A Zika vaccine – the case strengthens

LONDON, UK----7th September 2016----ExpertREACT. The promise of significant funds from the Obama Zika emergency measure should spur vaccine development in the wake of tougher new recommendations to prevent sexual transmission. Biotech/Academic DNA approaches currently lead the way.

The Zika virus, which was designated a global emergency by the WHO back in February 2016 continues its march forward. As of the latest WHO situation report (1st September 2016) 72 countries have now reported evidence of mosquito-borne Zika transmission since 2007 **(1).** The vast majority of infected countries are within the Americas but with Singapore being added in the last weeks the virus now becomes further entrenched in South East Asia adding another populous continent to its global footprint. Indonesia, Thailand, Bangladesh and Maldives had previously been categorized but not within WHO Category 1 "Countries with a first reported outbreak from 2015 onwards."

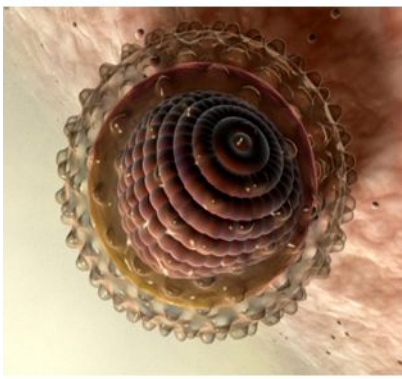
As well as mosquito-borne transmission, since February 2016, 11 countries have also reported evidence of person-to-person transmission which is of major concern for countries with little or no mosquito vector. Moreover, all nasty characteristics of this viral infection such as birth defects, CNS malformations, pregnancy losses, GBS and other syndromes continue to accumulate in case number as the year draws into its last quarter. Because most countries do not report the actual numbers of Zika infections, experts state it is still not possible to comment on the exact global trend of the Zika outbreak. Surprisingly, the global risk assessment of this latest pandemic has not changed.

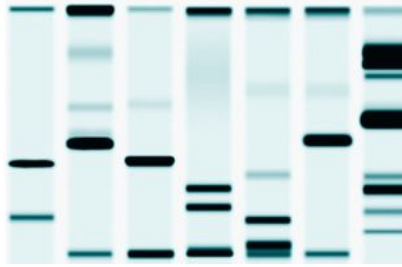
Currently there are no licensed countermeasures for Zika infection and disease. This includes vaccines, therapies or preventive drugs. The WHO guidance (updated February 2016) urges pregnant women to **consider avoiding travel** to areas reporting local Zika virus transmission and to discuss travel plans with their doctors. The US CDC has issued guidelines for special populations visiting friends and families in areas with Chikungunya, Dengue or Zika highlighting the collective importance of the *flavivirus* threat **(2).** Insect repellents registered with the Environmental Protection Agency (EPA) such as DEET, picaridin, IR3535, oil of lemon eucalyptus (OLE), or para-menthane-diol are recommended also for pregnant women.

Particular emphasis is now being placed on practicing safe sex for Zika prevention with the surprisingly stringent CDC recommendation that **all people** who live or have traveled to an area with Zika "should consider condoms to protect their sex partners". Recently (September 6th 2016) the WHO expanded its Zika sexual transmission advice for asymptomatic males **(3)** as researchers have reported evidence that the Zika virus can persist for as long as six months in semen. Previously the safe sex recommendations were for six weeks. *"This is the same length of time as is recommended for symptomatic males. This recommendation now also applies to females, whether or not they have had symptoms. The 6-month duration of safer sexual practice upon return has not changed."*

In terms of specific countermeasures recent weeks have seen a number of significant announcements at the governmental level. In the US, the US Department of Health and Human Services' Office of the Assistant Secretary for Preparedness and Response (ASPR) is funding the accelerated development of a Zika vaccine through 1 of its Centers for Innovation in Advanced Development and Manufacturing (CIADMs) **(4)** The CIADMs (similar to pandemic influenza, Ebola and anthrax measures) will be led by Emergent Biosolutions. Emergent will progress an investigational new drug request to FDA to begin clinical studies using a technology similar to that within dengue vaccines. *"Over the next 30 months, BARDA will provide more than $17.9 million to Emergent with the potential for additional work for a total of approximately $21.9 million. At any stage in development, BARDA could transfer the technology to other vaccine manufacturers to utilize the technology for to produce and market the Zika vaccine."*

Another BARDA/HHS announcement led to Japanese company, Takeda's vaccine business unit being selected to develop a vaccine to support the Zika response in the US and affected regions around the world **(5).** Initial funding from BARDA is for $19.8 million to cover the vaccine development through Phase 1, with potential funding of up to $312 million if ASPR/BARDA exercises all options to take the vaccine through Phase 3 trials and filing of the Biologics License Application (BLA) in the US.





