celerion
Translating Science to Medicine

Preventative Vaccines for Insect-Borne Diseases

Celerion is your partner for developing vaccines for insect-borne infections. Initial vaccine studies, designed to characterize the antigenic response to the vaccine, can be done in healthy subjects in areas where the disease is not prevalent (no complication of natural immunity from prior infection with the pathogen). Celerion's experience in managing these early clinical studies at multiple sites in multiple countries, combined with our expertise in immunogenicity assessments in our state-of-the-art bioanalytical laboratories including complex sample preparation (washed PBMCs), have proven critical in the successful early studies of vaccines for Zika, Chikungunya and Lyme Borellia. Key questions to be addressed during early clinical development are:

- What characterizes the antigenic response to the vaccine?
- Does an immune correlate of protection (ICP) exist for vaccines for the disease or can one be defined during early clinical development that would set a target (e.g. desired antibody titer) for subsequent clinical studies?
- What is the optimal dosing regimen to achieve optimal protection?
- Is a booster vaccination beneficial?
- What is the time between initial vaccination and achieving an adequate immune response?
- What immunogenicity exists after vaccination other than the desired immune response against the pathogen?

Once the dose and optimal antigenicity of the vaccine has been established, preventative efficacy studies can be conducted in areas prone to the specific infection. These studies address the ultimate question: what percentage of vaccinated subjects who are living in geographical areas harboring the insect hosts are protected from infection?

Infectious diseases spread to humans through the bite of insects have plagued mankind for centuries. Plague and malaria outbreaks have altered history and social behavior. Modern communications and public health have made the world more aware of emerging infectious threats spread by insects including Zika, West Nile fever and Lyme's disease. Advances in immunology and protein therapeutics have resulted in a broad spectrum of novel therapies to stimulate the immune system to prevent and potentially treat insect-borne diseases.

The pathogenesis of the diseases (Figure 1) share some common characteristics that impacts vaccine development. Life-cycle of the pathogen involves a phase where it resides inside an insect host. Therefore, incidence range is largely defined by geographical range of the insect host. These diseases are non-seasonal except how weather effects the survival and life-cycle of the insect host.

Figure 1. Characteristics of Insect-borne Infections That Are Current Targets for Vaccine Development

Disease	Infectious Organism	Insect Vector	Geographic Range	Comments on Vaccine Development
Lyme's Disease	Borellia burgdorferi (spirochete bacteria)	Ixodes (Deer Ticks)	Forested areas of NA, Europe and Central Asia	LYMERix sold 1998-2002 in US. Incidence increasing rapidly in US. New vaccines in phase 2/3 development.
Plague	Yersinia pestis (bacteria)	Fleas on Rodents	Cases in Central Africa, Peru, Bolivia, Western US, Central Asia, China	So far successfully treated with modern antibiotics. Vaccine valuable for remote areas.
Dengue Fever	Flavivirus Dengue 1,2,3 or 4	Aedes aegypti and Aedes albopictus (mosquito)	Endemic through tropics and subtropics	One marketed vaccine in 3 countries. Other Vaccines in phase 1 and 2 development – several preclinical. Must be active against all serotypes.
Zika	Zika Virus	Aedes aegypti and Aedes albopictus (mosquito)	Wet equatorial and subtropical regions of world. Also transmitted by sex. Now pandemic	Transmission mother to fetus associated with microcephaly. A few vaccines in phase 1 and 2 development – several preclinical.
Chikungunya	Togaviridae alphavirus	Aedes aegypti and Aedes albopictus (mosquito)	Tropics and subtropics – first found in US in 2013	Vaccine candidates in phase 1 and 2 testing. Several preclinical.
Encephalitis	Japanese Encephalitis Virus	Aedes family of mosquitos	Asia and Western Pacific	IXARIO approved in 2009. 3 others on market.
	Equine Encephalitis Viruses	Also animal to human transmission of insect infected animals	Eastern, Western and Venezuelan forms -	Vaccines in phase 1 and preclinical. Interest in a pan-equine vaccine.
	West Nile Virus		2100 cases in US in 2015	1 in 150 infections is serious. Vaccine in preclinical development
Malaria	Plasmodium falciparum (parasite)	Female Anophales mosquito	Tropical and subtropical regions of the world	P.falciparum is most dangerous form of malaria parasite. No effective vaccine. Several vaccines in preclinical and phase 1 and 2 testing often involving government funding
	P. vivax' P. malariae, P.ovale			
Leishmaniasis	Leishmania dorovani (parasite)	Phlebotomine sand flies	Focal areas in subtropics, tropics and southern Europe	Cutaneous or visceral (organ) infections. Vaccines in preclinical, phase 1 and 2 development.