Revista Electrónica de Biomedicina
Electronic Journal of Biomedicine

ISSN: 1697-090X

APPLICATION OF RESONANT RECOGNITION MODEL ANALYSIS TO ZIKA VIRUS ENVELOPE PROTEIN.

Prof. José Luis Hernández Cáceres, PhD.

**Facultad De Ciencias Médicas "Diez de Octubre".
Universidad de Ciencias Médicas de La Habana.
La Habana. Cuba.**

Email: cacerjlh @ infomed.sld.cu

Rev Electron Biomed / Electron J Biomed 2015;3:15-20.

Comentario del revisor Prof. José María Eiros Bouza, PhD, MD. Catedrático de Microbiología. Facultad de Medicina. Universidad de Valladolid.

Comentario del revisor Prof. Sandro Bustamante. M.Sc. Programa de Farmacología Molecular y Clínica. ICBM - Facultad de Medicina Universidad de Chile. Santiago de Chile. Chile.

RESUMEN: APLICACIÓN DEL MODELO DE RECONOCIMIENTO RESONANTE AL ANÁLISIS DE LAS PROTEÍNAS DE LA CUBIERTA (E) DEL VIRUS DEL ZIKA

Se aplicó el Método de Reconocimiento Resonante a un grupo de secuencias de aminoácidos de siete proteínas de la capa externa del virus del Zika.

Se identificó un pico principal a la frecuencia resonante de Cosic de f=0.337. Este valor se corresponde con una frecuencia electromagnética en el espectro visible (color verde-548 nm).

Nuestros resultados sugieren la posibilidad de irradiar el cuerpo con luz monocromática como una alternativa practicable para tratar la fiebre por virus del Zika, sobre todo para evitar el desarrollo de microcefalia fetal asociada a la infección en pacientes embarazadas.

PALABRAS CLAVE: Modelo de Reconocimiento Resonante, Virus del Zika, Proteína, Frecuencia Electromagnética, Infección.

SUMMARY

Resonant Recognition Model Analysis was applied to a group of seven envelope protein sequences of Zika virus. One main peak was identified at Cosic´s Resonant frequency of f=0.337. This corresponds to an actual electromagnetic frequency in the visible spectrum (green color-548 nm).

Our results point to the plausibility of whole body irradiation with monochromatic light as a low cost and effective means for treating Zika Fever especially for avoiding fetal microcephaly development among pregnant patients.

Key words: Resonant Recognition Model, Zika Virus, Protein, Electromagnetic Frequency, Infection.

INTRODUCTION

On February 1st, 2016, Zika virus (ZIKV) was declared a Public Health Emergency of International Concern[1]. The figures of Zika fever (ZF) cases are up to 7 digits globally[2-4], and the hypothesis of association of ZIKV with microcephaly as well as Guillain-Barre and ophthalmic anomalies is receiving mounting support[5].

A vaccine for ZIKV is not expected before 2019, and currently available antivirals are ineffective. There is concern regarding the efficacy of a ZIKV vaccine for curbing a ZF pandemic. This justifies the search for alternative ways for ZIKV combat. As stated by Malone et al[6]:"In the absence of currently available vaccines, the likely long timeline for vaccine development, and the open questions about the basic pathogenesis of Zika virus infection, parallel development of other prophylactics and therapeutics must be explored."

The idea of applying ideas and concepts from the Resonant Recognition Model (RRM) for infectious diseases control has been proposed for treating Ebola Virus Disease[7] as well as for malaria[8-9]. The proposed intervention is to irradiate the host (or the vector) with low power monochromatic radiation at a specific wavelength in the range from ultraviolet to terahertz, depending on the specific process/interaction. Experimental evidence supporting RRM as a universal mechanism for protein-to-protein interaction is ample[10-12]; however the idea of using low-power light for infection treatment has not been tested experimentally yet.

The existence of a mouse model for ZIKV[13], as well as the possibility to apply affordable radiation sources (e.g. LED´s7) supports the possibility to test the validity of the hypothesis as well as the plausibility of the proposed procedure.

The main idea of the RRM is that proteins do recognize each other as well as their substrates/receptors via exchanging electromagnetic radiation[8-11]. This process follows a resonance scenario, and the exchanged energies are in the range of 10-20-10-18 J (0.1-10 eV)[14].

A key aspect of the RRM approach is to predictthe resonant frequencies. The procedure has been introduced by Irena Cosic[8-11]. For it, one or various proteins that are determinative for fulfilling a given function are analyzed. We hypothesize that through RRM analysis an alternative procedure for ZF treatment can be proposed. Here we are analyzed the envelope (E) 251-AA protein that plays a main role in the antigenic response as well as in the recognition of the host cell. Our results suggest that irradiation with low power monochromatic light (548nm) could be a useful choice for ZF treatment.

