



DISEASE WATCH | IN THE NEWS

Playing the host

An estimated 50–100 million dengue virus infections occur every year, and dengue fever is the most frequently detected arthropod-borne viral disease in humans. Little is known about the proteins (dengue virus host factors; DVHFs) in the human host and arthropod vector that are required for the propagation of dengue virus infection. Currently, few tools are available for genome-wide analysis of the *Aedes* mosquito vectors that carry dengue virus. In a recent issue of *Nature*, however, researchers led by Mariano Garcia-Blanco from Duke University in Durham, North Carolina, USA, report the results of their genome-wide RNA interference screen in the related dipteran *Drosophila melanogaster*, which they say has generated the "...first version of what will eventually be a comprehensive

list of DVHFs". The screen of a 22,632 double-stranded RNA library identified 116 candidate insect DVHFs, most of which had not previously been shown to be involved in dengue virus propagation. The authors went on to use a short interfering RNA screen to identify 42 human DVHFs, and conclude that the level of conservation between insect and human factors indicates potential new therapeutic targets. *Nature*

Optimal defence

In recent years, the treatment of chronic inflammatory conditions such as rheumatoid arthritis has been revolutionized by the availability of anti-tumour necrosis factor (anti-TNF) immunotherapeutic agents. However, one particular side effect of such treatment that

is of interest to microbiologists is the reactivation of latent tuberculosis (TB) infection. In a recent paper in *Journal of Clinical Investigation*, Bruns *et al.* looked at the effects of treating patients with rheumatoid arthritis with the anti-TNF monoclonal antibody infliximab. The authors found that infliximab treatment induced a marked decrease in the frequency of a particular perforin- and granulysin-rich CD8⁺ T cell subset, T_{EMRA} cells. T_{EMRA} cells express TNF on their surface, and were shown to bind infliximab and consequently become sensitive to the actions of complement-mediated lysis. The role of CD8⁺ T cells in the cell-mediated immune response to *Mycobacterium tuberculosis* infection has been keenly debated in recent years. Bruns *et al.* conclude from this work that "...CD8⁺ T_{EMRA} cells are required for optimal host defence against TB". *J. Clin. Invest.*

Swine flu

The major infectious disease news story this month was of course swine flu (now referred to as influenza A (H1N1)). The story began to be reported in the mainstream media towards the end of April, when WHO Director Margaret Chan issued a statement in which she drew attention to the outbreak as "a public health emergency of international concern". The outbreak has centred on Mexico, where it is thought to have started in mid-March, possibly in the town of La Gloria in Veracruz state. As of 6 May, more than 1,000 cases of influenza A (H1N1) infection had been confirmed in more than 20 countries. Also by that date, 29 deaths had been reported in Mexico and 1 death had been reported in the United States. Most infections have been in otherwise healthy individuals, and in general the symptoms have been mild. All isolates examined have been susceptible to the antivirals oseltamivir and zanamivir, but resistant to amantadines.

The situation in the last week of April remained somewhat confused, as the number of suspected cases increased rapidly and WHO raised the influenza pandemic alert level to phase 5. By the beginning of May, however, a slightly clearer picture was beginning to emerge, although many key questions remained unanswered. Initially, there was some confusion over the origins of the virus. It now seems likely that it is the product of a reassortment between swine viruses, one of which is the H3N2 triple reassortant that has been circulating in pigs in the Midwestern United States for more than 10 years and contains genes of human and avian origin. Sequence analysis also revealed that the virus does not encode a functional PB1-F2 protein, which was a known virulence determinant of the 1918 H1N1 virus and the H5N1 avian flu virus.

Internationally, containment efforts have focused on the early administration of antivirals to infected individuals and their close contacts, and non-pharmaceutical interventions, including precautionary closure of schools and colleges. As we went to press, health officials worldwide seemed to be cautiously optimistic that such control measures were working to contain the infection. Despite this, WHO was keen to stress that all national health authorities should remain vigilant and warned that the current situation may represent a 'herald wave', as the virus might return in a more virulent form in the next flu season. *CDC/WHO*



A cold sequence of events

Infection with human rhinovirus (HRV) is the major cause of the common cold, and HRV infection is also an important contributor to asthma exacerbation. As such, the costs of HRV infection in the United States are estimated at US\$60 billion per year. Surprisingly, however, little is known about the basic molecular and evolutionary characteristics of HRVs. Historically, HRVs have been classified into 99 different serotypes on the basis of their capsid proteins. Only a limited number of complete genome sequences are available but on the basis of this information, two different HRV species are recognized, HRV-A and HRV-B, although the existence of a third species, HRV-C, has recently been proposed. Now, researchers have fully sequenced each of the 99 different HRV serotypes from the HRV reference repository, along with 10 field samples, and the results were reported in a recent issue of *Science*. Sequence analysis confirmed the existence of HRV-C and hinted that there could be a fourth HRV species, HRV-D. Other highlights from the study include the fact that a number of HRV serotypes seem to have arisen through recombination events. The availability of this genomic resource should provide a major boost to rhinovirus researchers. *Science*

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 Connotea (<http://www.connotea.org>), under the username NatureRevMicrobiol.