of the population, but it can also cause life-threatening disease. To gain some insight into its evolution *in vivo* and thus the events that lead to invasive disease, Wilson and colleagues compared the commensal population of methicillin-sensitive *S. aureus* (MSSA) in the nasal flora of one patient to the population that caused a blood infection in the same patient. Using high-throughput whole-genome sequencing, they were able to identify eight genetic changes in MSSA that accompany this transition from a commensal to a pathogenic lifestyle. Importantly, these changes were absent from the *S. aureus* population present in asymptomatic carriers. Half of these changes were loss-of-function mutations that gave rise to protein truncations, including one in a transcriptional regulator that is known to have a role in pathogenicity. ***Proc. Natl. Acad. Sci. USA***

Two better than one?

BRANDX

A combination of two drugs has shown promising results against *Mycobacterium tuberculosis*. With the emergence of highly resistant strains of the bacterium, such as XDR and MDR, new protocols are desperately needed to treat tuberculosis, which kills millions of people worldwide each year. Speaking at the American Chemical Society meeting, Blanchard and colleagues reported that treatment with two drugs, the broad-spectrum antibiotic meropenem and the β-lactamase inhibitor clavulanic acid, can kill *M. tuberculosis*, including drug-resistant strains. The key to this success is clavulanic acid, which blocks the action of the bacterial β-lactamase, the enzyme responsible for conferring antibiotic resistance by deactivating the administered antibiotic. These results are encouraging, but clinical trials will now be necessary to test the safety and effectiveness of this drug combination. **Science Daily**

In the News was compiled with the assistance of David Ojcius, University of California, Merced, USA. David's links to infectious disease news stories can be accessed on his Twitter page (@Ojcius).