EBV and Molecular Mimicry in Multiple Sclerosis

Toward a Common Research Agenda in Infection-Associated Chronic Illnesses
NAS

June 29, 2023

William Robinson, MD, PhD

Stanford University
VA Palo Alto

Epstein-Barr Virus (EBV)

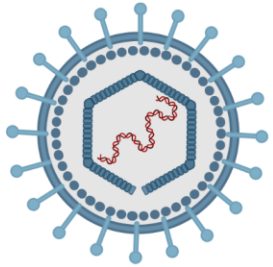
Multiple sclerosis

Rheumatoid arthritis

Sjögren's syndrome

SLE

EBV



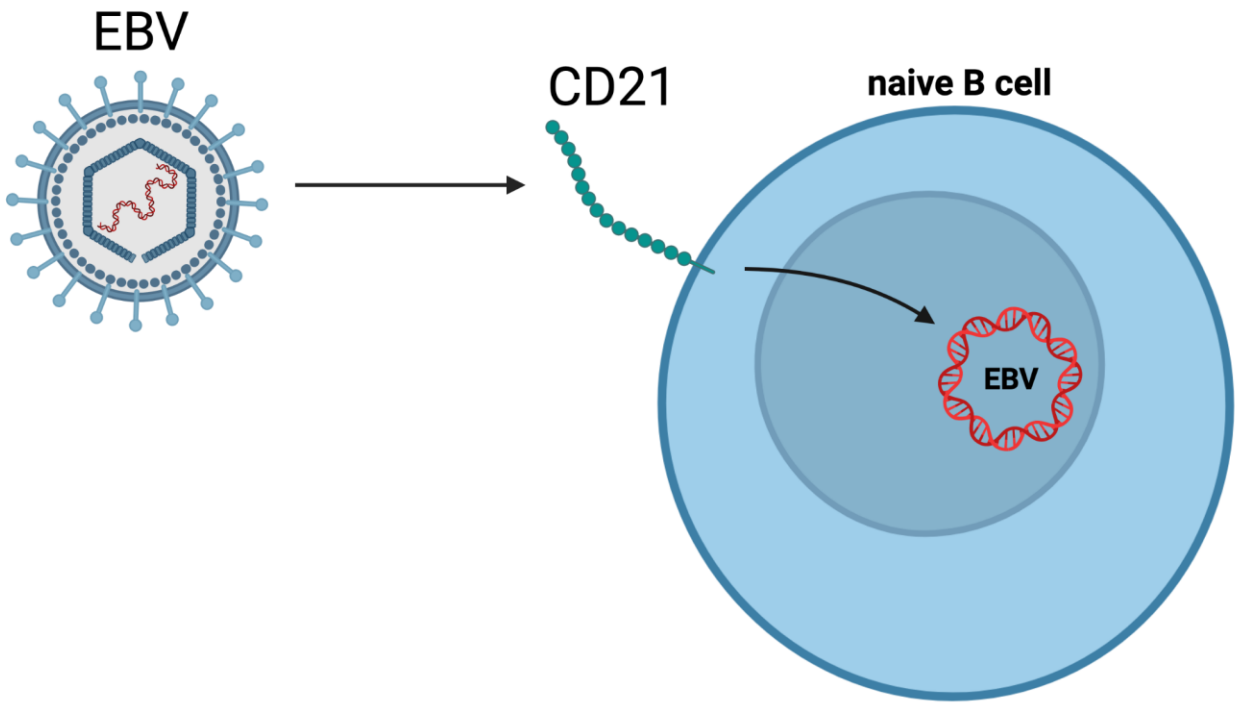
EBV Infection and Latency

Multiple sclerosis

Rheumatoid arthritis

Sjögren's syndrome

SLE



EBV Infection and Latency

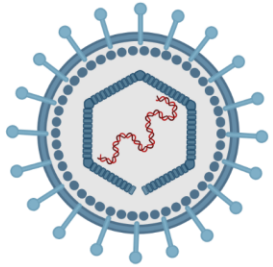
Multiple sclerosis

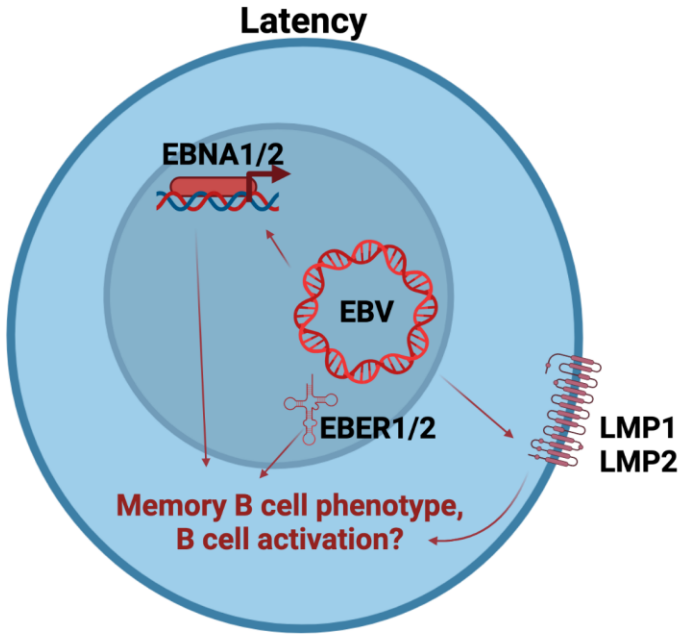
Rheumatoid arthritis

Sjögren's syndrome

SLE

EBV





EBV Infection and Latency

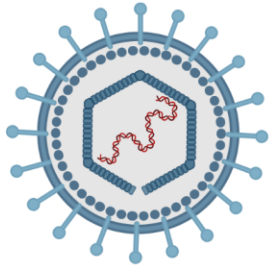
Multiple sclerosis

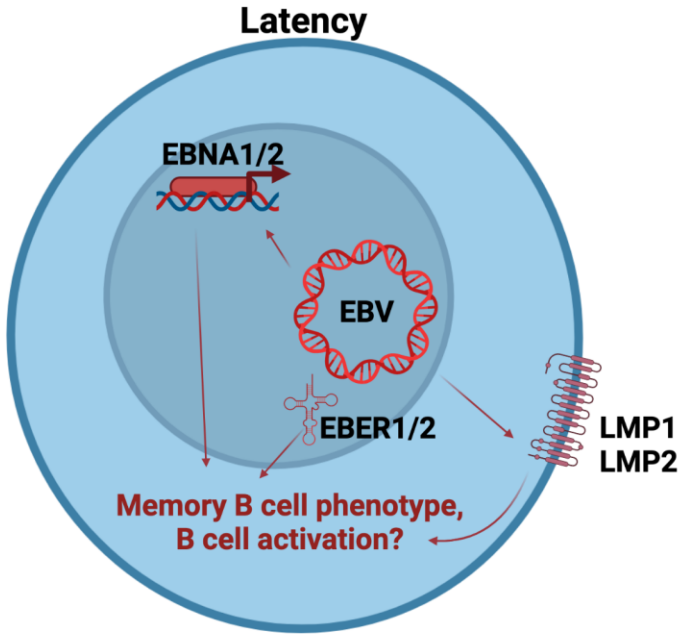
Rheumatoid arthritis

