List of attached documents in PDF

1. CV of the PI
2. PDF of CDC link for the classification of MPXV clade I and II and biosafety level and procedures. This link refers to follow guidelines from BMBL book, chapter VIII-E Viral Agents for culture work.
3. Pages 269-270, Chapter VIII-E Viral Agents on MPXV from BMBL 6th edition book that explains working with MPXV and other pox viruses in different biosafety levels.
4. Printout of CDC information on monitoring and risk assessment of MPXV disease
5. Product sheet of MPXV clade II

Curriculum Vitae

Name: **Saguna Verma, Ph.D.**

Current title & department: Professor and Graduate Co-Chair, Department of Tropical Medicine, Medical Microbiology and Pharmacology, John A. Burns School of Medicine

Current Address: 651 Ilalo Street, BSB 320-E, Honolulu, Hawaii 96813
Telephone: 808-692-1662, Fax: 808-692-1984
E-mail: saguna@hawaii.edu

Professional Training and History

Education

1982-85	B.S.	Zoology, Chemistry, Botany; Devi Ahilya University, Indore, India
1985-87	M.S.	Biochemistry; Devi Ahilya University, Indore, India
1989-93	Ph.D.	Life Sciences (Concentration: Endocrine Biochemistry); Devi Ahilya University, Indore, India

Professional Positions Held

1989-1991	Junior Research Fellow supported by Council of Scientific & Industrial Research (CSIR) Fellowship, School of Life Sciences, Indore, India
1992-1993	Senior Research Fellow supported by CSIR, School of Life Sciences, Indore, India
1994-1999	Project Scientist, Genes and Proteins Laboratory, National Institute of Immunology, New Delhi, India
1999-2002	Break in career to raise two kids
2003-2005	Junior Researcher, Retrovirology Research Laboratory, Department of Tropical Medicine and Medical Microbiology (DTMMMP), John A. Burns School of Medicine (JABSOM), University of Hawaii at Manoa (UHM), Honolulu, Hawaii
2005-2010	Assistant Researcher, DTMMMP, JABSOM, UHM, Honolulu, Hawaii
2010-2014	Assistant Professor (tenure-track), DTMMMP, JABSOM, UHM, Honolulu, Hawaii
2014-2016	Associate Professor (tenure-track), DTMMMP, JABSOM, UHM, Honolulu, Hawaii
2016-2020	Associate Professor (tenured), DTMMMP, JABSOM, UHM, Honolulu, Hawaii
2020-	Professor, DTMMMP, JABSOM, UHM, Honolulu, Hawaii
2019-	Graduate Co-Chair, DTMMMP, John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, Hawaii

Awards and Honors

1985	Merit Scholarship in B.S. by the Devi Ahilya University, Indore, India
1989-1993	University Grants Commission-Council of Science and Industrial Research Fellowship (CSIR), India
1992	Madhya Pradesh Council of Science and Technology, India YOUNG SCIENTIST, Merit certificate in 7th Young Scientist conference organized by Council of Science and Technology, India
2005	Hawaii State-Biomedical Research Infrastructure Network (BRIN) Travel Award to attend the Symposium on Kawasaki Disease, San Diego, California
2011	J. Immunology paper selected for *'In this Issue'* highlighting top papers in February issue, Journal of Immunology
2012	Invited speaker, Keystone Symposium '*Innate Immunity: Sensing the Microbes and Damage Signals*' in Keystone, Colorado

2013 Invited speaker at the `*Block symposium*' of the Annual Meeting of American Association of Immunologists
2015 Recipient of the `*Careers in Immunology Fellowship'* award by the American Association of the Immunologists
2017 Invited speaker at the '*NIH/NIAID Symposium: Molecular Mechanisms and Immune Consequences of Pathogen Reservoirs'* at Rockville, Maryland
2018 *J. Virology* 2017 paper on the Zika virus infection and host response in human testicular cells was highlighted in the Editors news story in the Jan 2018 issue of *Nature Medicine*
2019 Recipient of American Association of Immunologists Laboratory Travel grant to cover the cost of PI and a student to attend AAI annual meeting in San Diego
2019 Keynote speaker at the prestigious joint meeting of North American Testis Workshop/American Socciety of Andrology held on April 3-6, 2019 in Chicago
2020 Invited speaker at the meeting 'Viruses' at Barcelona, Spain, February 2020
2021 Invited speaker at the annual meeting of Society of Study of Reproduction, December 2021

Society Memberships

2008-present American Society of Microbiology
2009-present American Society of Virology
2013-present American Association of Immunologists

Teaching and Mentoring

Instructional Activities

Courses taught for the Department of Tropical Medicine, Medical Microbiology and Pharmacology as Instructor

2006 TRMD 699, `*Oxidative stress and human diseases*, (1 credit) – Co-Instructor of the Journal club portion of this graduate directed research course (16 hr)
2007 TRMD 699, `*Inflammation and human diseases*' (1 credit) – Co-Instructor of the Journal club portion of this graduate directed research course
2009 TRMD 690 (1 credit) – Instructor, Seminar of Tropical Medicine, Medical Microbiology and Pharmacology
TRMD 604, guest lecture on `*Inflammasomes as guardian of cytosolic sanctity in infection and immunity*'
2010 TRMD 699, Directed research mentoring (1 M.S. student, 3 credits)
TRMD 609, Advanced Medical Immunology- Co-instructor of this graduate advanced level course (3 credits). Topic covered was `*Vaccine adjuvants and innate immune responses'* (8 hr)
TRMD 604, guest lecture on `*Inflammasomes as guardian of cytosolic sanctity in infection and immunity*'
TRMD 601, `*Inflammation and human diseases*' (1 credit)
2011 TRMD 705, Infection and Immunity (3 credit hrs)- Instructor of this advance immunology course
TRMD 604, guest faculty to teach advances in innate immunity
TRMD 601, `*Inflammation and human diseases*' (1 credit)
TRMD 699, Directed research mentoring (2 M.S. students, TMMMP and MBBE, 6 credits)
2012 TRMD 604, guest faculty to teach advances in innate immunity
TRMD 699, Directed research mentoring to 2 Ph.D students (total 6 credits)

2013	TRMD 610, Infection and Immunity (3 credits)- Instructor of advance immunology course TRMD 604, guest faculty to teach advances in innate immunity TRMD 699, Directed research mentoring to 2 Ph.D students (total 8 credits)
2014	TRMD 609, Advanced Medical Immunology- Co-instructor of this graduate advanced level course (3 credits). Topic covered was `*MyD88 signaling'* (8 hr) TRMD 604, guest faculty to teach advances in innate immunity TRMD 699, Directed research mentoring to 2 Ph.D students (total 8 credits)
2015	TRMD 610, Infection and Immunity (3 credits)- Instructor of advance immunology course TRMD 601, `*Inflammation and human diseases*' (1 credit) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits)
2016	TRMD 604, guest faculty to teach advances in innate immunity TRMD 601, `*Inflammation and human diseases*' (1 credit) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits)
2017	TRMD 610, Infection and Immunity (3 credits)- Instructor of advance immunology course TRMD 601, `*Inflammation and human diseases*' (1 credit) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits)
2018	TRMD 609, Advanced Medical Immunology- Co-instructor of 3credit course Topic covered was `*cross-talk between PRRs* (10 hr) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits)
2019	TRMD 601, `*Inflammation and human diseases*' (1 credit) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits)
2020	TRMD 601, `*Inflammation and human diseases*' (1 credit) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits) TRMD 610, Infection and Immunity (3 credits)- Instructor of advance immunology course
2021	TRMD 601, `*Inflammation and human diseases*' (1 credit) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits)
2022	TRMD 601, `*Inflammation and human diseases*' (1 credit) TRMD 699, Directed research mentoring to 2 graduate students (total 8 credits) TRMD 610, Infection and Immunity (3 credits)- Instructor of advance immunology course
2023	TRMD 699, Directed research mentoring to 3 graduate students (total 10 credits) TRMD 654, Advances in HIV/AIDS (2 credits)- Instructor of advance immunology course

Course developed and approved in 2011: TRMD 610 (Infection and immunity) for PhD level students: A three credit advanced course covering special topics in (i) Recognition of pathogen (ii) Cross talk between innate and adaptive immunity (iii) Cutting edge topics in infectious disease immunity and (iv) CNS infections

