

Networks against dengue

SUMMARY

About a third of the world's population is at risk of contracting dengue. In Vietnam, where this disease is of enormous public health importance, research by Dr Cameron Simmons is providing new insights into the relationship between the virus that causes this disease and its human host. On the back of this work, preparations are under way for the first-ever clinical trials of an antiviral treatment for dengue, due to take place in Vietnam in 2009.



Background

In a typical year, there are some 100 million cases of dengue fever around the world, notably in South-east Asia and Central and Southern America. Yet in spite of the extraordinary scale of this public health problem, there are as yet no animal models of the disease and no licensed vaccines to protect against the dengue virus, and no drugs to treat infection have ever made it to clinical trials.

In Ho Chi Minh City in Vietnam, Cameron Simmons is studying the relationship between the dengue virus and its human host. With the support of a Wellcome Trust Career Development Fellowship, Dr Simmons is supervising dozens of local students working towards their own careers as independent scientists.

Advance

Dr Simmons has developed a network of collaborations across southern Vietnam that has given him an invaluable opportunity to study the disease in thousands of people with dengue. In infants, for example, Dr Simmons and colleagues have found that low levels of maternal antibodies correlate reasonably (but not absolutely) with increased disease severity but, surprisingly, the link between viral load and disease is weak at best.

The researchers also aim to investigate associations between human genes and the occurrence of dengue shock syndrome, a life-threatening complication of the disease. "We are collecting and beginning to analyse the genetic polymorphisms [variations] of very large numbers of children with dengue shock syndrome compared to a control population," Dr Simmons says. The hope is that this information will help to identify the molecular pathways that make some Vietnamese children more susceptible than others to the disease. "If you can understand which pathways are important, then you've got a rational basis from which to develop new medicines that might improve patient outcomes from this serious disease," he says.

At the same time, Dr Simmons and The Broad Institute (USA) have been characterising the genetic variation in the dengue virus genome as part of a collective effort under the umbrella of the Genome Resources in Dengue (GRID) consortium. This international effort should help to reveal whether some virus subtypes pose a greater danger to humans than others. Ultimately, this database will be of immense value for the rational implementation of vaccines and identification of drug targets.

How it's making a difference

Dr Simmons's research on dengue virus infections has helped to support the clinical development of the first-ever antiviral treatment for dengue fever (in collaboration with the Novartis Institute for Tropical Diseases, Singapore), which has been pencilled in for clinical trials in Vietnam towards the end of 2009.

In parallel with Dr Simmons's work on dengue, the researchers in Ho Chi Minh City have also claimed success against several other infectious diseases, including H5N1 influenza. By scrutinising the immune response of those who survived this frequently fatal influenza, he and his colleagues, in collaboration with scientists in Switzerland and the USA, have identified human antibodies against H5N1, and have produced monoclonal antibodies that might one day be used (together with a cocktail of existing antiviral drugs) to save lives in Vietnam and elsewhere in the event of an H5N1 outbreak. "Not only do these antibodies neutralise the virus that was circulating in Vietnam some five years ago, they are still capable of neutralising viruses in circulation right now, he says."

In May 2008, Dr Simmons was awarded a Wellcome Trust Senior Research Fellowship in Basic Biomedical Science.

References

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www.broad.mit.edu/annotation/viral/Dengue

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WELLCOME TRUST GRANTS

Research Career Development Fellowship: 'Cellular immune responses and disease pathogenesis during dengue infection', 2004; project grant: 'Generation and characterisation of human monoclonal antibodies to highly pathogenic H5N1 viruses', 2006