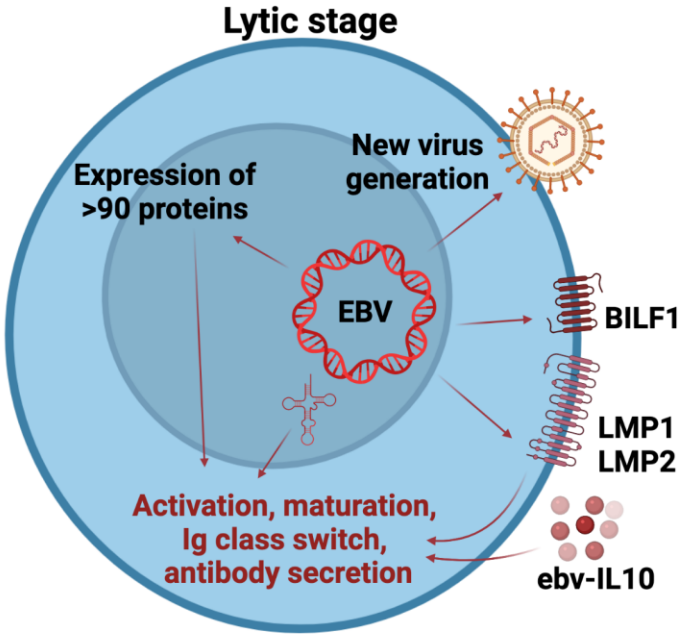
Sjögren's syndrome

SLE

EBV







EBV Mediated Diseases

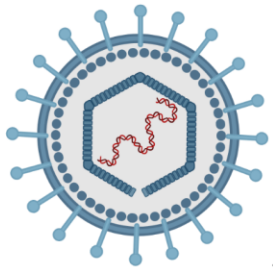
Multiple sclerosis

Rheumatoid arthritis

Sjögren's syndrome

SLE

EBV

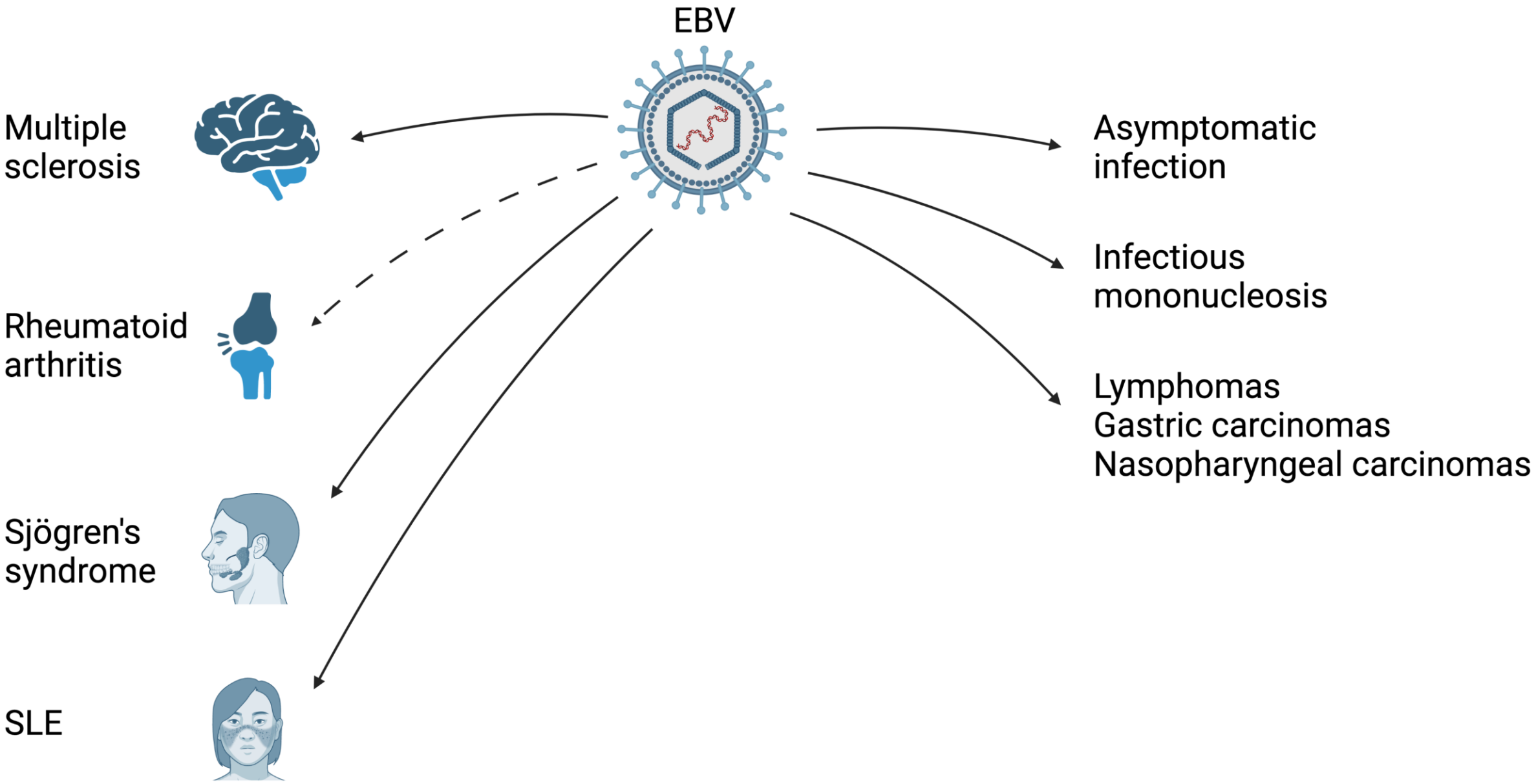


Asymptomatic infection

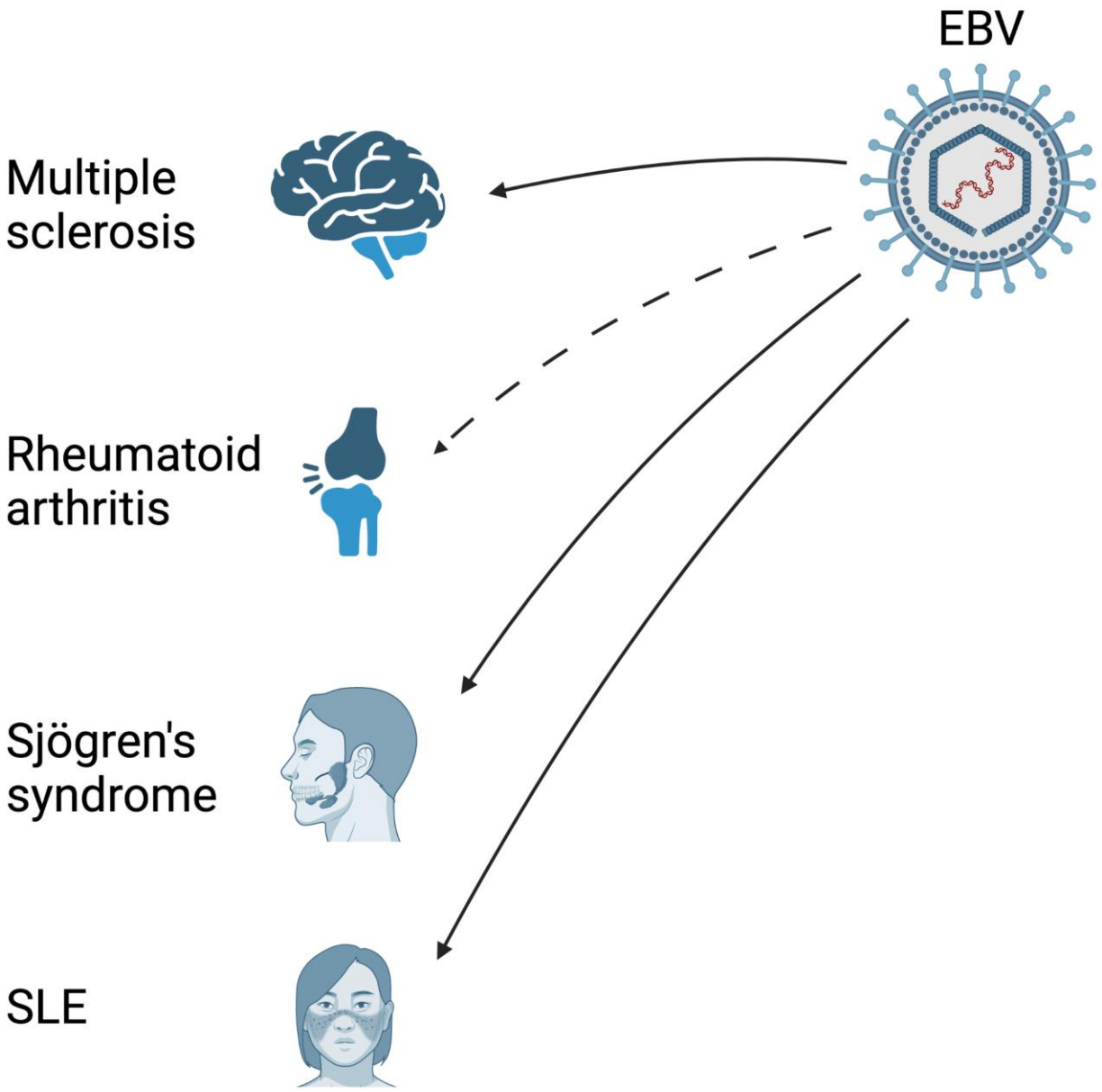
Infectious mononucleosis

Lymphomas
Gastric carcinomas
Nasopharyngeal carcinomas

EBV Mediated Diseases



EBV in Autoimmunity



REPORT

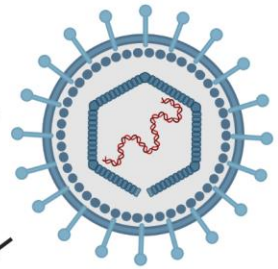
MULTIPLE SCLEROSIS

Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis

Kjetil Bjornevik[1]†, Marianna Cortese[1]†, Brian C. Healy[2,3,4], Jens Kuhle[5], Michael J. Mina[6,7,8], Yumei Leng[6], Stephen J. Elledge[6], David W. Niebuhr[9], Ann I. Scher[9], Kassandra L. Munger[1]‡, Alberto Ascherio[1,10,11]*‡

