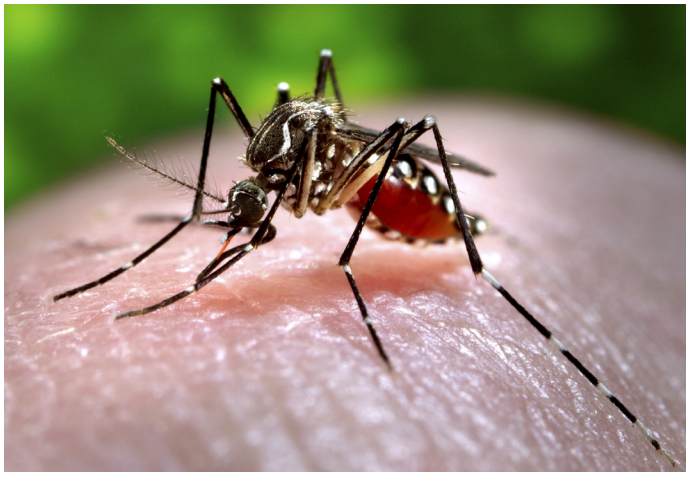
Multivalent Dengue Vaccine

Available to license: A universal Dengue vaccine to induce cellular immune responses against all dengue virus serotypes.

Dengue fever is the most rapidly spreading mosquito-borne viral disease in the world. The World Health Organisation estimates that almost half of the world's population lives in at-risk areas, with ~390 million new infections every year. The disease is caused by four dengue virus (DENV) serotypes, infection with one serotype only confers protection against re-infection with the same serotype. Multiple serotypes commonly circulate together in a particular geographical region and secondary infection with a different serotype carries the risk of developing haemorrhagic fever and shock due to antibody-dependent enhancement (ADE) where non-neutralising antibodies facilitate virus entry into host cells, leading to increased infectivity. Following infection with a secondary DENV serotype, the immune response can be skewed by the memory of the previous infection, with the titre of antibodies specific to the earlier virus being higher than for the currently infecting serotype; a phenomenon known as "antigenic sin".

A safe and effective DENV vaccine must induce strong, long-lived and equal protection against all four serotypes in order to avoid the risk of ADE or antigenic sin. Most DENV vaccines in development have been designed to induce protective antibodies against external proteins of each of the four virus serotypes and are formulated with components from each of the four serotypes.

An alternative approach has been pioneered at the University of Oxford's Jenner Institute. Researchers have developed a vaccine to induce protective T-cell immunity against all four serotypes of DENV with minimal risk of inducing ADE or antigenic sin.



Oxford Invention

The Jenner researchers have developed a DENV vaccine using non-replicating viral-vectored vaccines to induce T-cell responses against a single immunogen incorporating the most conserved non-structural DENV proteins. This vaccine has been designed to generate full protection against all DENV serotypes.

The vaccine was designed using a bioinformatics approach, to identify the most conserved and functionally critical protein sequences in all four serotypes of DENV, representative of the true global virus population. The researchers have developed a single immunogen comprising the most conserved segments of the internal NS3-NS5 genes across all four serotypes. This single, pan-serotype, universal dengue antigen has been expressed in a simian adenoviral vector and in the vector modified vaccinia Ankara, for use in a heterologous prime-boost vaccination regimen.

Cellular Immune Response against all DENV serotpes

Immunogenicity trials of the DENV vaccine in mice have shown the induction of abundant T cells against all four serotypes represented in the novel dengue antigen, and studies in macaques show vaccine safety and immunogenicity.

The Jenner DENV vaccine is being currently evaluated in a DENV challenge model, which uses several strains of the virus which have been adapted to infect mice. In this model, induction of DENV-specific cytotoxic T-cells should prevent DENV infection in the mice.

For further information please contact:
technology@innovation.ox.ac.uk
www.innovation.ox.ac.uk
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