

The *Culex pipiens quinquefasciatus* Genome Project

Background

Culex species are important vectors of human pathogens in the United States and world-wide, including the aetiologic agents of West Nile encephalitis, Eastern equine encephalitis, Venezuelan equine encephalitis, Japanese encephalitis, St. Louis encephalitis, Ross River encephalitis, Murray Valley encephalitis, Rift valley fever, and lymphatic filariases (see maps below). The most important of the *Culex* vectors are members of the *Culex pipiens* complex, a very closely related group of species (or incipient species - the taxonomy remains unclear) that originated in Africa but has spread by human activity to tropical and temperate climate zones on all continents but Antarctica. More than 100 million people are infected worldwide with the *Wuchereria bancrofti* form of lymphatic filariasis that is transmitted primarily by *Cx. pipiens* complex mosquitoes in urban and suburban settings, and approximately 43 million filariasis cases are seriously disabled (UNDP/World Bank/WHO/TDR and WHO/UNICEF "Research on Rapid Geographical Assessment of Bancroftian Filariasis" July, 1997). It has been estimated that 750 million people are exposed to filariasis every year (WHO Expert Committee on Filariasis, 1992).

The genome sequence of a member of the *Cx. pipiens* complex will greatly simplify the identification of mosquito genes required for pathogen transmission, potentially enabling the development of new strategies for combating and controlling these diseases. Furthermore, initiation of a *Cx. pipiens* complex species genome project would complement ongoing work with *Anopheles gambiae* (draft genome completed) and *Aedes aegypti* (draft genome underway) and lead to the completion of draft genomes of the three most important mosquito vectors of human pathogens. Comprehensive comparisons between representatives of these three mosquito genera will also greatly inform the evolutionary relationships among these species and perhaps lead to advances in our understanding of mosquito genes involved in important phenomena like vectorial capacity and insecticide resistance. The genome of a *Cx. pipiens* complex species will also be invaluable in helping illuminate mechanisms whereby the endosymbiotic organism *Wolbachia* (first discovered in *Cx. pipiens*) is responsible for phenomena like cytoplasmic incompatibility in mosquitoes and other insects.

The Strategy

In 2004 the *Culex* Genome Project Consortium in collaboration with the Broad Institute was awarded funding from the National Institute of Allergy and Infectious Diseases to commence Phase I of the *Culex* Genome Project. This phase consists of the construction and partial sequencing of seven normalized cDNA libraries prepared from *Culex*. Some of these libraries are prepared from mosquitoes infected with relevant human pathogens, such as West Nile Virus. A BAC library with a 12-fold coverage of the *Culex* genome has been constructed and its ends will be sequenced. In addition 20 selected BAC clones will be sequenced in their entirety.

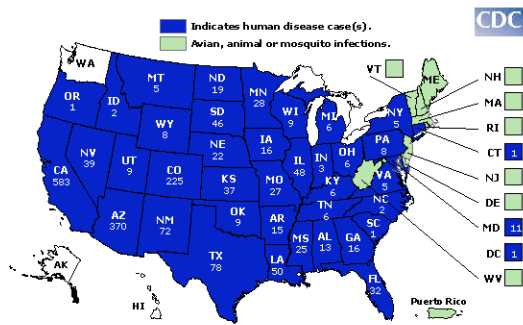
Phase II of the project will commence toward the completion of Phase I. Phase II involves the generation of a whole-genome assembly from an eight fold coverage of the genome together with an automated annotation of this assembly. The DNA sequencing and annotation will be shared between the Broad Institute and The Institute for Genome Research.

Steering Committee and Partners

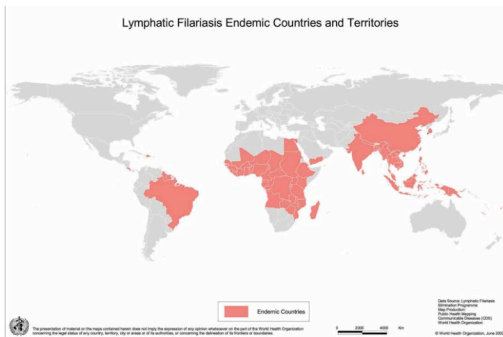
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Incidences of Human Disease vectored by *Culex* mosquitoes

The incidence of West Nile virus cases in the United States, 2004. CDC



The incidence of lymphatic filariasis in the world, CDC



The incidence of Japanese Encephalitis in Asia, CDC