Problem-based learning (PBL) lectures for JABSOM

2009-present	Biochemistry unit MD3 course for the JABSOM First year medical students on `*Lysosome function and Disorders'* Biochemistry unit MD3 course for the JABSOM First year medical students on `*Vitamins*'

Biochemistry unit MD4 course for the JABSOM First year medical students on `*Steroid metabolism'*
Biochemistry unit MD3 course for the JABSOM First year medical students on ` *RNA replication and translation'*
Biochemistry unit MD4 course for the JABSOM First year medical students on `*Vitamin D metabolism'*
Gastroenterology sub-unit MD4 course for the JABSOM First year medical students on ` *Immunopathology of Inflammatory Bowel Disease'*

Invited lectures in other departments

Fall 2007-2014	MBBE 651, `*Toll like Receptors as Sensors of Microbial Pathogens: Bringing Specificity to Innate Immunity*'
Spring 2008	MICR 690, `*Analysis of Disease Related Genes in Kawasaki Disease'*
Spring 2010	MICRO 690 on `*Can blocking the blood-brain barrier disruption improve WNV-associated neurological sequeale'*
Spring 2015	TROPMED 431 `Immunology of parasitic infection'
Spring 2013-present	CMB 622 on 'Neuroinflammation and blood-brain barrier'
Fall 2022	CMB621 on 'Introduction to Virology and antiviral immunity'

Invited talks in scientific and public meetings

Spring 2008	Invited lecture at the Pediatric CME program on `Kawasaki Disease: Blood-based markers for KD diagnosis'
Spring 2009	Invited public lecture `*Biology of West Nile virus'* for the JABSOM faculty and staff (1 hr lecture)
Spring 2010	Guest lecture RCMI forum on `*Can blocking the blood-brain barrier disruption improve WNV-associated neurological sequeale'*
Fall 2012	Invited oral presention at the Keystone Symposium 'Innate Immunity: Sensing the Microbes and Damage Signals'
Spring 2013	Invited oral prestention at the block symposium of the Annual Meeting of American Association of Immunologists
Summer 2013	Invited speaker at the special seminar series at Georgetown University, DC Invited speaker at the John Hopkins Bloomberg School of Public Health, DC
Summer 2014	Invited speaker at the seminar at the National Brain Research Institute, Manesar, India Invited speaker at the seminar at the Trsnslation Health Science Technology Institute, Gurgaon, India Invited speaker at the seminar at the School of Biotechnology, Jawaharlal Nehru University, India
Fall 2016	Visiting Professor at Jawaharlal Nehru University, India Invited speaker at the Viral Disease Biology program at the Rajiv Gandhi Center of Biotechnology, India
Fall 2017	Invited speaker at the '*NIH/NIAID Symposium: Molecular Mechanisms and Immune Consequences of Pathogen Reservoirs'* at Rockville, Maryland
Fall 2018	Invited speaker at the seminar at the Wake Forest Intitute of Regenerative Medicine, Winston-Salem, NC Invited speaker at the seminar at the United State Army Research Institute of Infectious Disease (USAMRIID), Fort Detrick, Maryland
Spring 2019	Keynote speaker at the prestigious joint meeting of North American Testis Workshop/American Soccietty of Andrology held in April 2019 in Chicago

Summer 2019	Invited speaker at the special seminar series at Center for Craniofacial Molecular Biology, University of Southern California, California
2020	Invited speaker at the meeting 'Viruses' at Barcelona, Spain, February 2020
2021	Invited speaker at the annual meeting of Society of Study of Reproduction, December 2020

Students Mentored for research:
Graduate students directly mentored as Chair: 9
Graduate students mentored as committee members: >20
Undergraduate students directly mentored: 10
International medical school students directly mentored: 2
Post-doctoral fellow mentored: 4

Research support

Hawaii Community Foundation (PI: Verma) 12/1/2023-6/30/2025
Understanding long-term effects of SARS-CoV-2 on testicular complications in hACE2 mice
Goal of this study is to define the short and long-term effects of SARS-CoV-2 infection on testicular injury and testis function in hACE2 mouse model

Hawaii Community Foundation (PI: Tallquist and Verma) 12/1/2020-6/30/2023
Modeling SARS-CoV-2 cardiac complications in hACE2 mice
Goal of this study is to define how SARS-CoV-2 infection affects cardiac fibroblasts, especially in the presence or absence of fibrosis from myocardial infarction in hACE2 mouse model

PIKO Pilot Project- Year 1 (PI: Verma) 6/1/2022-5/30/2023
Association of SARS-CoV-2 proteins with COVID-19 disease in Hawaii
Goal: To assess the levels of circulating virus antigens in COVID-19 patients and its association with disease severity

INBRE Collaborative Research Opportunity Award (MPI: Horgen and Verma) 7/1/2022- 6/30/2023
Screening for anti-SARS-CoV-2 activity of marine extracts from Hawaii
Goal: To screen natural marine extracts library from Hawaii for anti-SARS-CoV-2 properties

NIH-R21AI140248-01 (PI: Verma and Sadri-Ardekani) 5/18/2019-5/17/2022
Human testicular organoids as a model to dissect cell-type specific tropism and immune response to ZIKV
Goal is to use single-cell RNA sequencing approach to identify aniviral and cell death pathways modulated by ZIKV

Hawaii Community Foundation (PI: Verma) 5/1/2018-12/30/2022
AXL Receptor Regulates Zika Virus Entry and Immune Response in Human Testicular Cells
Goal of this study is to define mechansism of ZIKV entry in the testicular cells

FERRING COVID-19 Investigational Grant in Reproductive Medicine (PI: Sadri-Ardekani)
SARS-CoV-2 infection in human testis 3D organoid model 8/1/2020-7/31/2021
Goal is to assess if ACE2 expressing cells in the human testes can support SARS-CoV-2 infection
Role: Collaborator

NIH R21 AI129465-02 11/01/16 - 10/31/2019

Under attack: Modulation of the blood-testes barrier by Zika virus
Goal: To understand the mechanisms by which ZIKV establishes infection in the testes
Role: Principal Investigator

COBRE pilot grant 08/01/2017 - 07/30/2018
RNAseq analysis of the persistently infected tissue-reservoirs of the Zika virus
Goal: To understand tissue-specific responses to ZIKV' by using highly relevant nonhuman primate model that mimics human ZIKV disease
Role: Principal Investigator

American Association of Immunology 09/01/15-9/30/16
NLRC5 in immune control of WNV
Goal: To understand how NLRC5 affects innate-adaptive interface, specifically expression of MHC class I molecules in WNV infection
Role: Principal Investigator

Hawaii Community Foundation 07/01/14-12/30/16
Role of NLR Family protein 5 in flavivirus pathogenesis
Goal: To understand the mechansims associated with cytokine production and inflammatory response to WNV
Role: Principal Investigator

Pacific Center for Emerging Infectious Disease Research 08/01/10-07/30/15
NIH - COBRE (Yanagihara)
Project 2: Molecular mechanisms of West Nile virus neuroinvasion (PI: Verma)
The major goals of this project are to analyze matrix metalloproteinase and urokinase plasminogen activator signaling pathway in blood-brain barrier disruption after West Nile virus infection using both, in vitro and in vivo models.

