

Biosensor as a novel alternative approach for early diagnosis of monkeypox virus

Peyman Halvaei, MSc^a, Sajad Zandi, MSc^b, Milad Zandi, PhD^{c,*}

Dear Editor,

Monkeypox is an emerging zoonotic infection caused by a member of the Poxviridae family in the genus Orthopoxvirus. Close contact with infected humans, animals, and extinct objects may transmit the virus to humans. This infection takes about 7-14 days and causes fever, swelling in lymph nodes, headache, exhaustion, widespread physical pain, and skin lesions (rashes). Due to some difficulties in the clinical field to discriminate against monkeypox infection, laboratory confirmation of infection is provided by using nucleic acid amplification testing such as realtime or conventional PCR, as well as serological tests such as the enzyme-linked immunosorbent assay. Whether the accuracy and speed of these assessments may not light the current petition, the nature-based complexity of this emerging virus could demand scientists to develop the most highly sensitive, selective, and reliable alternative platforms for enhanced control or feast of the infection. Biosensor platforms have been recognized as an auspicious diagnostic tool for the accurate and rapid revealing of viruses as well as other severe diseases which may overcome the limitations associated with these current molecular and serological methods for monkeypox virus (MPXV) detection.

Monkeypox infection

Monkeypox is a kind of emerging zoonotic disease whose source and the natural cycle of the virus in nature are unknown, but there is evidence that rodents and monkeys normally transmit this disease to humans^[1,2]. MPXV can be transmitted through direct contact (scab, body fluid, and rash), touching monkeypox-contaminated objects and surfaces, respiratory secretions, and contact with infected animals (scratching, biting, or using products from infected animals). The infected person presents some clinical symptoms such as fever, febrile prodromal stage, headache, back pain, myalgia, prostration, fatigue, and skin rashes^[1-4]. Since these symptoms appear in various viral and nonviral diseases, more specific approaches such as laboratory diagnostic methods are needed to distinguish this infection.

Present MPXV detection approaches

In monkeypox infection, the laboratory technician takes a swab from the rash and sends it to the laboratory. A real-time or PCR test is performed in the laboratory based on validated protocols to identify the MPXV pathogen and establish specific viral DNA sequences. Another approach based on the individual immune response after infection is serological tests such as enzyme-linked immunosorbent assay to measure antimonkeypox antibodies in the blood^[1,5].

Limitations associated with the present MPXV detection approaches

The accuracy of PCR-based diagnosis depends on several factors such as sample collection, strain participation, disease stage progress, false-negative and fluctuating trends, the specificity of the primers, and mostly this approach is labor-intensive, timeconsuming, and entails skilled technicians with laboratory certification. And also the diagnosis of symptomatic or asymptomatic patients with a few mount a detectable immune response could be another issue in a serology test for precise detection^[1,5,6]. Therefore, in order to overcome the limitations associated with current detection methods, the development of rapid, specific, and highly sensitive approaches is critical in numerous clinical settings.

Biosensor as new approach for detection of MPXV

Biosensor is a device comprised of a biorecognition element to bind the target, a transducer to spread the amplified signal, and a computer to analyze the data. Taking into account the transducer, they are classified into electrochemical, optical, electrical, and mass sensors. Biosensors are of increasing interest for pathogen detection and disease diagnosis due to their improved sensitivity, portability, specificity, high performance, and automated data acquisition (Fig. 1). Biosensors by applying different biorecognition elements such as an antibody, nucleic acid, gene sequence, enzymes aptamer, and antimicrobial peptides have developed to detect several types of viruses such as coronavirus disease, swine influenza (H1N1), Ebola virus, Zika virus, avian influenza (H7N9), and dengue virus^[7].

^aDepartment of Tissue Engineering and Applied Cell Sciences, School of Advanced Technologies on Medicine, ^bDepartment of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran and ^cDepartment of Electrical Engineering, Malayer University, Malayer, Iran

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

^{*}Corresponding author. Address: Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran 1416634793, Iran. Tel: +98 937 287 6578. Fax: (+98 21) 8889 6696. E-mail address: miladzandi416@gmail.com (M. Zandi).

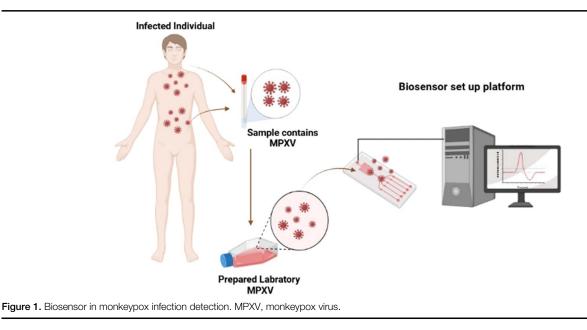
Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

International Journal of Surgery (2023) 109: 50-52

Received 2 November 2022; Accepted 8 November 2022

Published online 12 January 2023

http://dx.doi.org/10.1097/JS9.00000000000115



Data statement

The data in this correspondence article is not sensitive in nature and is accessible in the public domain. The data is therefore available and not of a confidential nature.

