

Flavivirus Vaccination

Organized by Fondation Mérieux

“Les Pensières” Fondation Mérieux Conference Center
Veyrier du Lac - France

December 6-8, 2010

Steering Committee:

- Farshad Guirakhoo
- Franz Heinz
- Joachim Hombach
- Jacques Louis
- John Roehrig

Meeting Coordination:

- Valentina Picot

des racines pour la vie • roots for life



Background

Flaviviruses comprise a family of more than 70 single-stranded RNA viruses, the majority of which are transmitted to their hosts by vectors such as mosquitoes or ticks.

Flavivirions are spherical and composed of a lipid membrane surrounding a capsid (C) protein bound to a viral RNA (positive)-sense, which together form the nucleocapsid core. The surface proteins are the glycosylated envelope (E) and membrane (M) proteins. The M protein is a mature form of the pre-membrane (prM) protein, important for infectivity and pathogenicity. The E protein is responsible for viral attachment to cellular receptors and specific membrane fusion. The E protein is the major target for virus-neutralizing and hemagglutination-inhibiting antibodies.

A single serotype has been identified for Japanese encephalitis (JE) yellow fever (YF), and tick-borne encephalitis (TBE) virus, whereas 4 serotypes exist for dengue virus, complicating its vaccine development. The prototype flavivirus is YF virus, which was first isolated in 1927 from "Asibi", a resident of Ghana. Despite the effective vaccines available against YF, JE, and TBE since many years, the numbers of human cases have increased in the last 2 decades, mainly due to changes in climate conditions and increased travel and urbanization. These diseases have become a major public health problem in a number of countries once again. There are currently >200,000 cases and 30,000 death for YF, and it is believed that JE is responsible for more than 50,000 cases of encephalitis annually, with at least 10,000 deaths. Some 2.5 billion people – two fifths of the world's population – are now at risk for dengue, and despite 50 years of efforts, there is no dengue vaccine available on the market. WHO currently estimates that there may be 50 million dengue infections worldwide every year. In 2007 alone, there were more than 890,000 reported cases of dengue in the Americas, of which 26,000 cases were diagnosed as Dengue Hemorrhagic Fever (DHF). There are almost 100 asymptomatic infections for every reported flavivirus case, and the case fatality rates vary from 1 to 30% depending on the infecting flavivirus.

The pathogenesis of flaviviruses is not completely understood. The first steps of infection involve the interaction of the virus with the host cells. The virus transmitted to the human body by mosquito or tick bite proliferates locally and in regional lymph nodes, and enters the blood vessels causing short-lived viremia lasting 5 to 15 days. The infection may be asymptomatic or spread to visceral organs or the central nervous system, triggering innate and adaptive immune responses by the host with the outcome of recovery, neurological sequelae, or death, depending on the virus species and host factors which affect susceptibility to the infections.

There is no specific treatment for flavivirus infections and the viruses cannot be eradicated given their animal reservoir. Hence, vaccination is the most effective approach to disease control.

Currently, there are effective vaccines against TBE, JE and YF available for travellers who will spend time in endemic or epidemic regions, as well as the population residing in these areas. These vaccines have been shown to be successful in combating the disease and reducing the number of human cases around the world.

Farshad Guirakhoo, Ph.D.

The Meeting's objectives:

1. To focus on epidemiology, antigenic and molecular structure, as well as on pathogenesis, and host immune responses against flaviviruses;
2. To review the safety and effectiveness of current and future vaccines such as TBE, JE, YF and dengue.

Each speaker has been asked to specifically address one or more of these objectives in their presentation. There will be a professionally prepared report of the Conference's presentations and discussions including specific responses to the above objectives.