NIH - R01AI089999-01 (Hoffman) 08/01/10-07/30/15
Selenoprotein K modulates calcium-dependent signaling in immune cells
The major goals of this project are to determine selenoprotein K (SelK) dependent immune responses and use WNV infection model to characterize role of SelK in disease pathogenesis.
Role: Collaborator

RTRN- RCMI 07/01/13-06/30/14
Epigenetic regulation of innate immune responses to flaviviruses
The goal of this project is to understand the role of epigenetic modulation, specifically histone deacetylases in regulating production of WNV-induced inflammatory cytokines.
Role: Principal Investigator

5 G12 RR/AI03061-21 (Shomaker/Yanagihara) 09/01/06-08/31/11
NIH/NCRR
Research Centers in Minority Institutions Program
Research Outcomes Accelerating Discoveries for Medical Applications and Practice
Activity 3 Tropical Infectious Diseases and Prevention
The proposed Tropical Infectious Diseases Detection and Prevention Core activity consisting of the Pathogen Reference and Reagent Core Facility, Molecular Pathology and Histology Core Facility and the Microarray Core Facility responds to an urgent local, regional and national need to position UHM in a leadership role to detect exotic infectious diseases that may be introduced to Hawaii and the continental United States from Asia. Our expectations are that at the end of the grant period, UHM will

be one of the premier institutions for tropical infectious diseases research and training in Asia and the Pacific.
Role: Molecular Virologist

Clinical and Translational Science Bridging Fund 09/01/09-08/30/10
NIH-RCMI (Yanagihara)
Cyclooxygenase 2 and glial cells – Role in WNVE-associated neuroinflammation
The major goal of this project is to determine the role of WNV-induced COX-2 in triggering pro-inflammatory cytokines and MMPs in the brain glial cells
Role: Principal Investigator

20050001 (Verma) 03/01/08-10/30/09
Hawaii Community Foundation
Role of Human Brain Microvascular Endothelial Cells in West Nile Virus Central Nervous System Invasion
The major goals of this project are to determine and delineate the mechanism(s) of infection and injury induced by West Nile virus to human brain microvascular endothelial cells and the trafficking of cell-free WNV into the CNS.
Role: Principal Investigator

Role: Principal Investigator
20050405 (Verma) 07/01/05-04/30/08
Hawaii Community Foundation
Oxidative Stress and its Implications in the Pathogenesis of West Nile Virus Infection
The goal of this project was to delineate the pathophysiological mechanisms underlying oxidative stress-induced disease pathogenesis.
Role: Principal Investigator

Pacific Center for Emerging Infectious Disease Research 01/01/04-06/31/05
NIH- P20 RR 018727 (Yanagihara)
Effects of Selenium deficiency on genomic mutations of RNA viruses.
The primary goal of this project was to investigate how West Nile virus may be affected by selenium deficiency within the cells in which they replicate.
Role: Principal Investigator

20050411 (Melish) 06/01/05-06/07/07
Hawaii Community Foundation
Kawasaki Disease: The Diagnosis Project- Host response
The goal of this project is to employ gene array technology to analyze specific host genes and signaling pathways involved in the pathogenesis of Kawasaki syndrome.
Role: Co-Investigator

Service activities

DTMMMP service

2010-present	Member of Department of TMMMP Graduate Student Selection Committee
2010	Served in the Selection Committee for the recruitment of `Infectious Disease Pathologist' in the TMMMP
	Served in the Selection Committee for the recruitment of `HIV Immunologist' in the TMMMP
2012	Served in the Selection Committee for the recruitment of 'Institutional Support Position # 79325' in the TMMMP
2015-present	Reviewer and Interviewer of the applicants for MHIRT funded program, DTMMMP

2016 Served in the Selection Committee for the recruitment of 'Virologist' in the TMMMP
2018-present Graduate Co-Chair, TMMMP

UH Manoa campus wide service

2013-2019 Voting member of the University of Hawaii's Institutional Animal Care and Use Committee
2015-2020 Reveiwer of the proposals for Undergraduate Research Opportunities Program (UROP) funding
2019- Member of the Honors Council that guides 60+ yr old Honors Program at the UH at Manoa

JABSOM service

2010-2013 Member of the Medical Students Selection Committee of the JABSOM, UHM (>80 hr per year)
2013-present Judge for the poster session at the JABSOM Biomedical Symposium
2014-2017 Interveiwer for the JABSOM Medical student applicants (30 hrs per year)
2015 Member of the committee for selecting speakers for 50th Anniversary celebration of the JABSOM
Served in the Selection Committee for the recruitment of `Associate Specialist' in the Dean's office
2014 Pilot grant reviewer for Hawaii Pediatric Association Research and Education Foundation, HI
2015-present Reviewer and Interveiwer for the Northern Pacific Global Health (NPGH) program Fellowship applicants
2017-18 Member of the committee for selection of the Associate Director of Research, JABSOM
2019 Member of the Medical Students Selection Committee of the JABSOM, UHM (>80 hr per year)
2021- Co-organizer of the JABSOM Annual BioMed Symposium

Public and professional services

Editorial Board

2013-present Editorial Board Member of the journal *Clinical Microbiology* published by OMICS Group Inc, NY, USA.
2019- Editorial Board Member of the journal *Scientific Reports*, Nature pulishing Group

Ad hoc Reviewer

Journals 2009-present-

Adhoc Reviewer for PNAS, Journal of Virology, Journal of General Virology, PLoS ONE, Virology, Japanese Journal of Infectious Diseases, Journal of Neuroinflammation, Journal of Genetics, Journal of Functional Foods, Mediators of Inflammation, Journal of Neurochemistry, Journal of Immunology, Microrganisms, PloS Neglected and Tropical Diseases, Journal of Virology, Plos Pathogens, Frontiers in Microbiology, AIDS Research and Human Retroviruses, Viruses, Scientific Reports and Nature Communications

Grant Reviews

2023 External reviewer of grant from French National Research Agency
2021-22 Member, NIH/CSR of **Virology B** (February 2021, June and October 2022)
2020 Member, NIH/CSR of **Clinical Neuroimmunology and Brain Tumor** (February 2020)

	Member, NIH/CSR of special emphasis panel **ZRG1-IDM-W-02** (August 2020)
2019	Member, NIH/CSR of **Topics in Virology, ZRG1 IDM-W** (November)
	Member, NIH/CSR of **Clinical Neuroimmunology and Brain Tumor** (June)
	Member, NIH/CSR of **Development and Brain Disorder** (June)
	Member, NIH/CSR of **ZRG1 IMM-R (50)** (July)
2018	Member, NIH/CSR of **Clinical Neuroimmunology and Brain Tumor** (February)
	Member, NIH/CSR of **ZRG1 BDCN-Q** (June)
	Member, NIH/CSR of **ZRG1 BDCN-M (91) S** (December)
2017	Member, NIH/CSR of **Clinical Neuroimmunology and Brain Tumor** (June)
	Member, NIH/CSR of **Clinical Neuroimmunology and Brain Tumor** (October)
	Member, NIH/CSR of **ZRG1 BDCN-Q** (November)
2016	Member, NIH/CSR of **Development and Brain Disorder** (October)
2015-16	Pilot Grant proposals for Clinical Translational Research-Infrastructure Network, USA
2014	COBRE Pilot small grant proposals
2015-	Fellowship proposals for the Northern Pacific Global Health program, USA
2015-	Research proposals for the UROP Program, UH
2014	RCMI Translational Research Networks Small Grants Pilot Program award, USA
2008-13	Hawaii Community Foundation, HI
2013	The Deutsche Forschungsgemeinschaft (German Research Foundation), Germany

Others

2008-2013	Member of the Scientific Advisory Committee of the Hawaii Community Foundation
2014-2016	President of American Society of Microbiology (Hawaii Chapter)
2019	External Doctorate Thesis Examiner, Monash University, Australia,

Publications in peer reviewed journals/Books

Book chapters

1. Kelly J and **Verma S.** Book chapter `Flaviviruses' in the book `Neuroinfections', edited by Paweł P. Liberski, Wojciech Kozubski and Michael Katz Warsaw, Poland, 2015, pp. 167-175.
2. GKaur, KWright, **S Verma**, A Haynes, JM Dufour, *The good, bad and ugly of testicular immune privilege* published in 'Molecular mechanisms in Spermatogenesis' (2021, Publisher: Springer Nature)

Original articles:

1. Giannakopoulos S, Pak J, Ward M, Bakse J, Tallquist M, and Verma S. SARS-CoV-2 infection leads to persistent testicular injury and functional impairments that resolve within a month of recovery in K18 hACE2 mice. 2024, in review *Nature Communications*.
2. Giannakopoulos S, Strange D, Jiyarom B, Abdelaal O, Bradshaw AW, Nerurkar VR, Ward M, Bakse J, Yap J, Vanapruks S, Boisvert W, Tallquist M, Sadri-Ardekani H, Clapp P, Murphy SV, **Verma S.** In vitro evidence against productive SARS-CoV-2 infection of human testicular cells: Bystander effects of infection mediate testicular injury. PLoS Pathogens 2023 May 18;19(5):e1011409.
3. Jiyarom B, Giannakopoulos S, Strange DP, Panova N, Gale M Jr, **Verma S.** RIG-I and MDA5 are modulated by bone morphogenetic protein (BMP6) and are essential for restricting Zika virus infection in human Sertoli cells. Front Microbiol 2022: 13: 1062499 doi: 10.3389/fmicb.2022.1062499
4. **Verma S,** Saksena S and Sadri-Ardekani H. ACE2 receptor in testes: Implications in COVID-19 pathogenesis. *Biology of Reproduction*, 2020 PubMed PMID 32427288