EBV in Autoimmunity

EBV



Multiple sclerosis

Rheumatoid arthritis

Sjögren's syndrome

SLE

REPORT

MULTIPLE SCLEROSIS

Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis

Kjetil Bjornevik[1]†, Marianna Cortese[1]†, Brian C. Healy[2,3,4], Jens Kuhle[5], Michael J. Mina[6,7,8], Yumei Leng[6], Stephen J. Elledge[6], David W. Niebuhr[9], Ann I. Scher[9], Kassandra L. Munger[1]‡, Alberto Ascherio[1,10,11]*‡

An Increased Prevalence of Epstein-Barr Virus Infection in Young Patients Suggests a Possible Etiology for Systemic Lupus Erythematosus

Judith A. James,*‡ Kenneth M. Kaufman,*‡ A. Darise Farris,‡ Elizabeth Taylor-Albert,*‡ Thomas J.A. Lehman,| and John B. Harley*‡§

Department of Medicine, University of Oklahoma Health Sciences Center, ‡Oklahoma Medical Research Foundation, and §U.S. Department of Veterans Affairs Medical Center, Oklahoma City, Oklahoma 73104; and |Hospital for Special Surgery, New York 10021

Arthritis & Rheumatology
Vol. 0, No. 0, Month 2022, pp 1–7
DOI 10.1002/art.41994

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

BRIEF REPORT

Antibody Responses to Epstein–Barr Virus in the Preclinical Period of Rheumatoid Arthritis Suggest the Presence of Increased Viral Reactivation Cycles

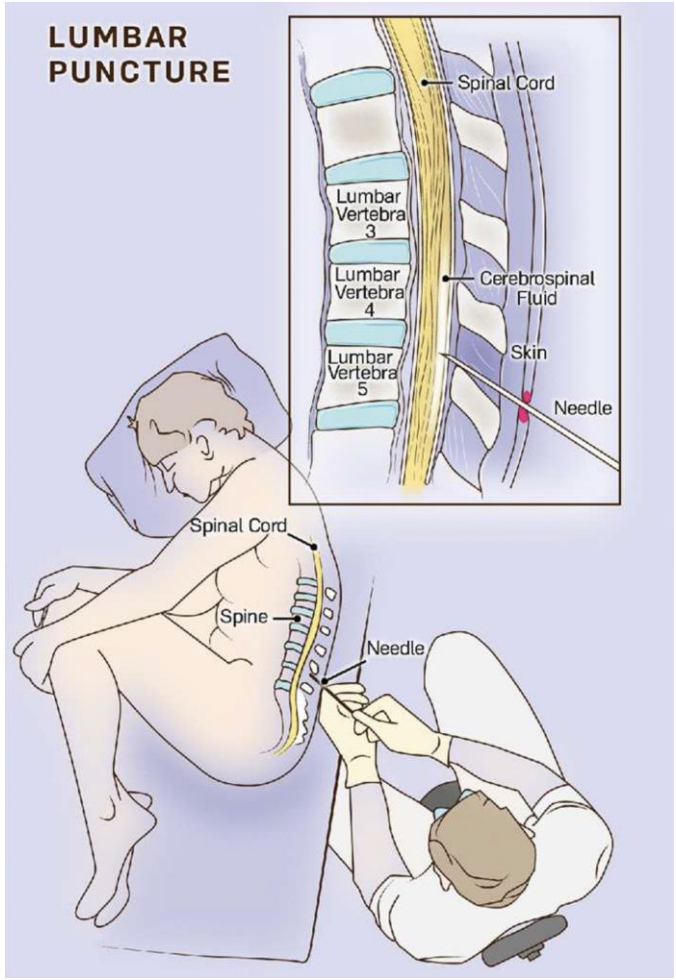
Sabrina Fechtner,[1] Heather Berens,[1] Elizabeth Bemis,[2] Rachel L. Johnson,[2] Carla J. Guthridge,[3] Nichole E. Carlson,[2] M. Kristen Demoruelle,[1] John B. Harley,[4] Jess D. Edison,[5] Jill A. Norris,[2] William H. Robinson,[6] Kevin D. Deane,[1] Judith A. James,[7] and V. Michael Holers[1]

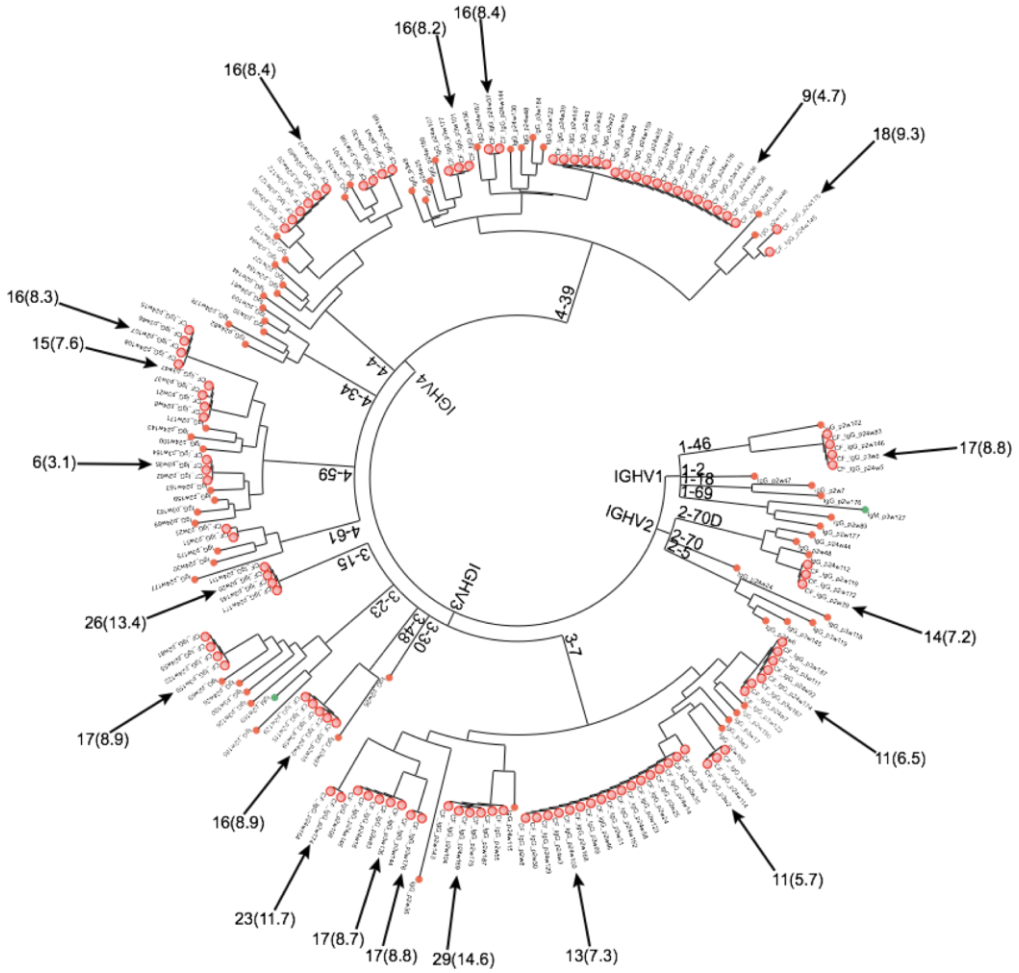
Serological Evidence for the Association Between Epstein-Barr Virus Infection and Sjögren's Syndrome

