OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference on
Vaccines & Vaccination
September 24-26, 2014 Valencia Convention Centre, Spain

A novel approach to the development of arboviral vaccines for dengue and chikungunya virus

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Arbovax employs an innovative technology (Patent No. 6, 589, 533) to develop safe and effective live-virus vaccines coupled with a low-cost system of manufacture. Arbovax created a strategy based on the straightforward concept of developing stable mutations of arboviruses that can replicate successfully in insect cells but grow poorly in mammalian cells, thus creating live, attenuated host-range mutant virus vaccines for any virus that has an insect vector and for which a cDNA clone can be produced. The first target is Dengue virus (DV), a mosquito-borne member of the Flavivirus family, which has four serologically distinct serotypes (DV1-4). Upwards of 100 million people are at risk for dengue infection each year, and with the increasing global spread of its mosquito vectors, including Aedes albopictus, the Asian tiger mosquito, this number is poised to dramatically increase. Currently no vaccine or therapeutic exists to counter DV. The use of live-virus vaccines for dengue is critical since virus-neutralizing epitopes have been found to be complexes only found in the whole, intact virus. Other types of vaccines which use denatured viral proteins or dengue virus domains taken out of the whole virus context may lead to the generation of sub- or non-neutralizing antibodies which in turn puts the patient at risk for developing dengue hemorrhagic fever upon secondary exposure. The immunogenicity and safety of three novel live, attenuated host-range DV vaccines containing deletions in the transmembrane domain of Dengue virus serotype-2 (DV2) E glycoprotein were evaluated in African green monkeys. Groups of 4 monkeys received one dose each of test vaccine candidate with no boost. Two vaccines, DV2ΔGVII and DV2G460P, generated neutralizing antibody in the range of 700- 900 PRNT50. All three vaccine strains decreased the length of viremia by at least 2 days. No safety concerns were identified. Vaccines for Chikungunya virus (CHIKV) were also developed by Arbovax using the same method tio generate host-range viral mutants. Chikungunya is an emerging mosquito-borne virus of the Alphavirus family. Infections with CHIKV can lead to severe rheumatic disease in humans. As with DV, there are no current vaccines or therapeutics available. We analyzed five host-range CHIKV vaccines in a mouse model and assessed for joint swelling, generation of neutralizing antibodies, and protection from challenge. One vaccine produced no inflammation and no detectible viremia post-challenge.

Biography

Malcolm E Thomas is President and CEO of Arbovax, a biotechnology company commercializing a unique and innovative platform technology that can be used to make vaccines against insect-borne viral diseases. Prior to Arbovax he was Vice President of Operations for StemCo Biomedical and before that, was Director of International Marketing for Bayer Biologicals and Vice President of Pacific Rim Operations for Becton Dickinson Biosciences. During his tenure with Becton Dickinson as Vice President for Asia Pacific he lived in Singapore for 5 years. He started his working life as a Research Scientist in the Biochemistry Department of the Wellcome Research Laboratories in the UK. He holds a BSc in Biochemistry (Hons) from the University of East Anglia in the UK.

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