5. Strange DP, Jiyarom B, Sadri-Ardekani H, Cazares L, Kenny TA, Ward MD and **Verma S**. Paracrine IFN response limits ZIKV infection in human Sertoli cells. *Frontiers in Microbiology* 2021,12:667146. doi: 10.3389/fmicb.2021.667146
6. Strange DP, Jiyarom B, Trivedi G, Zarandi NP, Xie X, Baker C, Sadri-Ardekani H, Shi P-Y and **Verma S.** Axl promotes Zika virus entry and modulates antiviral state of human Sertoli cells. *mBio* 10:e01372-19
7. Strange DP, Siemann DS, Green R, Belcaid, M, Gale Jr. M and **Verma S**. Transcriptome analysis of primary human Sertoli cells infected with Zika virus reveals unique insights into host-pathogen cross talk. *Scientific Reports* 2018, 8:8702 doi:10.1038/s41598-018-27027 4.
8. Strange DP, Zarandi NP, Trivedi G, Atala A, Bishop CE, Sadri-Ardekani H, and **Verma S**. Human testicular organoids as a novel tool to study Zika virus pathogenesis. *Emerging Infections and Microbes* 2018, 9;7(1): 82. doi: 10.1038/s41426-018-0080-7
9. Siemann DS, Strange DP, Maharaj PM, Shi P-Y and **Verma S**. Zika virus infects human Sertoli cells and modulates the integrity of the in vitro blood-testis barrier model. *Journal of Virology* 2017, 27;91(22) doi: 10.1128/JVI.00623-17
10. Lai CY, Strange DP, Wong TAS, Lehrer AT, **Verma S**. Ebola virus glycoprotein induces an innate immune response in vivo via TLR4. Front Microbiol. 2017 Aug 17;8:1571.
11. Nelson JT, Roe K, Orillo B, Shi P-Y, **Verma S.** Combined treatment with adenosine analog inhibitor NITD008 and histone deacetylase inhibitor represents an immunotherapy strategy to block WNV replication and ameliorate associated mortality. *Antiviral Research*, 2015
12. Kumar M, Roe K, Nerurkar PV, Orillo B, Thompson KS, **Verma S,** Nerurkar VR. "Reduced immune cell infiltration and increased pro-inflammatory mediators in the brain of Type 2 diabetic mice infected with West Nile virus." *Journal of Neuroinflammation* (2014), 11(1):80.
13. Roe K, Orillo B, **Verma S**. "West Nile virus-induced cell adhesion molecules on human brain microvascular endothelial cells regulate leukocyte adhesion and modulate permeability of an *in vitro* BBB model." *PlosOne,* 2014; 9(7):e102598.
14. Roe K, Gibot S, **Verma S.** "Triggering Receptors Expressed on Myeloid Cells (TREMs): New players in anti-viral immunity?" *Frontiers in Microbiology*, 2014, 5:627
15. Kumar M, Roe K, Orillo B, Muruve DA, Nerurkar VR, Gale Jr. M and **Verma S**. Inflammasome adaptor protein apoptosis-associated speck-like protein containing CARD (ASC) is critical for the immune response and survival in West Nile virus encephalitis. *Journal of Virology*, 2013; 87:3655.
16. Roe K, Kumar M, Lum S, Orillo B, Nerurkar VR and **Verma S**. West Nile virus-induced disruption of the blood-brain barrier in mice is characterized by the degradation of the junctional complex proteins and increase in multiple matrix metalloproteinases. *J. General Virology*, 2012;93:1193-203.
17. Kumar M, Roe K, Nerurkar PV, Namekar M, Orillo B, **Verma S**, and Nerurkar VR. Impaired virus clearance, compromised immune response and increased mortality in type 2 diabetic mice infected with West Nile virus. *Plos One,* 2012; 11:80
18. **Verma S,** Kumar M and Nerurkar VR. Cyclooxygenase-2 inhibitor blocks the production of West Nile virus-induced neuroinflammatory markers in astrocytes. *Journal General Virology* 2011;92(3):507-15.
19. **Verma S,** Hoffmann FW, Kumar M, Huang Z, Roe K, Nguyen-Wu E, Hashimoto AS, and Hoffmann PR. Selenoprotein K knockout mice exhibit deficient calcium flux in immune cells and impaired immune responses. *Journal of Immunology*, January 10, 2011;186:2127-37. PMCID: PMC3088479.
20. **Verma S,** Kumar M, Gurjav U, Lum S and Nerurkar VR. Reversal of West Nile virus-induced blood-brain barrier disruption and tight junction proteins degradation by matrix metalloproteinases inhibitor. *Virology* 2010;397:130-138.
21. Kumar M, **Verma S,** and Nerurkar VR. Role of pro-inflammatory cytokines released from West Nile virus-infected neurons in mediating neuroinflammation and neuronal death. *Journal of Neuroinflammation* 2010;7:73. PMCID: PMC2984415

22. **Verma S,** Lo Y.Y, Chapagain M, Gurjav U, Lum S, Kumar M, Lo H, Tanaka A and Nerurkar VR. Modulation of human brain microvascular endothelial cells tight junction proteins and cell adhesion molecules by WNV infection: Transmigration across the *in vitro* blood-brain barrier. *Virology* 2009;385:425-433.
23. **Verma S**, Molina Y, Lo Y.Y, Nakano C, Cropp B, Yanagihara R and Nerurkar VR. Effects of selenium deficiency on West Nile virus replication in an in vitro selenium-deficient model. *Virology Journal* 2008;5:66.
24. Chapagain M, **Verma S**, Mercier F, Yanagihara R, Nerurkar VR. Human polyomavirus JC infects brain microvascular endothelial cells independent of serotonin receptor 2A. *Virology* 2007;364:55-63.
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Press articles and community Interveiws since 2013

January 2018: Interviewed by Shraddha Chakradhar, Associate News Editor, *Nature Medicine* for her story on testes immune privilege and our research on Zika virus
June 2018: Interviewed by the JABSOM and UH News team for second Zika virus grant funding

April 2017: Presented talk as guest speaker on the World Malaria Day celebrated by the Student Immunization Initiative, Hawaii Chapter
May 2017: Interviewed by the *Hawaii Business Magazine* for the story on recent Zika virus research. Story published in the June edition of the magazine
December 2016: Interviewed by the JABSOM and UH News team for first Zika virus grant funding at UH
August 2014: Interviewed by the Assitant News Editor of a national TV channel in India, RajyaSabha TV

Centers for Disease Control and Prevention

Mpox

Mpox Home

Biosafety Laboratory Guidance for Handling and Processing Mpox Specimens

Updated December 8, 2023

> Category B (UN3373) categorization includes infectious substances transported for diagnostic or investigational purposes. Submitters should follow all appropriate Category B regulations for packaging and transporting specimens from suspect mpox patients for diagnostic testing.

All clinical specimens may contain potentially infectious agents or organisms. Take precautions when handling specimens suspected or confirmed positive for mpox virus. Timely communication between clinical and laboratory staff is essential to minimize the risk of laboratory transmission when handling and testing specimens from patients with possible mpox. Label specimens accordingly and alert the receiving laboratory to ensure that specimens are appropriately handled. Correct handling and storage of specimens during transportation are essential for accurate diagnostic testing.

General Guidance

Mpox virus is a member of the *Orthopoxvirus* genus within the *Poxviridae* family. Some federal regulations and guidelines apply to work conducted with the mpox virus. See Select Agent Regulations.