Jingxiu Xuan[1,2†], Zhiqian Ji[1†], Bin Wang[1†], Xiaoli Zeng[1], Rongjuan Chen[1,2], Yan He[1,2], Peishi Rao[1,2], Puqi Wu[1,2] and Guixiu Shi[1,2]*

[1] Department of Rheumatology and Clinical Immunology, The First Affiliated Hospital of Xiamen University, Xiamen, China, [2] Department of Science & Technology, Xiamen Key Laboratory of Rheumatology and Clinical Immunology, Xiamen, China

High B Cell Clonality in the Spinal Fluid of MS Patients

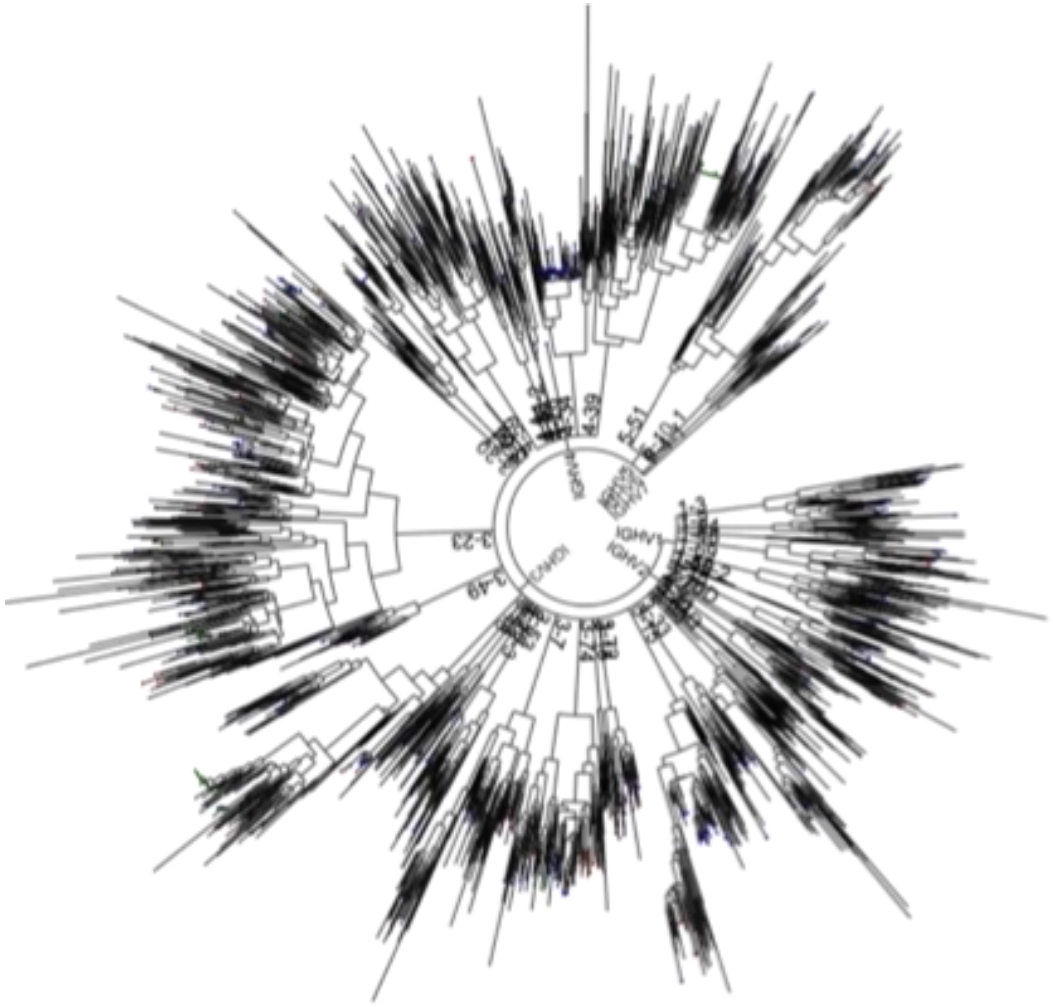




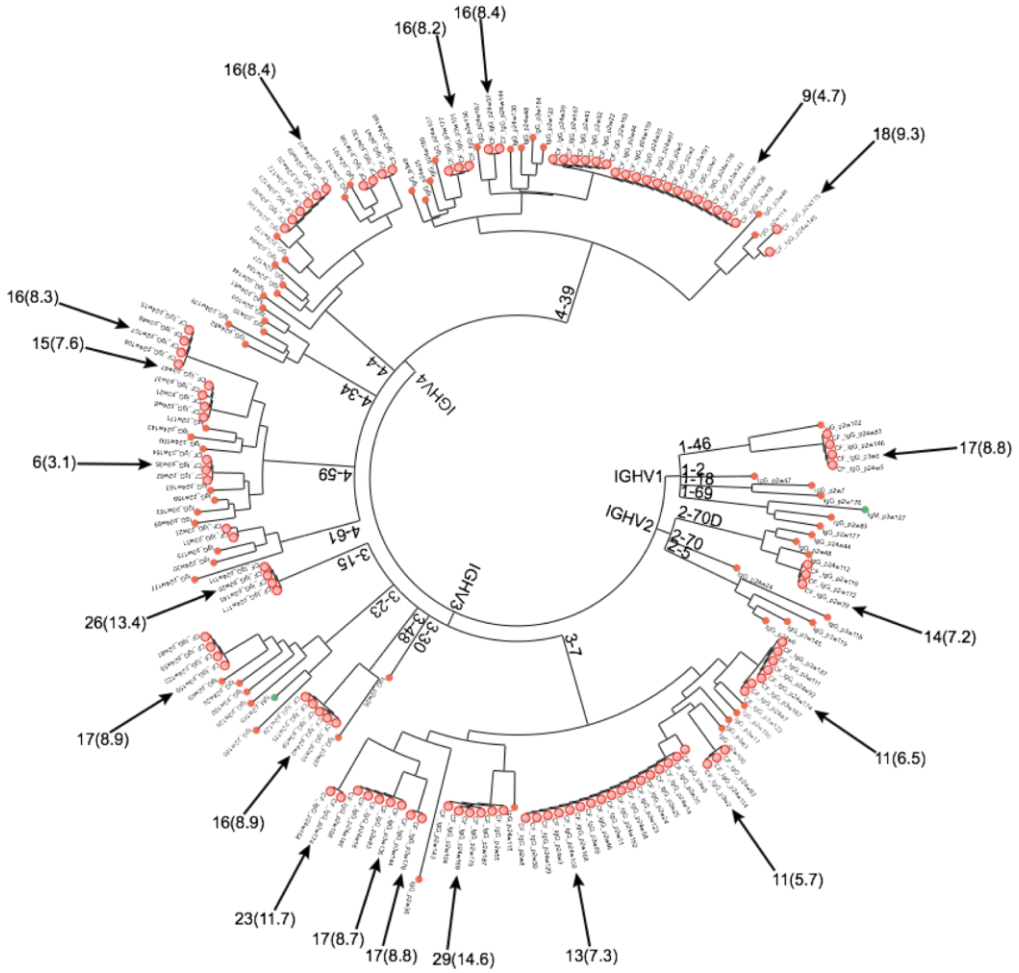
CSF

Lanz et al., *Nature*, 2022

High B Cell Clonality in the Spinal Fluid of MS Patients



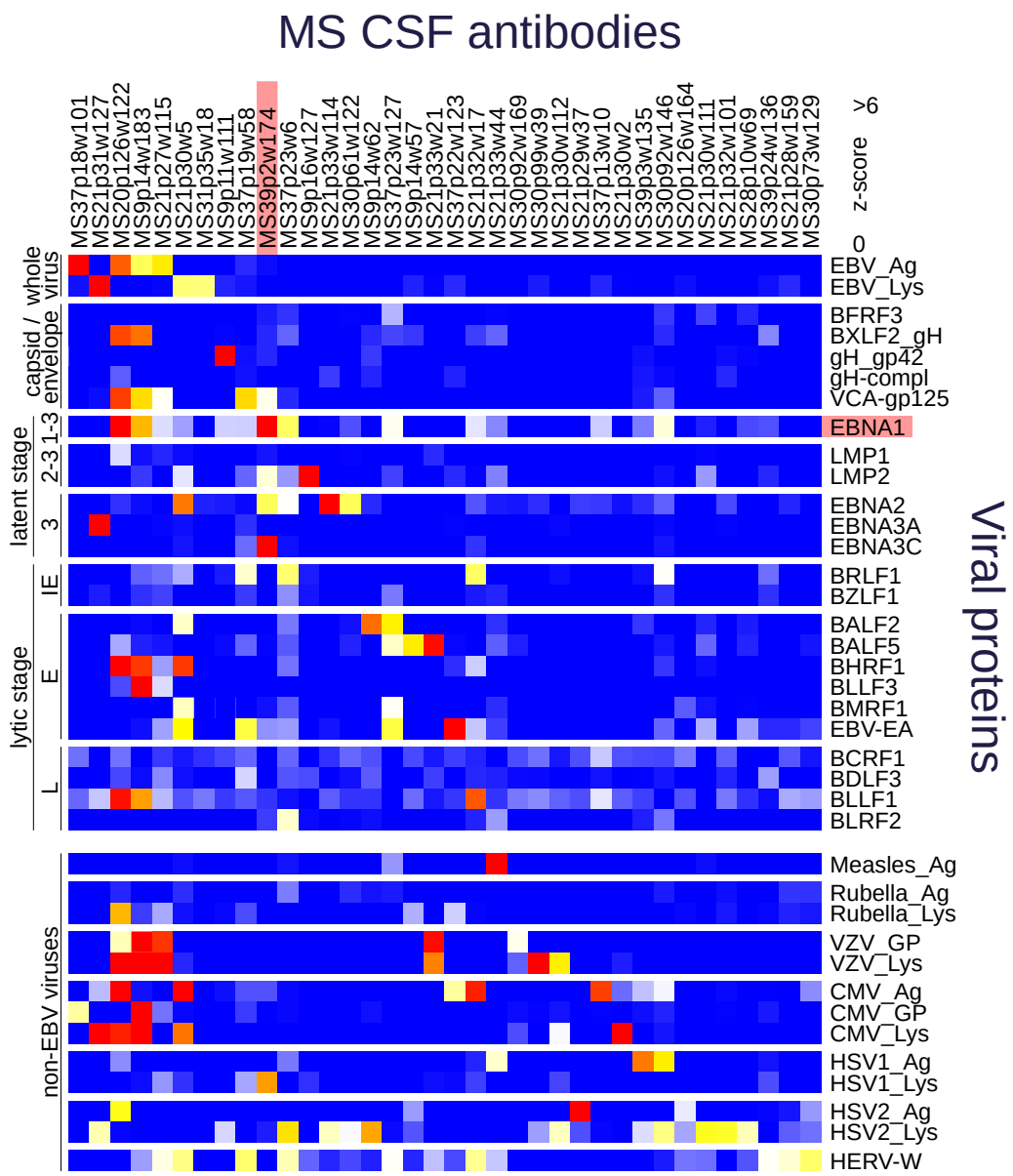
Blood

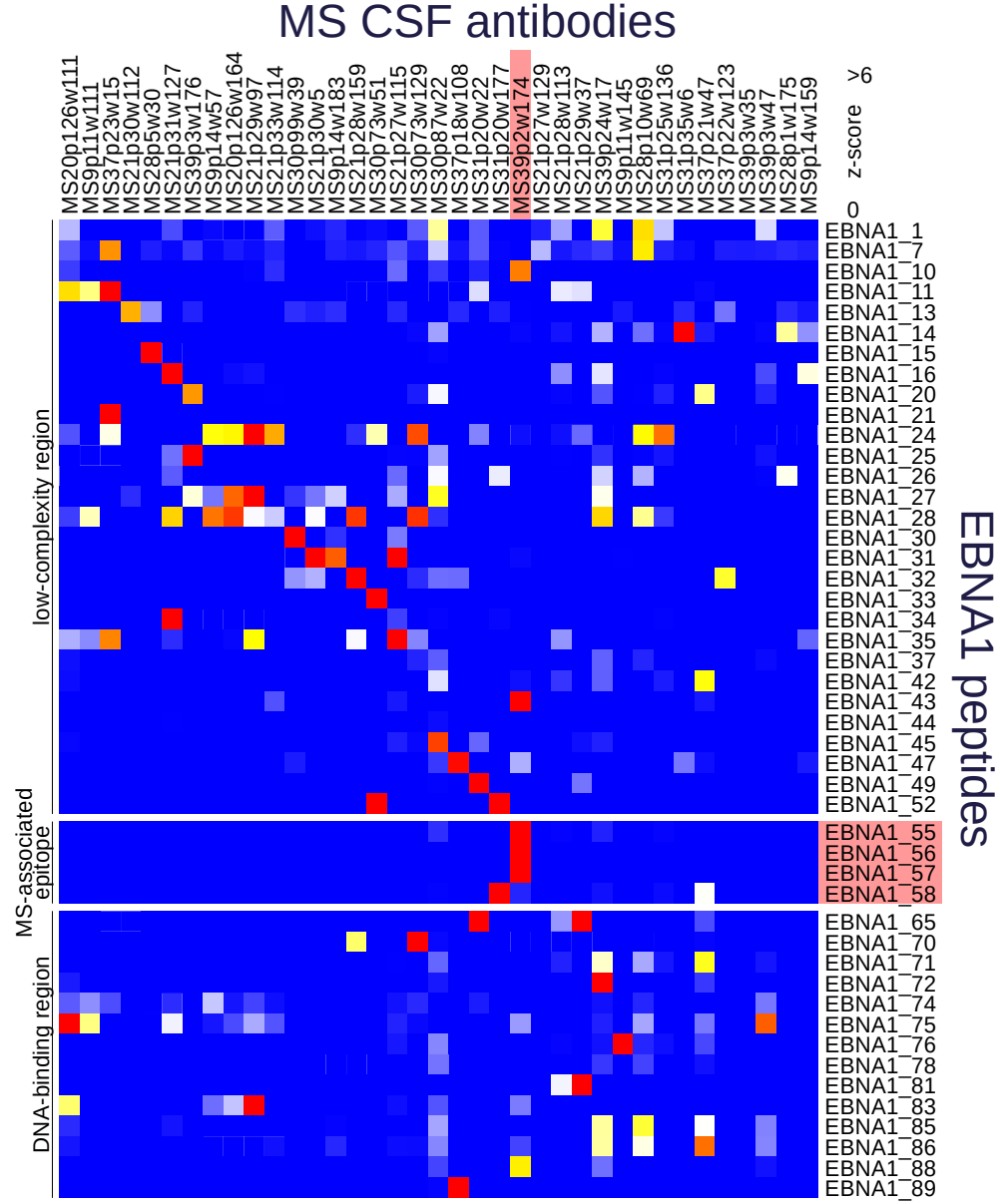


CSF

Lanz et al., *Nature*, 2022

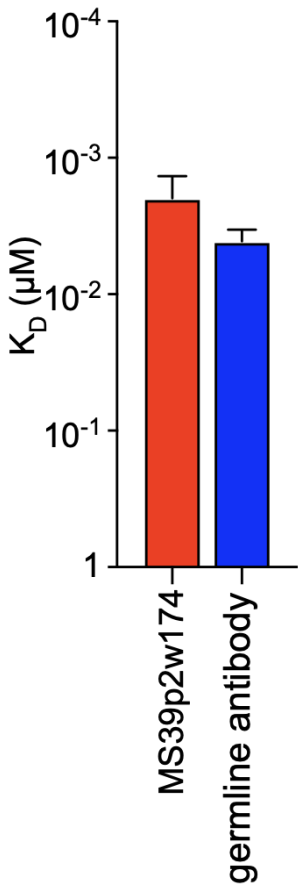
MS Spinal Fluid B Cells Bind Viral Antigens