METHODS

Resonant Recognition Model.

The following seven amino acid (AA) sequences for ZIKV (strain Mr 766) envelope (E) proteins were

downloaded from UniProt database:

W8QFD5 - W8QFD5_ZIKV
W8R1N8 - W8R1N8_ZIKV
W8Q6P9 - W8Q6P9_ZIKV
W8Q6P1 - W8Q6P1_ZIKV
W8QFC5 - W8QFC5_ZIKV
W8QIQ1 - W8QIQ1_ZIKV
W8QIP7 - W8QIP7_ZIKV

Each sequence contained 251 AA. Mutations were found in 12 different positions (8%).

The primary amino acid sequences were transformed into a numerical series following the Resonant Recognition Model (RRM) methodology8-11. For it, to each of the 20 amino acids in the entire sequence an electron-ion interaction potential (EIIP) value was assigned (Table 1).

Amino Acid	EIIP
S	0.0829
T	0.0946
Q	0.0761
Y	0.0516
G	0.005
A	0.0373
V	0.0057
L	0.0000
I	0.0000
C	0.0829
M	0.0823
P	0.0198
F	0.0946
W	0.0548
K	0.0371
D	0.1263
E	0.0058
R	0.0959
H	0.0242
N	0.0036

Table 1. EIIP values for each amino acid[10].
This value represents the average energy state of all of the valence electron associatedwith that amino acid.

The obtained numerical series was treated as a time series. Power spectrum was estimated for each sequence using a SciLab program based on Fourier analysis. For finding the consensus spectrum, all the six cross spectral vectors were submitted to scalar cross multiplication. The obtained product is considered as the consensus spectrum.

The RRM frequency was converted to a true electromagnetic frequency by determining the appropriatewavelength using the empirical function proposed by Cosic[10]: $fRRM = 201/\lambda$

RESULTS AND DISCUSSION.

RRM analysis revealed a major peak at fRRM=0.367. This peak could be regarded as the main candidate for further studies. This frequency corresponds to wavelength values of 548 nm (green color of visible light respectively).