According to Advisory Committee on Immunization Practices (ACIP) recommendations, employers should offer pre-exposure orthopoxvirus vaccination to workers at risk of occupational exposure. Two vaccines may be used to prevent mpox disease, JYNNEOS and ACAM2000. Individuals are considered fully vaccinated 14 days after the second dose of the JYNNEOS vaccine or four (4) weeks after the ACAM2000 vaccination. The Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th edition recommends vaccination for laboratorians who work directly with viral cultures or animals contaminated or infected with replication-competent orthopoxvirus (e.g., mpox virus). The BMBL and the ACIP recommend booster doses of JYNNEOS every 2 years and ACAM2000 every 3 years for people at occupational risk for virulent replicating orthopoxviruses (e.g., mpox virus). They also recommend booster doses at least every 10 years for those at occupational risk for less virulent orthopoxviruses (e.g., cowpox virus and vaccinia virus).

As with all procedures, laboratories should perform a site-specific and activity-specific risk assessment to identify and mitigate risks. Risk assessments and mitigation measures depend on the following:

- The procedures performed
- The hazards involved in the processes and procedures
- The competency level of the personnel who perform the procedures
- The laboratory equipment and facility
- The resources available
- The vaccination status of the personnel who perform the procedures

Follow Bloodborne Pathogens – Worker protections against occupational exposure to infectious diseases | Occupational Safety and Health Administration (OSHA) when handling clinical specimens, all of which may contain infectious agents or organisms. These recommendations include hand hygiene and specific personal protective equipment (PPE) determined by

the potential for exposure to blood, body fluids, and infectious material. PPE, such as laboratory coats or gowns, gloves, eye protection, respiratory protection, and face shield, can help protect the skin and mucous membranes of the eyes, nose, and mouth. Avoid procedures that could generate infectious aerosols.

For more information, see:

- Biological Risk Assessment: General Considerations for Laboratories
- Core Infection Prevention and Control Practices for Safe Healthcare Delivery in All Settings
- Occupational Safety and Health Administration (OSHA) Bloodborne Pathogens Standard
- Occupational Safety and Health Administration (OSHA) Personal Protective Equipment Standard
- Biosafety in Microbiological and Biomedical Laboratories (BMBL) 6th Edition, Section II – Biological Risk Assessment, pages 9-20 and Section IV -Laboratory Biosafety Level Criteria, pages 32-69
- Mpox: Experts Give Virus Variants New Names

Select Agent Regulations

Specimens specifically identified as Clade I monkeypox virus are regulated as a select agent (SA). Entities that possess, use, or transfer this material must comply with the HHS Select Agent and Toxin Regulations [42 CFR § 73]. Specimens specifically identified as Clade II monkeypox virus are excluded from SA regulations. However, if a generic mpox test that does not identify the clade was used, the material is regulated unless another exemption or exclusion applies.

Specimens identified as orthopoxvirus or non-variola orthopoxvirus are not select agents and, thus, are not regulated material. See SA Grams – 2022 | Resources | Federal Select Agent Program (selectagents.gov) for more information on the 2022 U.S. Mpox Outbreak & FSAP Regulations.

Biosafety Considerations for Diagnostic Testing

Facilities that process and test mpox lesion materials including swabs of lesion surface and exudate, and lesion crusts, should have the necessary equipment, engineering controls, personal protective equipment, appropriate diagnostic assays, and properly trained personnel. If the appropriate safety equipment or protocols are unavailable, consider referring specimens to an equipped reference laboratory that meets the recommendation above.

- Perform routine diagnostic specimen processing in Biosafety Level 2 (BSL-2) laboratory facilities following standard and special practices, safety equipment, and facility specifications recommended for BSL-2 according to site-specific and activity-specific biosafety risk assessments. Additional precautions to reduce exposure risk may include, but are not limited to:
  - Solid-front gowns with cuffed sleeves
  - Double gloves
  - Eye protection (safety glasses, snugly fitting goggles) or face protection (face-shield)
  - NIOSH-approved particulate respirator equipped with N95 filters or higher
  - Limiting the number of laboratory personnel who work during specimen manipulation
  - Laboratory with directional airflow
- Manipulate diagnostic specimens in a certified Class II Biosafety Cabinet (BSC) or other containment devices, especially if there is a potential to generate aerosols (e.g., vortexing or sonication of specimens in an open tube). Do not work with open vessels on the bench top unless it is safe to do so based on site and activity-specific risk assessments (i.e., the specimen has been fully inactivated utilizing an approved inactivation method).
- If you cannot perform a procedure within a BSC, use a combination of PPE and other containment devices (e.g., glove box, centrifuge safety cups, or sealed rotor) designed to create a barrier between the specimen and the laboratory personnel. Perform site-specific and activity-specific biosafety risk assessments to determine if your situation warrants additional biosafety precautions.

For further details, see:

- Biosafety in Microbiological and Biomedical Laboratories, 6th Edition, Section IV – Laboratory Biosafety Levels, pages 37-43 and Appendix N – Clinical Laboratories, pages 529-541

Routine Diagnostic Testing

If a patient is suspected or confirmed for mpox virus infection, testing to evaluate other illnesses on the clinical differential should continue while awaiting orthopoxvirus test results. Implement specific biosafety precautions depending on the specimen tested.

- For routine clinical procedures and testing of non-lesion specimens such as urine for urinalysis, blood for analysis [e.g., complete blood count (CBC), chemistries, microbiology] from suspected or confirmed mpox patients:
  - Perform in Biosafety Level 2 (BSL-2) laboratory facilities following standard and special practices, safety equipment, and facility specifications recommended for BSL-2 according to site-specific and activity-specific biosafety risk assessments. For additional routine diagnostic testing information, see BMBL Appendix N – Clinical Laboratories .
  - The quantity of orthopoxvirus in clinical specimens, such as blood and body fluids, is likely low. Take standard universal precautions to protect against potential infectious agents in any specimen. Consistently adhering to Standard Precautions | Section IV and biosafety protocols for protecting laboratory workers will prevent possible exposure to the mpox virus in clinical specimens. Limit the number of staff who test specimens and avoid any procedures that have the potential to generate infectious aerosols. See precaution guidance below to prevent exposures for Procedures with a High Likelihood of Generating Aerosols.

- For lesion specimens (including swabs of lesion surface and exudate, and lesion crusts) from patients who are suspected of having mpox and who are being concurrently tested for orthopoxvirus and other differentials [e.g., herpes simplex virus (HSV) or varicella-zoster virus (VZV), which are known to have the highest quantity of mpox virus]:
  - Perform in Biosafety Level 2 (BSL-2) laboratory facilities, following standard and special practices, safety equipment, and facility specifications recommended for BSL-2 according to site-specific and activity-specific biosafety risk assessments.
  - Additional PPE, mitigation, and practices should be assessed during the risk assessment process to reduce exposure risk. See Biosafety Considerations for Testing.
- For viral culture of lesion specimens from patients suspected to have mpox for diagnostic purposes other than mpox virus (e.g., HSV or VZV):
  - Perform in BSL-2 laboratory facilities, using additional precautions based on the laboratory's site-specific and activity-specific risk assessment to identify and mitigate risks. See Biosafety Considerations for Testing.
  - As stated above, lesions are known to have the highest quantity of mpox virus. Once laboratory personnel extract the viral DNA using a validated extraction protocol, the viral DNA is non-infectious. Laboratory personnel can work in a BSL-2 laboratory facility following standard and special practices, safety equipment, and facility specifications recommended for BSL-2 with this material. Instead of culturing lesion specimens, laboratory personnel should consider using diagnostic techniques that extract DNA or RNA, if possible. Refer to the Biosafety in Microbiological and Biomedical Laboratories (BMBL), 6th edition , Section IV -Laboratory Biosafety Level Criteria, and Section VIII-E Viral Agents.

Culturing Specimens for Mpox Virus

Culture-based testing for mpox virus should not be performed as a routine diagnostic procedure in clinical or diagnostic laboratories. Refer to the Biosafety in Microbiological and Biomedical Laboratories (BMBL), 6th edition , Section IV - Laboratory Biosafety Level Criteria BSL-3, and Section VIII-E Viral Agents.