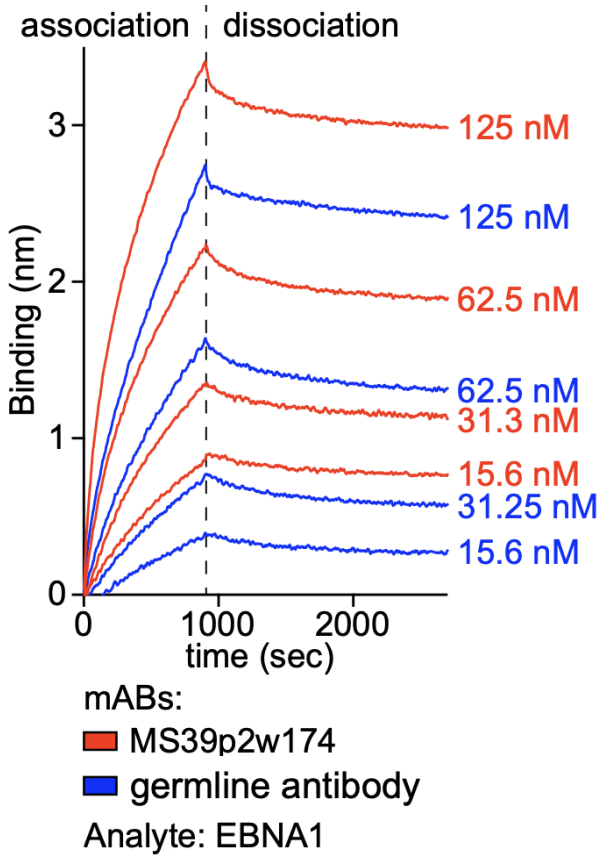




High Affinity Interaction with Pro/Arg-rich Region on EBNA1

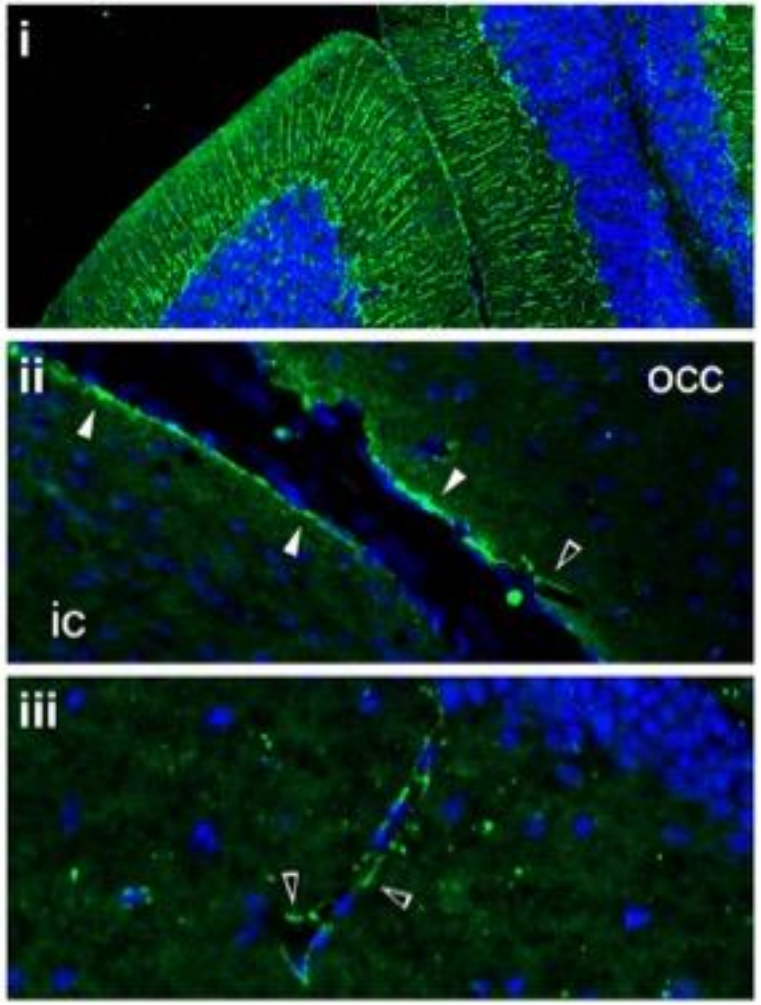
Ser386 AA394-399 Phe405

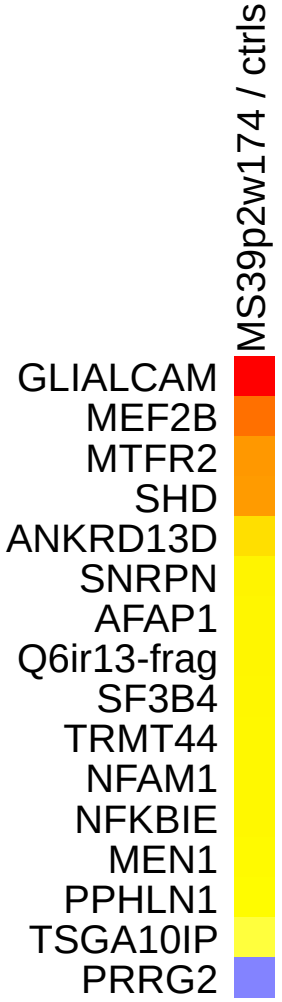




Lanz et al., *Nature*, 2022

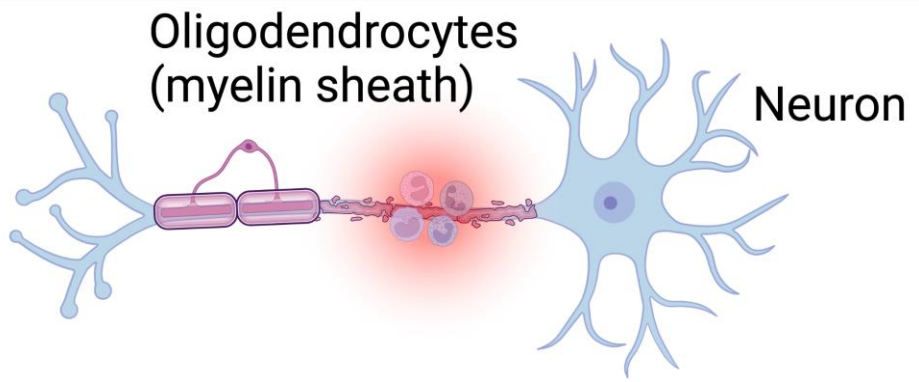
Cross-Reactivity to GlialCAM





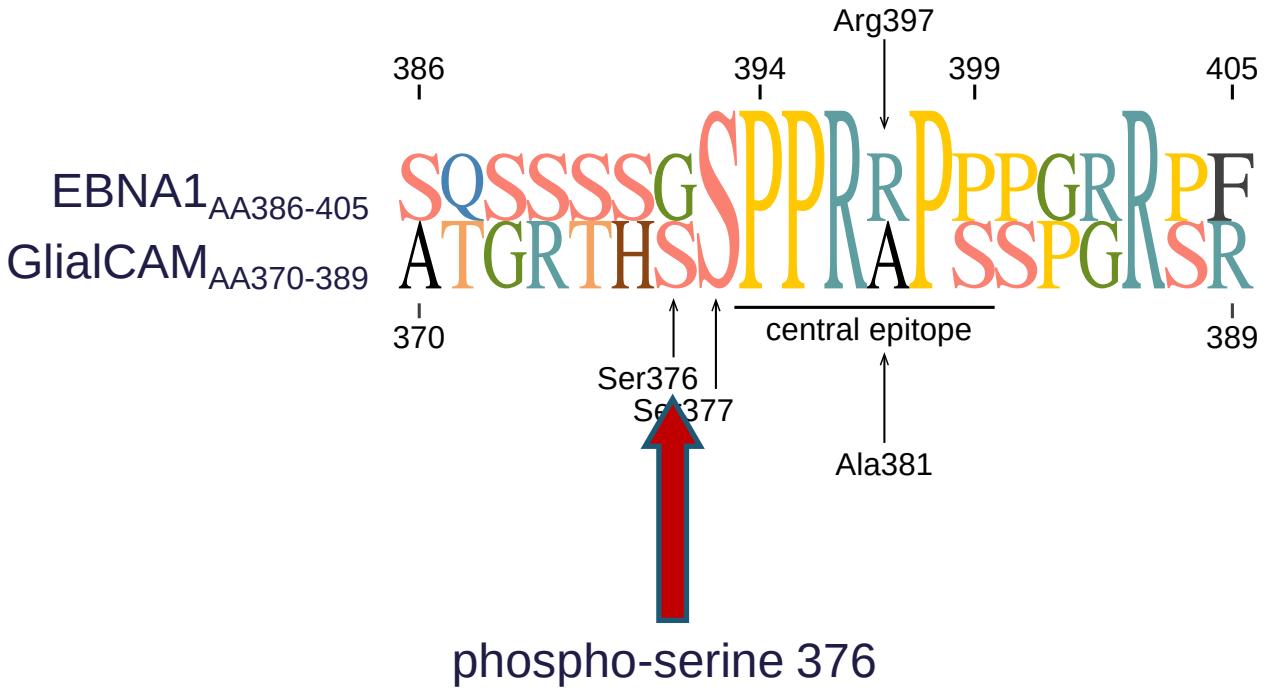