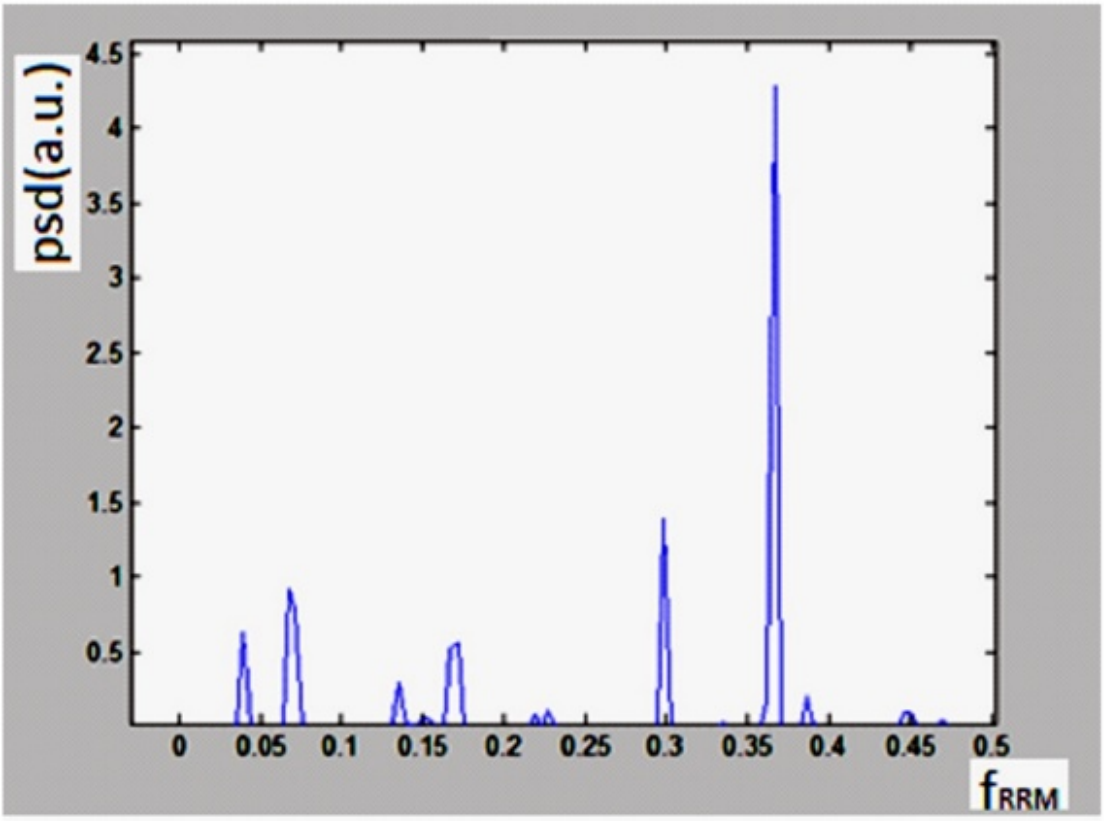

Figure 1. Consensus spectrum for the six ZIKV Envelope AA sequences studied.
Note the main peak at the RRM frequency of fRRM=0.367

So far, this seems to be the first attempt to apply RRM to the study of Zika envelope proteins. This structural protein was picked for this study given its key role in viral invasion. The envelope plays a major role in the conformation of the outer part of the virus. The outer part acts an antigen for antigen-antibody reactions, as well as in the interaction with the host membrane receptors during the entry of the virion into a human cell. Hence, countering the function of the envelope could be among the most effective ways of fighting ZIKV virulence.

Specifically, we are suggesting irradiating the patient with light at this wavelength. According to the RRM, exchange of photons between envelope proteins and host membrane receptors are required for local recognition between the main actors of the viral invasion. The presence of light coming from an external source should disrupt the recognition, and thus counter virion entrance into the cell. Given that wavelength would be expected between 500 nm and 700 nm (on the basis of the results presented here), a plausible intervention would be a whole body irradiation to patients. Considering the risk of microcephaly in newborns, the possibility to apply this treatment to pregnant patients should be especially considered.

The feasibility of this procedure is supported by the fact that exposure of the human skull to blue (465 nm) LEDs with a luminous flux density of about 10 $W \cdot m^{-2}$ elicits discernable changesthroughout the brain as inferred by fMRI activity[15].The availability of mouse model for ZIKV could provide a means for testing the plausibility of the proposed intervention. Following suggestion by Murugan et al, the application of monochromatic or narrow band, LED-generated wavelengths might attenuate the adverse activities associatedto ZIKV.The procedure would be non-invasive, relatively inexpensive, and if successful would support the alternativemodel that molecular reactions can be simulated or virtually controlled by the equivalent electromagnetic energy.

One of the most concern-sensitive issues of ZF is its association with microcephalia in children born from pregnant mothers with ZF. Exposing the mother´s womb to monochromatic light could be a practical outcome from the present study. As reported, LED-generated photons at wavelengths between 630 and 800 (nm) can travel 23 cm through the surface tissue and muscle between input and exit at a photo-detector[16]. This distance (23 cm) is compatible with the size of a pregnant uterus and thus can provide support for the technical feasibility of the proposed approach. Given the availability of animal models for ZF13, pre-clinical studies might be carried out at a relatively low cost.

CONCLUSIONS:

The application of RRM analysis to the envelope protein of ZIKV allowed identifying a candidate resonant frequency at fRRM=0.367; this corresponds to visible light at 548 nm.

These results suggest that whole body irradiation with low power monochromatic sources could be a practical solution, especially for avoiding fetal microcephaly development from pregnant patients.

Testing the plausibility of the proposed method is possible using a mouse model for the disease.

REFERENCES

1.- Heymann DL, Hodgson A, Sall AA, Freedman DO, Staples JE, Althabe F, et al (2016). Zika virus and microcephaly: why is this situation a PHEIC? Lancet. 2016.

2.- Jin J. Zika Virus Disease(2016). JAMA. 315:2482-2486.

3.- Aggarwal R, Aggarwal H, Basu M, Chugh P (2016). Zika virus disease. Int J Community Med Public Health; 3: 1352-1354.

4.- Fauci AS, Morens DM (2016). Zika Virus in the Americas - Yet Another Arbovirus Threat. N Engl J Med; 374:601-660.

5.- European Centre for Disease Prevention and Control. Rapid risk assessment. Zika virus epidemic in the Americas: potential association with microcephaly and Gullian -Barre` syndrome. Stockholm, Sweden: European centre for disease prevention and control;2015.

6.- Malone RW, Homan J, Callahan MV, Glasspool-Malone J, Damodaran L, Schneider ADB, et al. (2016) Zika Virus: Medical Countermeasure Development Challenges. PLoS Negl Trop Dis 10(3): e0004530.