Molecular Testing and Analysis of Bacterial or Mycotic Cultures

Perform the following procedures in a BSL-2 laboratory facility following standard and special practices, safety equipment, and facility specifications recommended for BSL-2[1] :

- Molecular analysis of extracted nucleic acid preparations
- Routine examination of bacterial and mycotic cultures for diagnostic purposes

[1]BSL-2 procedures apply, unless the viral cultures are being done with lesion specimens awaiting orthopoxvirus test confirmation. Refer to the Biosafety in Microbiological and Biomedical Laboratories (BMBL), 6th edition , Section IV - Laboratory Biosafety Level Criteria BSL-3, and Section VIII-E Viral Agents, when performing culturing of lesion specimens for diagnostic purposes other than mpox virus from an individual suspected of having mpox.

Clinical and Anatomic Pathology

The practice of pathology plays a critical role in determining accurate disease diagnoses by studying organ tissues and fluids. This includes microscopic evaluation and testing of cytology, surgical biopsy, and autopsy specimens.

Risks associated with surgical pathology and some cytology procedures occur when manipulating fresh tissue and body fluids from patients who may have an unknown or known infectious disease or virus, such as the mpox virus. Risks are increased in the surgical grossing room during manual specimen handling, tissue dissection, and the preparation of frozen tissue sections using a cryostat. These procedures can result in percutaneous exposures from punctures or cuts, droplet or aerosol exposures from blood and body fluid splashes, and surfaces contaminated with the virus. Clinical laboratory and support staff must be aware of these risks and provide effective mitigation procedures.

The following pathology specimen types are considered inactivated and can be handled in accordance with BSL-2 guidelines:

- Fixed fluid or tissue smears for routine diagnostic staining and microscopic analysis
- Formalin-fixed biopsy or autopsy tissues
- Glutaraldehyde-fixed grids for electron microscopic study

Sufficient incubation time in fixative should be utilized, dependent on tissue/biopsy size, to allow adequate fixative penetration. Orthopoxviruses (such as vaccinia virus and mpox virus) may require additional incubation time in the fixative. For larger tissue samples, additional incubation time should be utilized to ensure complete inactivation of the virus.

For information, see:

- Evaluation of Virus Inactivation by Formaldehyde to Enhance Biosafety of Diagnostic Electron Microscopy
- Reassessment of the rate of fixative diffusion
- Autopsy and Handling of Human Remains | Mpox | Poxvirus | CDC

Anatomic pathology uses different procedures and workflows than clinical pathology, so the risks and mitigation control needed to protect personnel may differ. At a minimum, all personnel practicing anatomic or clinical pathology should follow Standard Precautions | Section IV when handling clinical specimens, including hand hygiene and using PPE, such as laboratory coats or gowns, gloves, eye protection, or a disposable mask and face shield, to help protect the skin and mucous membranes of the eyes, nose, and mouth. See precaution guidance below to prevent exposures for Procedures with a High Likelihood of Generating Aerosols.

Site- and activity-specific biosafety risk assessments should be performed to determine if additional biosafety precautions are warranted.

Environmental Testing

At this time, the National Wastewater Surveillance System team recommends that untreated wastewater samples be pasteurized (60°C for 1 hour) before processing if they are suspected of containing mpox virus. This is due to the potential exposure of laboratory personnel during untreated wastewater processing.

Procedures with a High Likelihood of Generating Aerosols

Laboratory exposures to poxviruses occur primarily through needle-stick injuries, direct contact with the specimen, or aerosols that laboratory procedures may generate. Conduct procedures with a high likelihood of generating aerosols (e.g., vortexing or sonication) in a certified Class II BSC. Use additional precautions to create a barrier between the specimen and personnel. These additional precautions can include centrifuge safety cups, sealed centrifuge rotors, and additional PPE to reduce the risk of exposure to laboratory personnel. Perform site-specific and activity-specific biosafety risk assessments to identify and mitigate risks and to determine if your situation warrants additional biosafety precautions. Situations that may warrant additional biosafety precautions include high testing volumes, use of pneumatic tube systems, and automated testing platforms (e.g., laboratory robotic platforms, etc.). If testing a lesion specimen from a suspected mpox patient, CDC recommends that laboratory personnel perform complete viral inactivation before putting the specimen on any automated platform or placing the platform within a Class II BSC, if available, to perform the work.

If laboratory personnel cannot perform procedures that may generate aerosols in a BSC, acceptable methods of respiratory protection include NIOSH-approved respirators with N95 filters or higher. N95 filtering facepiece respirators provide the minimum level of respiratory protection. Facilities may consider using higher levels of respiratory protection, particularly if personnel cannot be correctly fitted to tight-fitting respirator models. These higher levels may include using loose-fitting NIOSH-approved powered air-purifying respirators equipped with particulate filters.

Decontamination

Perform routine cleaning and disinfection procedures using an EPA-registered, hospital-grade disinfectant with emerging viral pathogens claim. Products with Emerging Viral Pathogens claims may be found on EPA's List Q . Follow the manufacturer's directions for concentration, contact time, and care and handling.

Reevaluate current protocols for cleaning, use of PPE, patient placement, and hand hygiene; see Standard Precautions | Section IV. For example, high-touch surfaces such as patient waiting rooms and equipment present a higher probability of contamination in the work area and should be disinfected frequently. Increase the number of available cleaning supplies, distribute them throughout the laboratory and waiting areas, and encourage staff to clean surfaces and equipment frequently. Reusable PPE should be cleaned and disinfected according to manufacturer instructions because not all disinfectants are compatible, and some may degrade the PPE.

Laboratory Waste Management

Dispose of sharps in appropriate puncture-resistant containers to autoclave as infectious waste. All cultures, stocks, residual specimens, and mpox virus waste should be decontaminated before on-site disposal using an approved method, such as autoclaving. Materials decontaminated outside the immediate laboratory should be placed in a durable, leak-proof container and closed for transport from the laboratory. Follow local, regional, state, national, and international regulations for waste disposal. State and local waste disposal regulations vary; for more information, see:

- Environmental Protection Agency Regulations
- State Universal Waste Programs in the United States
- U.S. Department of Transportation's: Managing Solid Waste | F-2 pages 94–97
- Notice of Enforcement Discretion Regarding Mpox Medical Waste

Resources for Monitoring Healthcare Workers Exposed to Mpox Virus

Infection Control: Healthcare Settings

Pages 269-270 from the Chapter VIII-E: Viral agents, BMBL 6th edition book that explains biosafety level recommendations

Natural Modes of Infection

The most well-known orthopoxvirus is variola virus, which causes smallpox. After an extensive vaccination campaign, smallpox was declared eradicated in 1980. Monkeypox occurs sporadically in several West and Central African countries but remains endemic in the Democratic Republic of Congo. The importation of wild-caught animals from Ghana into the United States resulted in a 2003 monkeypox outbreak that affected multiple states. Vaccinia virus is used to make the current smallpox vaccine. Naturally-acquired infections with vaccinia virus exist outside of the United States.[104] Cases of human cowpox occur in Europe and Asia. Rodents are known or suspected to play a part in the transmission of monkeypox, cowpox, and vaccinia viruses.[99–101]

Laboratory Safety and Containment Recommendations

Vaccination with vaccinia virus can afford protection against infection from other species of orthopoxviruses. Smallpox vaccination occurs via scarification using a multi-puncture method with a bifurcated needle. The current U.S.-licensed smallpox vaccine, ACAM2000, uses a replication-competent vaccinia virus strain. Symptoms such as fever, headache, and swollen lymph nodes are prevalent following vaccination. Adverse events include localized reactions (e.g., robust take), unintentional transfer of virus (e.g., self-inoculation, ocular vaccinia), diffuse dermatologic complications (e.g., eczema vaccinatum, non-specific post-vaccination rash), progressive vaccinia, cardiac complications, fetal vaccinia, and postvaccinial central nervous system disease. Due to the severity of complications that can arise from vaccination, the vaccine is not recommended for persons with certain contraindications.[99,103,105,106]

Orthopoxviruses are stable in a wide range of environmental temperatures and humidity. Virus may enter the body through the mucous membranes (e.g., eye splashes, inhalation of droplets or fine-particle aerosols), broken skin (e.g., needlesticks, scalpel cut), ingestion, or by parenteral inoculation. Sources of exposure include fomites, infected human or animal tissue, excretions or respiratory secretions, or infectious cultures.[106]

