

Type: Oral Presentation

Final Abstract Number: 14.009

Session: Oral Presentations: Emerging Infectious Diseases & One Health

Date: Thursday, March 3, 2016

Time: 15:45-17:45

Room: G.05-06

A synthetic consensus anti-Spike protein DNA vaccine induces protective immunity against Middle East Respiratory Syndrome Coronavirus in non-human primates

K. Muthumani^{1,*}, D. Falzarano², E.L. Reuschel¹,
K. Kraynyak³, K. Ugen⁴, P. Kim⁵, J. Maslow⁵, J.J.
Kim³, N.Y. Sardesai³, G. Kobinger⁶, H.
Feldmann⁷, D. Weiner⁸

¹ Perelman School of Medicine at the University of Pennsylvania, Philadelphia, USA

² University of Saskatchewan, Saskatoon, Canada

³ Inovio Pharmaceuticals Inc, Plymouth Meeting, USA

⁴ University of South Florida Morsani College of Medicine, Tampa, USA

⁵ GeneOne Life Science, Seoul, Korea, Republic of

⁶ Special Pathogens, National Microbiology Laboratory, Winnipeg, MB, Canada

⁷ National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, USA

⁸ University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Background: First identified in 2012, Middle East respiratory syndrome (MERS) is caused by an emerging human coronavirus, which is distinct from SARS-CoV, and represents a novel member of lineage C betacoronaviruses. Since its identification, MERS-CoV has been linked to over 964 infections manifesting with severe morbidity and often mortality (i.e. approximately 400+ deaths) in the Arabian Peninsula, Europe, in the US and in Korea. Human-to-human transmission has been documented with nosocomial transmission appearing to be an important route of infection. The significant recent increase in cases of MERS in the Middle East, coupled with the lack of effective antiviral therapies or vaccines to treat or prevent this infection are significant causes for concern.

Methods & Materials: A synthetic DNA plasmid based vaccine containing a full-length consensus MERS-S protein sequence was constructed and the cellular and humoral immunogenicity of MERS-vaccine was evaluated in mice, macaques, and camels. Following immunization, NHPs were challenged with infectious MERS-CoV (EMC/2012) and monitored for signs of infection by clinical scoring and examinations. Viral load was measured by qRT-PCR and tissue sections were stained with H&E.

Results: An optimized DNA vaccine encoding the MERS spike protein induced potent cellular immunity and antigen specific neutralizing antibodies in mice, macaques and camels. Vaccinated rhesus macaque monkeys seroconverted rapidly and exhibited high levels of virus-neutralizing activity. Upon MERS viral challenge all of the monkeys in the control-vaccinated group developed characteristic disease, including pneumonia. Vaccinated macaques were protected and failed to demonstrate any clinical or radiographic signs of pneumonia.

Conclusion: A consensus DNA MERS-vaccine was able to generate both a strong T cell and neutralizing antibody response in multiple animal models, including camels, a natural host for MERS-CoV and a probable source of human infection. MERS-vaccine was

also able to protect NHPs from an infectious MERS-CoV challenge. These results demonstrate the promise of this consensus DNA MERS-vaccine as a candidate for vaccine modality against this emerging pathogen.

<http://dx.doi.org/10.1016/j.ijid.2016.02.083>

Type: Oral Presentation

Final Abstract Number: 14.011

Session: Oral Presentations: Emerging Infectious Diseases & One Health

Date: Thursday, March 3, 2016

Time: 15:45-17:45

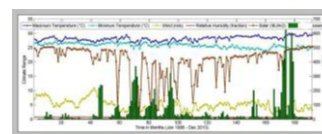
Room: G.05-06

Climate change and disease dynamics - A big data perspectiveD. Lopez¹, G. Sekaran^{2,*}

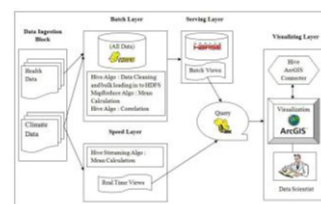
¹ VIT University, vellore, Tamil Nadu, India

² VIT University, Vellore, India

Background: The objective of this research is to predict disease scenarios based on environmental conditions change and climatic variability by combining regional climate models with mathematical models for disease transmission. Malaria and dengue fever are the most important vector borne diseases in the tropical and sub-tropical countries. Integration of large repositories of geospatial and health data derived from traditional stream as vital statistics, surveillance and hospitalization, and non-traditional sources including social media networks provide valuable insights into the spatio-temporal determinants of health and wellbeing.

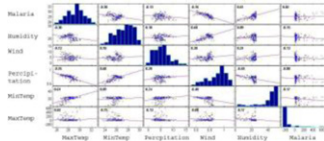


Methods & Materials: Data on infectious affected by vector borne diseases (Malaria) are collected from various private and public health centres, for the period starting January 1998 to December 2013 in Tamil Nadu, India. Daily weather data is collected from Regional Meteorological Centre, Chennai (Figure 1). The suggested approach is implemented as a Big Data system using lambda architecture and MapReduce data processing model (Figure 2). Pearson correlation coefficient is computed in the proposed framework to find the climatic factors that greatly influence the transmission of the vector borne diseases.