7.- Murugan NJ, Karbowski LM,Persinger MA. (2015) Cosic's Resonance Recognition Model for Protein Sequences and Photon Emission Differentiates Lethal and Non-Lethal Ebola Strains: Implications for Treatment. Open J Biophys, 5: 35-43.

8.- Hernandez Caceres JL,Cosic D, CosicI (2015): Application of the Resonant Recognition Model to the Study of Plasmodium Proteins Involved in Malaria Infection. MD Medical Data; 7: 007-014

9.- Cosic I, Hernández Caceres JL, Cosic D (2015): Possibility To Interfere With Malaria Parasite Activity Using Specific Electromagnetic Frequencies. Nonlinear Biomedical Physics; 3(11).

10.- Cosic, I. (1994) Macromolecular Bioactivity: Is It Resonant Interaction Between Macromolecules? IEEE Transactions of Biomedical Engineering, 41, 1101-1114.

11.- Hernández Caceres JL, Cosic I,Cosic D. (2014). Retroviral Proteases Viewed Through The Resonant Recognition Model. Medical Review, 6(2), 117-123.

12.- Dotta BT, Murugan NJ, Karbowski LM, Lafrenie RM, Persinger MA (2014). Shifting the Wavelengths of Ultraweak Photon Emissions from Dying Melanoma Cells: Their Chemical Enhancement and Blocking Are Predicted by Cosic's Theory of Resonant Recognition Model for Macromolecules. Naturwissenschaften, 101, 87-94.

13.- Rossi SL,Tesh RB, Azar SA, Muruato AE,Hanley KA,Auguste AJ, Langsjoen RM, Paessler S, Vasilakis N,Weaver SC (2016). Characterization of a Novel Murine Model to Study Zika Virus. Am J Trop Med Hyg.94:1362-1369

14.- Persinger M.A. (2010).10?20 Joules as a Neuromolecular Quantum in Medicinal Chemistry: An Alternative Approach to Myriad Molecular Pathways. Current Medicinal Chemistry, 17: 3094-3098.

15.- Starck T, Nisslia J, Aunio A, Abou-Elseoud A, Remes J, Nikkinen J, Timonen M, Takala T,

Tervonen O,Kiviniemi, V. (2012) Stimulating brain tissue with bright light alters functional connectivity in brain at resting state. World Journal of Neuroscience, 2: 81-90.

16.- Whelan HT., Buchmann EV., Dhokalia A., Kane M P, Whelan NT, Wong-Riley MT, Eells JI, Gould LJ, Hammamieh R, Jett, M. (2003). Effect of NASA light-emitting diode irradiation on molecular changes for wound healing in diabetic mice. Journal of clinical laser medicine and surgery, 21: 67-74.

CORRESPONDENCE:
Prof. José Luis Hernández Cáceres, PhD.
Facultad De Ciencias Médicas "Diez de Octubre".
Universidad de Ciencias Médicas de La Habana.
Josefina n°.112 e/ Revolución y Gelabert.
La Habana
CP 10500. CUBA
Email: cacerjlh @ infomed.sld.cu

Comentario del revisor Prof. José María Eiros Bouza, PhD, MD. Catedrático de Microbiología. Facultad de Medicina. Universidad de Valladolid.

El modelo de reconocimiento resonante que propone el Dr. Hernández Cáceres ha sido modelizado ya para *Plasmodium* por su propio grupo de la Universidad "Diez de Octubre" de La Habana. Como cualquier contribución debiera ser probado en algún modelo plausible.

Su planteamiento para minimizar la microcefalia en el contexto de la infección por Zika resulta inédito hasta el momento presente. Ya conocíamos su aplicación en el campo de algunos enzimas víricos como las proteasas de los retrovirus. Desde nuestra Revista su difusión permitirá que otros investigadores planteen cuestiones o matices a su propuesta.

Comentario del revisor Prof. Sandro Bustamante. M.Sc. Programa de Farmacología Molecular y Clínica. ICBM - Facultad de Medicina Universidad de Chile. Santiago de Chile. Chile.

El artículo Application of Resonant Recognition Model Analysis to Zika Virus Envelope Protein del Profesor José Luis Hernández Cáceres, propone un análisis teórico respecto de la posibilidad de utilizar energía electromagnética en el rango de la luz visible como una herramienta potencialmente terapéutica contra la infección por el virus Zika.

El virus Zika es particularmente preocupante por relacionarse con el desarrollo de anomalías en el desarrollo como la microencefalia. Este interesante y novedoso análisis a través del modelo de reconocimiento resonante, sugiere que potencialmente se podría intervenir con la sola aplicación de luz a la longitud de onda y potencia adecuadas, sin reacciones adversas para la madre y el feto. Es un aporte a la discusión científica.