Routine vaccination with ACAM2000 is recommended for laboratory personnel who directly handle cultures or animals contaminated or infected with replication-competent vaccinia virus, recombinant vaccinia viruses derived from replication-competent vaccinia strains (i.e., those that are capable of causing clinical infection and producing infectious virus in humans), or other orthopoxviruses that infect humans (e.g., monkeypox, cowpox, and variola).[106] Vaccination is advised every three years for work with monkeypox and variola viruses, and every 10 years for cowpox and vaccinia viruses. Vaccination is not required for individuals working in laboratories that only manipulate replication-deficient strains of vaccinia virus (modified virus Ankara [MVA], NYVAC, TROVAC,

and ALVAC). Vaccination may be offered to healthcare workers, animal care personnel, and vaccinators who have contact with contaminated materials. Vaccination does not protect against non-Orthopoxvirus species.[103,106]

Research with variola virus is restricted to two WHO-approved BSL-4 and ABSL-4 facilities; one is the CDC in Atlanta, GA, and the other is the State Research Center of Virology and Biotechnology (VECTOR) in Koltsovo, Russia. ABSL-3 practices, containment equipment, and facilities are recommended for monkeypox work in experimentally or naturally infected animals. BSL-2 facilities with BSL-3 practices are advised if vaccinated personnel perform laboratory work with monkeypox virus. BSL-2 and ABSL-2 containment plus vaccination are recommended for work with vaccinia and other human pathogenic poxviruses. The lowering of containment to BSL-1 for the manipulation of attenuated poxviruses and vectors (e.g., modified virus Ankara [MVA], NYVAC, TROVAC, and ALVAC) in areas where no other human orthopoxviruses are being used may be considered. However, higher levels of containment are recommended if these strains are used in work areas where other orthopoxviruses are manipulated. Vaccination is not required for individuals working only in laboratories where no other orthopoxviruses or recombinants are handled. BSL-2 and ABSL-2 plus vaccination are recommended for work with most other poxviruses. Note that for research subject to the *NIH Guidelines*, approval to lower containment from BSL-2 must be requested from NIH Office of Science Policy.[107]

Special Issues

The CDC provides information on a variety of topics relating to variola, monkeypox, and vaccinia viruses online at https://www.cdc.gov. For non-emergency information on potential human infections, smallpox vaccination, or treatment options, the CDC Poxvirus Inquiry Line can be contacted at 404-639-4129 or CDC-Info can be reached at 800-232-4636. To obtain smallpox vaccine, CDC Drug Services can be reached by phone at 404-639-3670 or by email at drugservice@cdc.gov. Clinicians or health departments may contact the CDC Emergency Operations Center in critical circumstances.

Select Agent Congo Basin monkeypox, Variola major, and Variola minor are Select Agents requiring registration with CDC for possession, use, storage, and/or transfer. See Appendix F for additional information.

Transfer of Agent The importation of poxviruses into the United States and/or their interstate transport may be subject to the rules and regulations of the CDC Import Permit Program, CDC Division of Select Agents and Toxins, and/or the USDA Animal and Plant Health Inspection Service. The exportation of poxviruses may require a DoC permit.

Mpox Monitoring and Risk Assessment for Persons Exposed in the Community

Updated November 25, 2022

This guidance is intended for people who have had mpox **exposures in the community**. Guidance for exposures in healthcare settings can be found here: Infection Prevention and Control of Mpox in Healthcare Settings.

Who should be monitored and for how long?

Anyone with an exposure to people or animals with mpox should monitor their health or be monitored for signs or symptoms consistent with mpox for 21 days after their last exposure. Information about human-to-human transmission of monkeypox virus is described in How it Spreads | Mpox | Poxvirus | CDC.

What to monitor

Monitoring should include assessing the person for signs and symptoms of mpox, including a thorough skin and mouth (oral) exam in good lighting. Skin examination can be performed by the person in isolation, a caregiver, or a healthcare provider and should include examination of the genitals and anus for rash or lesions.

Development of rash, signs, or symptoms

During the 21-day monitoring period:

- If a rash occurs:
  - An individual should follow isolation and prevention practices until (1) the rash can be evaluated by a healthcare provider, (2) testing is performed, if recommended by their healthcare provider, and (3) results of testing are available and are negative.
- If other signs or symptoms are present, but there is no rash:
  - An individual should follow isolation and prevention practices for 5 days after the development of any new sign or symptom, even if this 5-day period extends beyond the original 21-day monitoring period. If 5 days have passed without the development of any new sign or symptom and a thorough skin and oral examination reveals no new skin changes such as rashes or lesions, isolation and prevention practices for mpox can be stopped.
  - If a new sign or symptom develops at any point during the 21-day monitoring period (including during a 5-day isolation if applicable), then a new 5-day period should begin where the individual follows isolation and prevention practices.

Isolation and prevention practices can be ended prior to 5 days if a healthcare provider or public health authority believes the rash, signs, or symptoms are not due to mpox and there is a clear alternative diagnosis made that doesn't require isolation. The decision on when to end symptom monitoring and home isolation, either during the 21-day monitoring period or any 5-day extension, should be made with input from public health authorities.

Activity restriction during monitoring

Individuals exposed to monkeypox virus can continue their routine daily activities (e.g., go to work or school) as long as they do not have signs or symptoms consistent with mpox.

To date, there have been no cases of mpox transmitted by blood transfusion, organ transplantation, or implantation, transplantation, infusion, or transfer of human cells, tissues, or cellular or tissue-based products (HCT/Ps). As a precaution, patients with exposures should not donate blood, cells, tissue, breast milk, or semen while they are being monitored for symptoms. Given the morbidity and mortality among individuals awaiting organ transplantation, persons who have been exposed, but who are asymptomatic and without evidence of monkeypox virus infection, could be considered for organ donation following appropriate risk-benefit considerations.

How to monitor

Decisions on how to monitor exposed persons are at the discretion of public health authorities. In general, the type of monitoring recommended reflects the risk for transmission, with more active-monitoring approaches used for people who have had higher-risk exposures. Self-monitoring approaches are usually sufficient for people with exposures that carry a lesser risk for transmission. Evsen higher-risk exposures may be appropriate for a self-monitoring strategy if public health authorities determine that it is appropriate. Ultimately, the person's exposure risk level, their reliability in reporting signs or symptoms that might develop, the number of people needing monitoring, time since exposure, and receipt of post exposure prophylaxis (PEP) are all factors when determining the type of monitoring to be used.

How to monitor people unable to communicate onset of symptoms

Some people may be unable to communicate onset of symptoms, such as newborns, young children, or people with cognitive disorders. Parents and other caregivers should watch for changes in behavior and temperament that could signal that the person is experiencing uncomfortable symptoms such as fatigue or headache.

- Exposed people do not need to quarantine, but on a case-by-case basis, clinicians or public health officials could consider restricting programs, activities, or events that would pose high risk of transmission to other people (e.g., group play/education environments).
- Decisions about whether to limit activities in people who have been exposed to mpox but are unable to communicate onset of symptoms should consider the risk of their exposure incident (how likely they are to develop mpox infection) and the risk that transmission would pose to other people (e.g., immunocompromised family members, young children).

Exposure risk assessment for community settings

Each risk level category in the table below is intended to highlight the need for monitoring and assist with determining the need for postexposure prophylaxis (PEP). The exposure risk level of any incident may be recategorized to another risk level at the discretion of the treating clinician or public health authorities due to the unique circumstances of each exposure incident.

Mpox typically spreads through prolonged close, skin-to-skin contact with a person who has mpox, or their contaminated materials (e.g., clothing, bed sheets). Transmission during quick interactions (e.g., brief conversation), between people in close proximity has not been reported for any persons with mpox.

There may be settings in which contact tracing is not feasible due to the characteristics of the setting (e.g., level of crowding, types of interactions occurring). In settings where contact tracing is not feasible, people who spent time in the same area as someone with mpox should be considered to have intermediate or lower degree of exposure.