Results: This paper proposes a new architecture for modeling the climate change and vector borne diseases in real-time. A variety of big data analytical algorithms and data visualization approaches were used in the proposed big data based disease surveillance system to present the geographic regions at risk during this century. We found that maximum temperature is positively correlated while incidences of malaria and minimum temperature, wind,

rainfall, humidity are negatively correlated with malaria incidence (Figure 3).



Conclusion: The proposed early warning system is developed for continuous monitoring of information related to climatic change and public health as they unfold. These systems are in most instances, timely surveillance systems that collect information on epidemic prone diseases in order to trigger prompt public health interventions. Developing countries like India needs effective surveillance system and equity in health delivery programs for taking corrective actions to improve health conditions of vulnerable populations.

<http://dx.doi.org/10.1016/j.ijid.2016.02.084>

Type: Invited Presentation

Final Abstract Number: 15.001

Session: Plenary III: Malaria: Past, Present and Future

Date: Friday, March 4, 2016

Time: 09:00–09:45

Room: Hall 4 (Plenary Hall)

Malaria: Past, present and future

N. White

Mahidol-Oxford Tropical Medicine Research Unit,
Bangkok, Thailand



Abstract: Malaria has always exerted a heavy toll on mankind. At the turn of the 20th century millions died each year in India alone. No other infectious disease has had more impact on the human genome, particularly in tropical regions. In the past 150 years malaria has been first controlled and then eliminated in Europe, North America and Russia. This was achieved mainly by a dual attack on the malaria vector –the anopheline mosquito, and the malaria parasite in the human host. The successes in temperate regions led to a global eradication effort endorsed by the World Health Assembly in 1955. The campaign was armed with an effective insecticide, DDT, and an excellent new antimalarial drug, chloroquine. However by 1969 it was acknowledged that the ambitious goal of global eradication could not be achieved. Over the next three decades many of the successes of the eradication effort were reversed and malaria resurged across the tropical world. The resurgence was associated with resistance to the available insecticides and to the available antimalarial drugs. The tide has turned again over the past 15 years with substantial increases in international support for malaria control activities, widescale deployment of insecticide treated mosquito nets, and the belated introduction of highly effective artemisinin combination treatments for uncomplicated malaria and artesunate for severe malaria. Global malaria mortality and morbidity have fallen substantially. Malaria eradication is now back on the agenda. The challenges now are how to maintain the political and financial support for malaria control and elimination as case numbers fall, to reach those areas where control activities are still weak, to address seriously control of *P. vivax*, and to overcome two looming familiar threats; insecticide and drug resistance. Resistance to pyrethroids is increasing and resistance to artemisinin in *P. falciparum* has emerged in South-East

Asia, and now extends to the border of India. Artemisinin resistance has not been contained, and combination partner drug resistance has predictably followed. Spread of resistance to Africa would be disastrous. A moderately effective vaccine has been developed and new drugs are in the pipeline, but they will not generally available for years. The future is uncertain.

<http://dx.doi.org/10.1016/j.ijid.2016.02.085>

Type: Invited Presentation

Final Abstract Number: 16.001

Session: Infectious Encephalitis: Advances and Unknown

Date: Friday, March 4, 2016

Time: 10:14–12:15

Room: Hall 1

Flavivirus encephalitis and other neurological syndromes (Japanese encephalitis, WNV, Tick borne encephalitis, Dengue, Zika virus)



T. Solomon

University of Liverpool, Liverpool, United Kingdom

Abstract: Flaviviruses are some of the most important causes of encephalitis, and other neurological syndromes globally, and have an ability to spread to new areas causing large outbreaks.

Some are zoonotic, transmitted from animals to humans via mosquitoes (e.g. Japanese encephalitis virus – JEV, and West Nile virus – WNV) or ticks, (Tick-borne encephalitis virus – TBEV). For other flaviviruses humans are the natural hosts; these include dengue virus (DENV), and Zika virus (ZIKV).

The clinical epidemiology of neurological disease caused by flaviviruses varies. JEV is numerically the most important cause of encephalitis with up to 70,000 cases annually across Asia. Almost all those living in rural Asia become infected during childhood, but only a small proportion develops neurological disease. Clinical features include a non-specific febrile illness, aseptic meningitis, febrile seizures, encephalitis, with Parkinsonian movement disorders, and myelitis, causing a poliomyelitis-like flaccid paralysis. There is no specific treatment, but good supportive care is essential. Recognition and control of JE has been improved in recent years through better surveillance, improved diagnostics, on disability and disease burden and greater use of vaccines.

Being a mosquito-borne zoonotic Flavivirus, WNV is broadly similar to JEV. Its arrival and spread across the Americas in the last 15 years has taught us a great deal about the emergence of such viruses among populations of animals and humans that have not been exposed previously: disease tends to be seen in the elderly and sick.

TBEV is seen in cooler parts of Asia and Europe where ticks predominate. Humans tend to become exposed to infected ticks in wooded areas through tourism or work. The disease is well controlled in countries with strong vaccination programmes.

For dengue and Zika virus humans are the natural hosts, and so most patients present with a febrile syndrome, which may include a rash. However the neurological manifestations of dengue, including encephalitis, have been recognised increasingly over the last twenty years. The neurological associations of Zika virus infection are beginning to be recognised with the ongoing large outbreaks in South America.

<http://dx.doi.org/10.1016/j.ijid.2016.02.086>