Several common types of biosensors for viral infection detection

Field-effect transistor-based biosensors

Comparing different methods in MPXV detection

These biosensors consist of a three-electrode structure with a drain, source, and a gate that utilize semiconductor materials such as graphene which provide fast, ultrasensitive, flexible, and low-noise detection of viral infections like severe acute respiratory syndrome coronavirus 2 in clinical samples with a Limit of Detection of 1 fg/ml^[8].

Localized surface plasmon coupled fluorescence biosensor

This fiber-optic biosensor stimulated by localized surface plasmon is easy-to-use, and simple which attracted the detection of the swine flu virus (H1N1) and coronavirus disease-2019^[9].

Surface plasmon resonance biosensor

These sensors are generated by optical illumination and have several advantages such as free-labeling, sensitivity, easy processing, low-cost pricing, and real-time monitoring capabilities that make them professional for the detection of Dengue, Ebola, and Zika in low Limit of Detections^[7].

Electrochemical biosensor

These biosensors due to their selectivity and sensitivity are the most common for the detection of H1N1, H5N1, H7N9, HBV,

Table 1

MPXV detection methods	Approaches	Advantages	Limitations
NAATs	PCR	Identifying the MPXV agent and spotting specific viral DNA sequences	Accuracy, sensitivity False-negative and fluctuating trends, the specificity of the primers
Serological tests	ELISA	Measuring antimonkeypox antibodies in the blood	Labor-intensive, time-consuming, and skilled technicians' requirements Accuracy, sensitivity Specificity, time-consuming, and diagnosis of symptomatic or asymptomatic patients with a few mounts a detectable immune response
Biosensors	FET-based biosensors	Rapid and specific, ultrasensitive, flexible and low- noise	Dependence on biomarkers, biorecognition elements, and transducer
	LSPCF biosensor	Easy to operate, and simple	Dependence on biomarkers, biorecognition elements, and transducer
	SPR biosensor	Label-free, sensitive easy-to-use, economical, and real-time monitoring capabilities	Dependence on biomarkers, biorecognition elements, and transducer
	EC biosensor	Rapid and specific and highly sensitive selective, stable, and reliable	Dependence on biomarkers, biorecognition elements, and transducer

EC, electrochemical; ELISA, enzyme-linked immunosorbent assay; FET, field-effect transistor; LSP, localized surface plasmon; LSPCF, localized surface plasmon coupled fluorescence; MPXV, monkeypox virus; NAAT, nucleic acid amplification test; SPR, surface plasmon resonance.

Zika virus, Dengue virus, and coronavirus disease-2019^[10] (Table 1).

Conclusion

Diagnostic methods used in laboratories or diagnostic centers require expensive equipment or trained personnel for operation. The development of biosensors as quick, dependable, safe, and high-sensitivity diagnostics tools can be very significant in the diagnosis of MPXV.

Ethical approval

This article does not require any human/animal subjects to acquire such approval.

Sources of funding

None.

Authors' contribution

P.H. and S.Z. wrote the manuscript. M.Z. designed, final edited, and supervised the manuscript. Next, all authors critically reviewed the manuscript for relevant intellectual content. All authors critically reviewed and approved the final version of the manuscript.

Conflicts of interest disclosure

The authors declare no conflict of interest for this article.

Research registration unique identifying number (UIN)

None.

Guarantor

Milad Zandi, PhD in medical virology, senior researcher in emerging and reemerging viruses, Department of Virology, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98 937 287 6578, E-mail: miladzandi416@gmail.com.

References

- Altindis M, Puca E, Shapo L. Diagnosis of monkeypox virus an overview. Travel Med Infect Dis 2022;50:102459.
- [2] Shafaati M, Zandi M. State-of-the-art on monkeypox virus: an emerging zoonotic disease. Infection 2022;50:1425–30.
- [3] Shafaati M, Zandi M. Monkeypox virus neurological manifestations in comparison to other orthopoxviruses. Travel Med Infect Dis 2022;49: 102414.
- [4] Shafaati M, Zandi M, Choudhary OP. Monkeypox virus crosstalk with HIV; where do we stand now? Int J Surg 2022;105:106897.
- [5] Karem KL, Reynolds M, Braden Z, et al. Characterization of acute-phase humoral immunity to monkeypox: use of immunoglobulin M enzyme-linked immunosorbent assay for detection of monkeypox infection during the 2003 North American outbreak. Clin Vaccine Immunol 2005;12:867–72.
- [6] Petersen E, Kantele A, Koopmans M, et al. Human monkeypox: epidemiologic and clinical characteristics, diagnosis, and prevention. Infect Dis Clin 2019;33:1027–43.
- [7] Teklemariam AD, Samaddar M, Alharbi MG, et al. Biosensor and molecular-based methods for the detection of human coronaviruses: a review. Mol Cell Probes 2020;54:101662.
- [8] Nehra A, Singh KP. Current trends in nanomaterial embedded field effect transistor-based biosensor. Biosens Bioelectron 2015;74:731–43.
- [9] Hsieh B-Y, Chang Y-F, Ng M-Y, *et al*. Localized surface plasmon coupled fluorescence fiber-optic biosensor with gold nanoparticles. Anal Chem 2007;79:3487–93.
- [10] Mollarasouli F, Kurbanoglu S, Ozkan SA. The role of electrochemical immunosensors in clinical analysis. Biosensors 2019;9:86.