Interim Community Exposure Risk Assessment and Recommendations

For Monitoring and Postexposure Prophylaxis (PEP) in Individuals Exposed to Mpox Virus in a Community Setting

High Degree of Exposure

Exposure Characteristics

- Contact between an exposed individual's broken skin or mucous membranes with the skin lesions or bodily fluids from a person with mpox **-OR-**
- Any sexual or intimate contact involving mucous membranes (e.g., kissing, oral-genital, oral-anal, vaginal, or anal sex (insertive or receptive)) with a person with mpox **-OR-**
- Contact between an exposed individual's broken skin or mucous membranes with materials (e.g., linens, clothing, objects, sex toys) that have contacted the skin lesions or bodily fluids of a person with mpox (e.g., sharing food, handling or sharing of linens used by a person with mpox without having been disinfected† or laundered)

Recommendations

- Monitoring: Yes
- PEP¶: Recommended

Intermediate Degree of Exposure

Exposure Characteristics

- Being within 6 feet for a total of 3 hours or more (cumulative) of an unmasked person with mpox without wearing a surgical mask or respirator **-OR-**
- Contact between an exposed individual's intact skin with the skin lesions or bodily fluids from a person with mpox **-OR-**
- Contact between an exposed individual's intact skin with materials (e.g., linens, clothing, sex toys) that have contacted the skin lesions or bodily fluids from a person with mpox without having been disinfected† or laundered **-OR-**
- Contact between an exposed individual's clothing with the person with mpox's skin lesions or bodily fluids, or their soiled linens or dressings (e.g., during turning, bathing, or assisting with transfer)

Recommendations

- Monitoring: Yes
- PEP¶: Informed clinical decision making recommended on an individual basis to determine if the benefits of PEP outweigh the risks

Lower Degree of Exposure

Exposure Characteristics

- Entry into the living space of a person with mpox (regardless of whether the person with mpox is present), and in the absence of any exposures above

Recommendations

- Monitoring: Yes
- PEP¶: None

No Risk of Exposure

Recommendations

- Monitoring: No
- PEP¶: None

Exposure Characteristics

- No contact with the person with mpox, their potentially infectious contaminated materials, nor entry into their living space

¶ JYNNEOS and ACAM2000 are available for PEP

† Disinfection using a disinfectant registered with the U.S. Environmental Protection Agency (EPA), such as those with an emerging viral pathogens claim found on EPA's List Q

Factors that may increase the risk of mpox transmission include (but are not limited to): the person with mpox had clothes that were soiled with bodily fluids or secretions (e.g., discharge, skin lesion crusts or scabs on clothes) or was coughing while not wearing a mask or respirator, or the exposed individual is not previously vaccinated against smallpox or mpox. People who may be at increased risk for severe disease include (but are not limited to): young children (<1 year of age), individuals who are pregnant or immunocompromised, and individuals with a history of atopic dermatitis or eczema.

Last Reviewed: November 25, 2022

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NR-58622 Monkeypox Virus, hMPXV/USA/MA001/2022 (Lineage B.1, Clade IIb) *(Viruses)*

Price: All BEI Resources products are provided at no cost to registered researchers.

Description:	hMPXV/USA/MA001/2022 (Lineage B.1, Clade IIb)
Organism:	Monkeypox Virus
Biosafety Level:	3
Availability Status:	In Stock
Store at:	-60°C or colder
Contributor:	CDC
Comments:	Quantity limit per order for this item is 1. This item can be ordered twice a year. Orders over this limit will be sent to NIAID for approval before shipment. Monkeypox virus, hMPXV/USA/MA001/2022 was isolated from a human in Massachusetts, USA in May of 2022, during an outbreak of monkeypox. Monkeypox virus, hMPXV/USA/MA001/2022 belongs to Clade IIb (previously west African clade) and lineage B.1. The complete genome of monkeypox virus, hMPXV/USA/MA001/2022 has been sequenced (GenBank: ON563414.3 and GISAID: EPI_ISL_13052289). Each vial contains approximately 0.5 mL of cell lysate and supernatant from *Cercopithecus aethiops* kidney epithelial cells (BSC-40; ATCC ® CRL-2761™) infected with monkeypox virus, hMPXV/USA/MA001/2022. Additional information and tools are available at the Bacterial and Viral Bioinformatics Resource Center (BV-BRC). **The MATERIAL can be used for any legitimate purpose required to rapidly prevent, detect, prepare for, and respond to, the spread or transmission of MPXV, and to include use and sharing of the MATERIAL in conjunction with other public health institutions and like partners.**
Citations:	Acknowledgment for publications should read "The following reagent was deposited by the Centers for Disease Control and Prevention and obtained through BEI Resources, NIAID, NIH: Monkeypox Virus, hMPXV/USA/MA001/2022 (Lineage B.1, Clade IIb), NR-58622."

ATTACHMENTS

- Product Information Sheet
- Certificate of Analysis by Lot

PERMITS

For a list of permits that may be required for shipping this product and to set the permit information preferences; please select a country from the drop down below.

Country : USA

- If shipping to the U.S. State of Hawaii, you must provide either an import permit or documentation stating that an import permi

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KNOWLEDGE BASE

- How much do the reagents cost?
- How are viruses propagated at BEI Resources?
- Is the passage history available for viruses?

All compliant version documentation requests will be addressed within two business days of receipt.

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Product Information Sheet for NR-58622

Monkeypox Virus, hMPXV/USA/MA001/2022 (Lineage B.1, Clade IIb)

Catalog No. NR-58622

This reagent is the property of the U.S. Government.

For research use only. Not for use in humans.

Contributor:

Centers for Disease Control and Prevention, Atlanta, Georgia, USA

Manufacturer:

The University of Texas Medical Branch, Galveston, Texas, USA

Product Description:

Virus Classification: *Poxviridae*, *Orthopoxvirus*
Species: Monkeypox virus
Strain/Isolate: hMPXV/USA/MA001/2022
Original Source: Monkeypox virus, hMPXV/USA/MA001/2022 was isolated from a human in Massachusetts, USA in May of 2022, during an outbreak of monkeypox.[1]
Comments: Monkeypox virus, hMPXV/USA/MA001/2022 belongs to Clade IIb (previously west African clade) and lineage B.1.[2] The complete genome of monkeypox virus, hMPXV/USA/MA001/2022 has been sequenced (GenBank: ON563414.3 and GISAID: EPI_ISL_13052289).

Material Provided:

Each vial contains approximately 0.5 mL of cell lysate and supernatant from *Cercopithecus aethiops* kidney epithelial cells (BSC-40; ATCC® CRL-2761™) infected with monkeypox virus, hMPXV/USA/MA001/2022.

Note: If homogeneity is required for your intended use, please purify prior to initiating work.

Packaging/Storage:

NR-58622 was packaged aseptically in screw-capped plastic cryovials. The product is provided frozen and should be stored at -60°C or colder immediately upon arrival. For long-term storage, the vapor phase of a liquid nitrogen freezer is recommended. Freeze-thaw cycles should be avoided.

Growth Conditions:

Host: *Cercopithecus aethiops* kidney epithelial cells (BSC-40; ATCC® CRL-2761™)
Growth Medium: Eagle's Minimum Essential Medium (EMEM; HyClone) supplemented with 2% fetal bovine serum (FBS; Gibco) and 1% penicillin/streptomycin solution, or equivalents
Infection: Cells should be 70% to 80% confluent
Incubation: 3 to 5 days at 37°C
Cytopathic Effect: Cell rounding and sloughing

Citation:

Acknowledgment for publications should read "The following reagent was deposited by the Centers for Disease Control and Prevention and obtained through BEI Resources, NIAID, NIH: Monkeypox Virus, hMPXV/USA/MA001/2022 (Lineage B.1, Clade IIb), NR-58622."

Biosafety Level: 3

Appropriate safety procedures should always be used with this material. Laboratory safety is discussed in the following publication: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, and National Institutes of Health. Biosafety in Microbiological and Biomedical Laboratories. 6th ed. Washington, DC: U.S. Government Printing Office, 2020; see www.cdc.gov/biosafety/publications/bmbl5/index.htm.

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Use Restrictions:

The MATERIAL can be used for any legitimate purpose required to rapidly prevent, detect, prepare for, and respond to, the spread or transmission of MPXV, and to include use and sharing of the MATERIAL in conjunction with other public health institutions and like partners.

References:

1. GenBank
2. GISAID

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