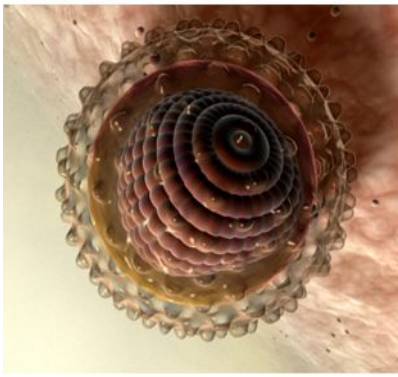
CONTINUED…..

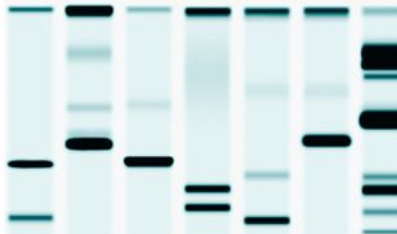
Considering Takeda's relatively new vaccine business has not yet progressed a vaccine to ex-Japanese markets, the announcement is a great boost to the unit no doubt leveraging from development capabilities built from its dengue and norovirus programs which in turn were acquired from Inviragen and Ligocyte acquisitions respectively. Takeda plans to develop an inactivated, adjuvanted whole Zika virus vaccine which is more similar to an influenza-like vaccine approach. Other major vaccine companies such as Sanofi (in partner with WRAIR), GSK (NIH), Pfizer, Johnson and Johnson have announced Zika efforts. Political pressure is now higher than ever with President Obama seeking to pass a Zika funding bill ($1.9 bn) albeit with resistance from congress.

In addition to the above announcements which focus on preclinical candidates, as of September 7th 2016 we observe that DNA-based Zika candidates are already recruiting for Phase I studies **(6).** US NIAID are developing two ZIKV vaccine candidates: a DNA-based vaccine (based on technology employed for NIAID's West Nile virus vaccine) and a live vaccine that uses a similar approach to Dengue virus vaccines. The DNA based vaccine, VRC-ZKADNA085-00-VP will be administered to 120 individuals (18 – 35 yrs) as two injections over various time points. The study (NTC02840487) is estimated to complete in December 2017.

US biotech, Inovio Pharmaceuticals (partner: GeneOne Life Science Inc) which is focusing on a range of viral based pathogens is investigating ZIKA-001 a synthetic DNA vaccine (GLS-5700) which encodes for the pre-membrane, membrane and envelope regions of Zika virus. The company has initiated a Phase I study (NCT02809443) Open-label, dose-ranging study to evaluate the safety, tolerability, and immunogenicity of GLS-5700 administered ID followed by electroporation in dengue virus-naïve adults. The study is estimated to complete in May 2018. Inovio have also launched another Phase I trial in Puerto Rico (NCT02809443).

Looking forward (and back) US government funding (should it be fully approved and available) will increase momentum in the development of a Zika vaccine. Similar funding gave us a suitable armamentium against pandemic influenza and bioterrorism threats. These are case studies we shouldn't ignore. With experts now concerned about the longer term health impact of Zika and infection in younger children, "Zika: worse than Thalidomide" there is more reason than ever to develop a vaccine **(7).**





References and Notes:

1) WHO Situation Report. Zika Virus Microcephaly. 1st September 2016. Available at: http://www.who.int/emergencies/zika-virus/situation-report/1-september-2016/en/. Accessed September 2016

2) US Centers For Disease Control and Prevention. Guidelines for Travelers Visiting Friends and Family in Areas with Chikungunya, Dengue, or Zika. Available at: http://wwwnc.cdc.gov/travel/page/travelers-vfr-chikungunya-dengue-zika Accessed September 2016

3) Prevention of sexual transmission of Zika virus. Interim guidance update, 6th September 2016. Available at: http://www.who.int/csr/resources/publications/zika/sexual-transmission-prevention/en/. Accessed September 2016

4) HHS calls on center for innovation to accelerate Zika vaccine development. June 27th 2016. Available at: http://www.hhs.gov/about/news/2016/06/27/hhs-calls-center-innovation-accelerate-zika-vaccine-development.html. Accessed September 2016.

5) Takeda to develop Zika Vaccine with up to $312 million in funding from US Government. September 2nd 2016. Available at: https://www.takeda.com/news/2016/20160902_7524.html Accessed September 2016.

6) Clinicaltrials.gov

7) Lyon J. Zika: worse than Thalidomide? *JAMA*. Published online August 24, 2016. doi:10.1001/jama.2016.11054

A printable version of this article can be purchased upon request.

http://www.vaczine-analytics.com/products-expertreactPRINT.asp