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Tropical Medicine & Surgery

Short Communication

A Short Communication on Detection of the Dengue Virus Using Gold Nanoparticles

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DESCRIPTION

Recently, our group published a paper describing the detection of the dengue virus using nanoparticles conjugated to antibodies. The article presents itself in a useful, interesting and comprehensive way as a potential diagnostic tool for patients. In this brief commentary, we extend our contributions, focusing on the hidden challenges and proposing solutions to some of your problems encountered, in addition to highlighting all the efficiency of this new methodology. According to the World Health Organization (WHO), more than 1 billion people in the world are affected by a set of diseases called neglected, which mainly affect poor populations living in tropical and subtropical developing countries [1]. Among these diseases, we have dengue [2]. Dengue is an infectious viral disease that has four serotypes (DENV 1-4). The transmission of the virus occurs through the bite of female mosquitoes of the genus Aedes, mainly *A. aegypti*. This mosquito is the same vector as Chikungunya, Yellow Fever and Zika virus. In Brazil, dengue is endemic throughout the national territory, with 247,393 cases notified in 2018, 1,544,987 in 2019 and 987,173 in 2020 [3]. We are the fifth largest country in the world in territorial extension, with many regions of native forest, where access occurs mainly by boats, causing a greater difficulty for an effective and simple diagnosis for dengue. The disease presents the following symptoms such as high fever, muscle and joint pain, headache, skin blemishes, pain in the back of the eye, characteristic rash, nausea, vomiting and in some cases, it can occur an evolution of the disease starting a more serious condition, called hemorrhagic dengue. Diagnosing dengue fever can be difficult because its signs and symptoms can be easily confused with those of other diseases such as Chikungunya, Zika virus, Malaria and Typhoid fever, which can result in misdiagnosis for the patient [2,3].

Dengue diagnosis is usually performed by bioassays, such as growing the virus in a cell culture from a sample taken from the patient, detecting virus-specific antibodies in the blood, or detecting virus antigens. However, these methods are too complex, time-consuming, lacking the necessary sensitivity and specificity or too expensive to be widely deployed in distant regions. It is necessary to develop a new methodology for the rapid, simple and effective diagnosis of this disease, to provide adequate treatment to patients. Therefore, our group has invested in the development of a fast and effective methodology, using nanotechnology as a basis. Gold nanoparticles (AuNPs) were used as a platform for building a point of care with easy application and high sensitivity. The method is relatively simple to make, using only two reagents: gold (III) chloride trihydrate 99.99% (HAuCl4) and sodium citratedehydrate 99%, which produces nanoparticles with an average diameter of 22 nm. The modification of the AuNPs surface was followed by the formation of self-organized monolayers with 11-Mercapto Undecanoid Acid (MUA), and activated with 98% N-hydroxysuccinimide solution and N-(3-dimethylaminopropyl) -N 'EthylCarbodiimide Hydrochloride (EDC-NHS) to create cross-linking links with the antibodies. Monoclonal antibodies were used in the work to promote a specific connection with the virus present in the samples. One of the points that our group intends to study in the future is the substitution of monoclonal antibodies for polyclonal ones, which can provide better connections with different regions of the virus, since they originated from different B lymphocytes, being produced in mammals or birds, in addition to the lower cost of synthesis. The non-change in color can be attributed to the size of the virus, which is 50 nm in diameter, and may not be large enough to cause changes in the resonance between the electrons in the conduction band of AuNPs (free electrons), as observed in larger virions, such as canine distemper, which has a diameter of 150 nm, previous described by our group [4]. The molecular interactions close to the AuNPs' surface, caused changes in the peak of the Localized Surface Plasma Resonance (LSPR) spectrum and were analyzed by the spectrophotometer. One of the reasons for developing this methodology was to use low-cost equipment with easy portability compared to other methodologies used in the diagnosis of dengue, such as real-time PCR.

The surface of AUNPS was characterized by transmission electron microscopy. The images obtained show an increase in

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Received: March 22, 2021; **Accepted**: April 05, 2021; **Published**: April 12, 2021

Citation: Basso CR, Castro GRD, Pedrosa VDA (2021) A Short Communication on Detection of the Dengue Virus Using Gold Nanoparticles. Trop Med Surg. 9: S1.001.

the average diameter and morphological changes, indicating other compounds. To complement the study, the surface Plasmon resonance technique was used, providing results on the adsorption and desorption kinetics on the surface of the gold sensor. This methodology detects the virus in a simple and effective way, significantly reducing the examination time and enabling the test to be conducted in remote areas with difficult access and little structure. Correct detection before the onset of symptoms brings benefits such as local epidemiological control, since the spread of the disease occurs mainly due to dispersion and lack of vector control, requiring the elimination of mosquito breeding sites. The challenge for our group would be to develop a colorimetric test, Point-of-Care (POC) that can monitor the diseases at initial stage.

This work generated a patent called "Method of Detection of Viral Disease and Diagnostic Kit", by Universidade Estadual Paulista Julio De Mesquita Filho-Brazil, under process number: BR1020180160389. This invention produces a simple and reliable diagnostic tool with higher sensitivity, in which real-time binding of the antigen to the antibody conjugate-gold nanoparticles, which allows working directly with human samples (blood, saliva, urine), and provides an alternative to PCR molecular diagnostics.

ACKNOWLEDGMENTS

The authors are grateful to Fapesp Brazil (process numbers: 2019/20573-1 and 2019/13411-5) for grants and for the financial support.

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