GlialCAM

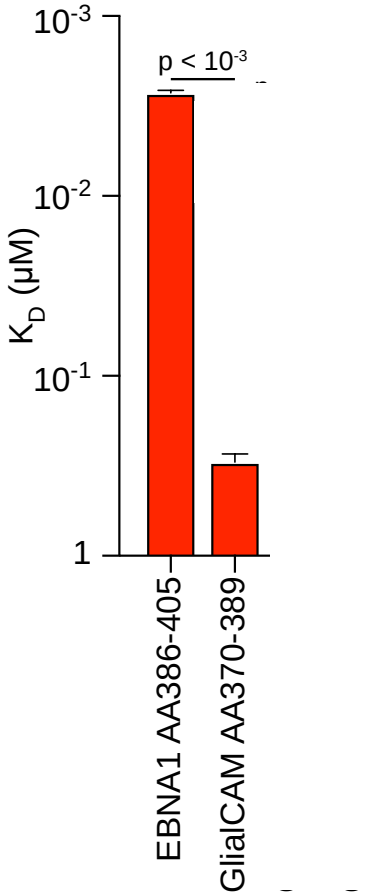
- Glial cellular adhesion molecule
- Glial water and chloride homeostasis
- Expression in astrocytes and oligodendrocytes



Lanz et al., *Nature*, 2022

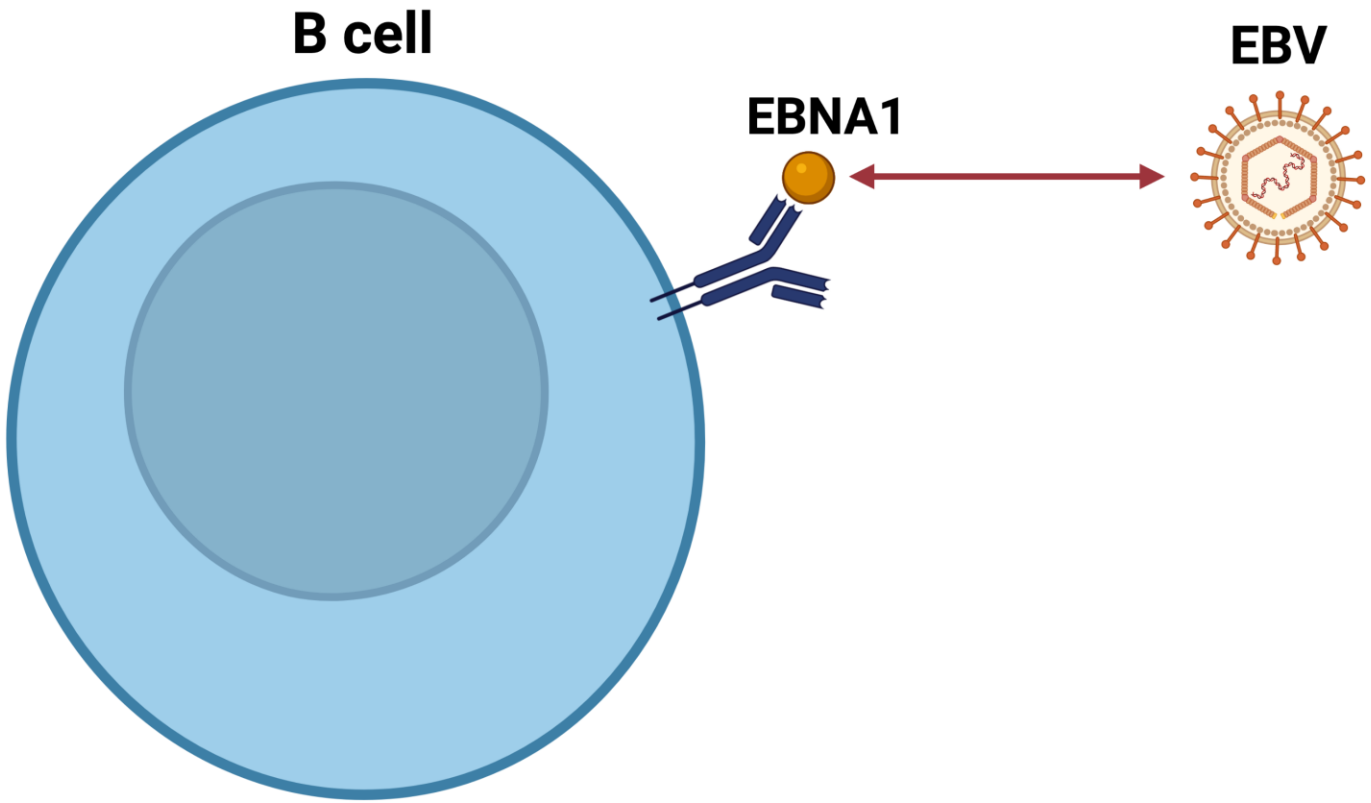
Affinity Maturation and Serine Phosphorylation are Necessary for High Affinity Interaction