MONDAY, December 6th, 2010

WELCOMING SESSION		
17h30-18h30	► <i>Registration</i>	
18h30-18h45	Welcome Address	Fondation Mérieux
18h45-19h30	Keynote lecture: Perspective in development of vaccines against Flaviviruses	Thomas Monath
19h45	► Welcome Dinner	

TUESDAY, December 7th, 2010

SESSION I	Infection with Flaviviruses: Disease burden, Epidemiology ► Chaired by: John Roehrig	
08h30-08h50	Epidemiology and disease burden of infection with dengue viruses	Duane Gubler
08h50-09h10	<i>Discussion</i>	
09h10 – 09h30	Epidemiology and disease burden of infections with encephalitic flaviviruses	John Roehrig
09h30-09h50	<i>Discussion</i>	
09h50-10h20	► Coffee Break	
10h20-10h40	Epidemiology and disease burden of infection with the yellow fever virus	Alan Barrett
10h40-11h00	<i>Discussion</i>	

SESSION II Molecular structure of Flaviviruses; Cellular receptors of Flaviviruses; Flaviviruses cell entry mechanisms ►Chaired by: Franz Heinz		
11h00-11h20	Molecular and antigenic structure of flaviviruses	Franz Heinz
11h20 -11h40	<i>Discussion</i>	
11h40-12h00	Immature dengue, a veiled pathogen	Jolanda Smit
12h00 -12h20	<i>Discussion</i>	
12h20-12h40	Structural basis and mechanisms of neutralization	Kim Dowd
12h40-13h00	<i>Discussion</i>	
13h00-14h30	►Lunch	
14h30-14h50	Structural basis and mechanism of ADE	Juthathip Mongkolsapaya
14h50-15h10	<i>Discussion</i>	
SESSION III Pathogenesis and Immune Response; Mechanisms underlying in vivo protection; Neutralization and enhancement of infections ►Chaired by: Joachim Hombach		
15h10-15h30	Clinical aspects of dengue: the potential impact of vaccines	Jeremy Farrar
15h30-15h50	<i>Discussion</i>	
15h50-16h20	►Coffee Break	
16h20-16h40	Innate Immune responses to infection with flaviviruses: role in protection and pathogenesis	Michael Diamond
16h40-17h00	<i>Discussion</i>	
17h00-17h20	Cellular immunity to dengue virus immunity and pathogenesis: humanized mice as a new animal model	Anuja Mathew
17h20-17h40	<i>Discussion</i>	
17h40-18h00	Innate and adaptive immunity to vaccines in development	Bruno Guy
18h00-18h20	<i>Discussion</i>	
18h20-18h30	ANRS EP46 - NOVAA The yellow fever vaccine immunity in HIV infected patients : development of new assays for virological and immunological monitoring in HIV infected patient	François Simon
19h00	►Dinner	

WEDNESDAY, December 8, 2010

SESSION IV	Vaccination against Flaviviruses: Vaccines in development ▶ Chaired by Farshad Guirakhoo	
8h30-8h50	IMOJEV™ A new single dose recombinant vaccine for Japanese encephalitis	Farshad Guirakhoo
8h50-9h10	<i>Discussion</i>	
09h05-9h25	RepliVax vaccine for tick borne encephalitis	Harry Kleanthous
9h25-9h40	<i>Discussion</i>	
9h40-10h00	A new cell culture inactivated vaccine for Yellow Fever	Dennis W. Trent
10h00-10h15	<i>Discussion</i>	
10h15-10h45	▶ Coffee Break	
10h45-11h05	Recombinant live attenuated dengue vaccine based on YF 17D virus	Jean Lang
11h05-11h20	<i>Discussion</i>	
11h20-11h40	Live attenuated and inactivated approach for dengue vaccine	JF Toussaint TBC
11h40-11h55	<i>Discussion</i>	
11h55-12h15	Recombinant live attenuated dengue vaccine candidates based on the delta-30 mutation	Stephen Whitehead
12h15-12h30	<i>Discussion</i>	
12h30-14h00	▶ Lunch	
14h00-14h20	Recombinant live attenuated dengue vaccine based Dengue2 (DENVax)	Dan Stinchcomb
14h20-14h35	<i>Discussion</i>	
14h35-14h50	▶ Coffee Break	
14h50-15h05	Recombinant Subunit vaccine	Beth Anne Coller
15h05-15h35	<i>Discussion</i>	
15h35-15h55	Closing lecture: Implementation of Dengue Vaccination: Role of Public-Private Partnerships	Scott Halstead
15h55-16h30	<i>Discussion, Conclusions and end of meeting</i>	