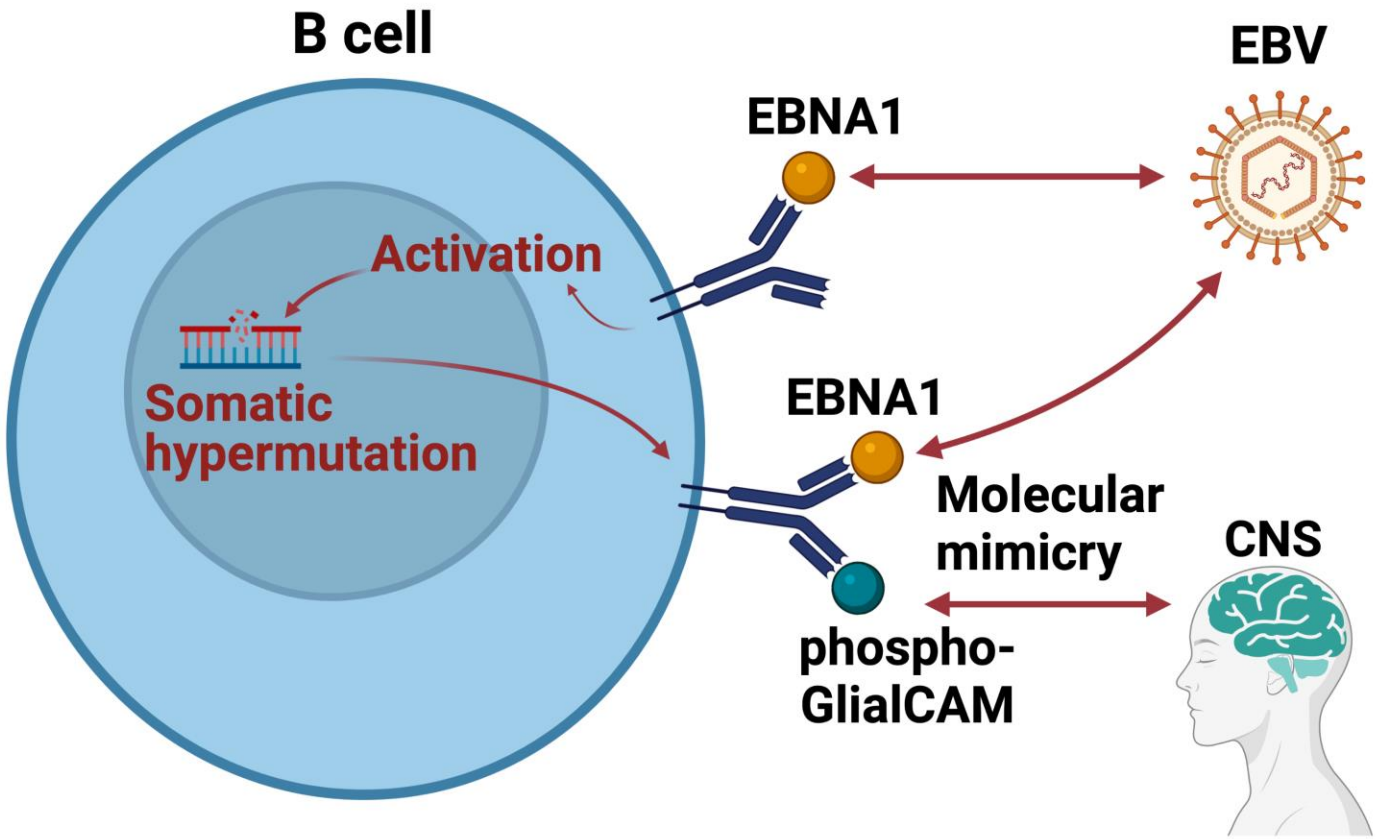
Lanz et al., *Nature*, 2022

Molecular Mimicry between EBNA1 and GlialCAM



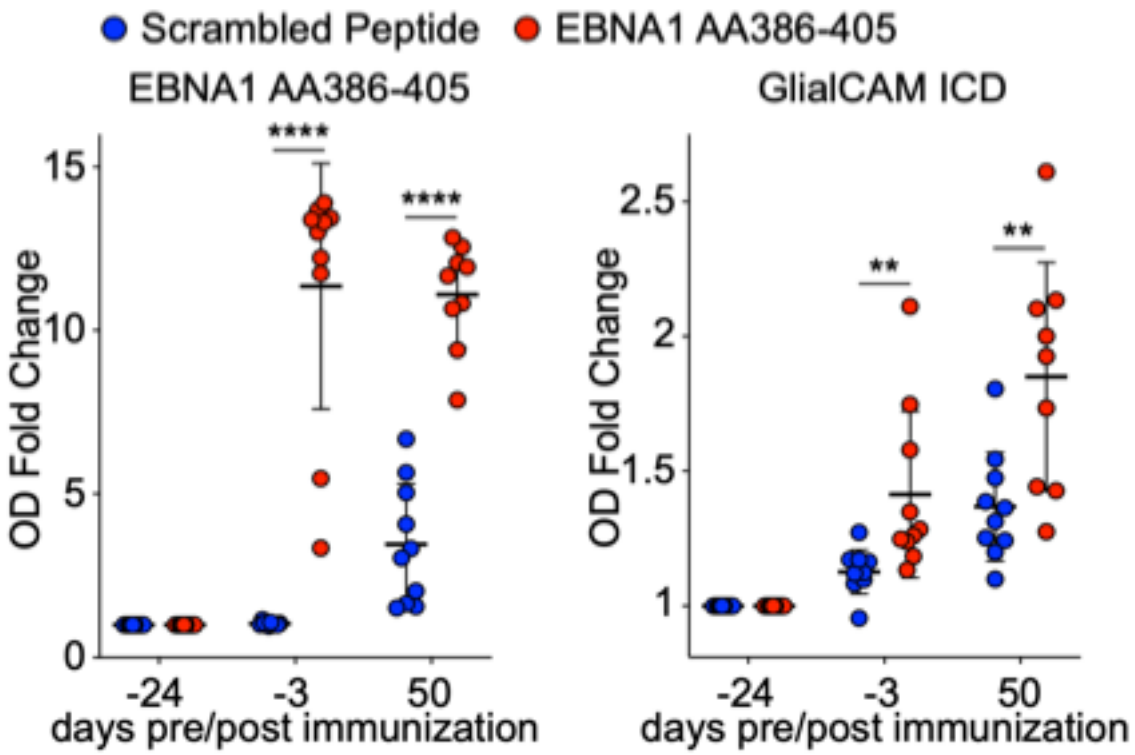
Lanz et al., *Nature*, 2022

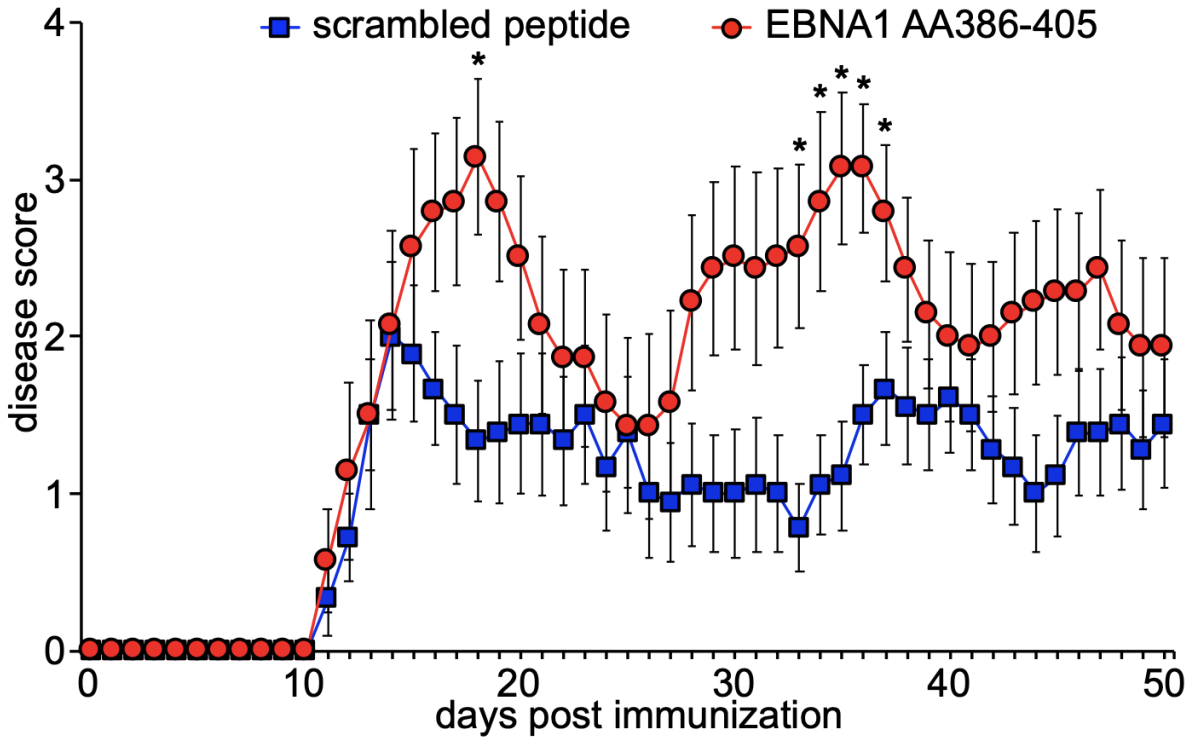
Molecular Mimicry between EBNA1 and GlialCAM



Lanz et al., *Nature*, 2022

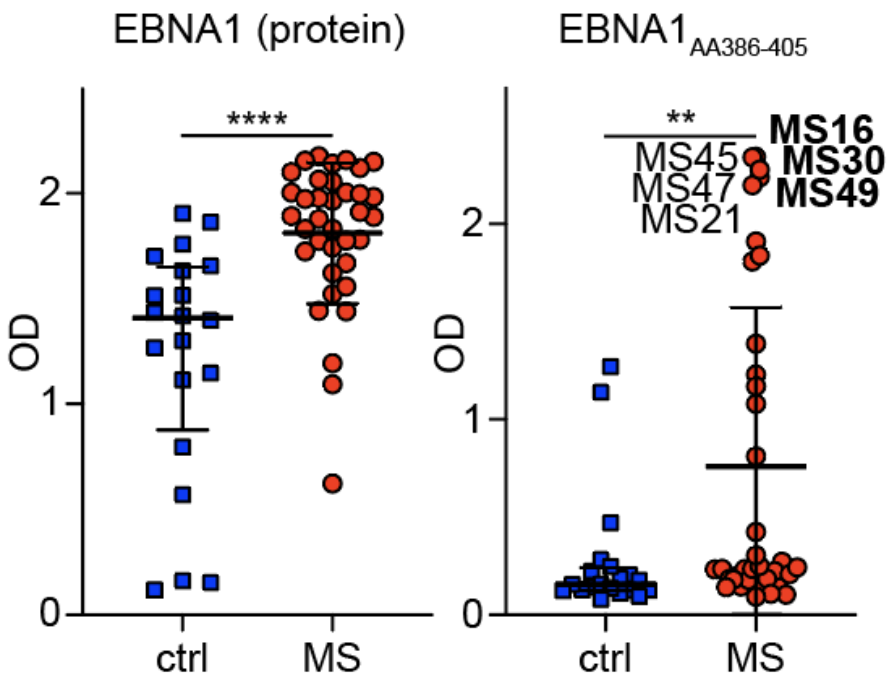
EBNA1 Immunization Generates Anti-GlialCAM Antibodies and Aggravates Neuroinflammation





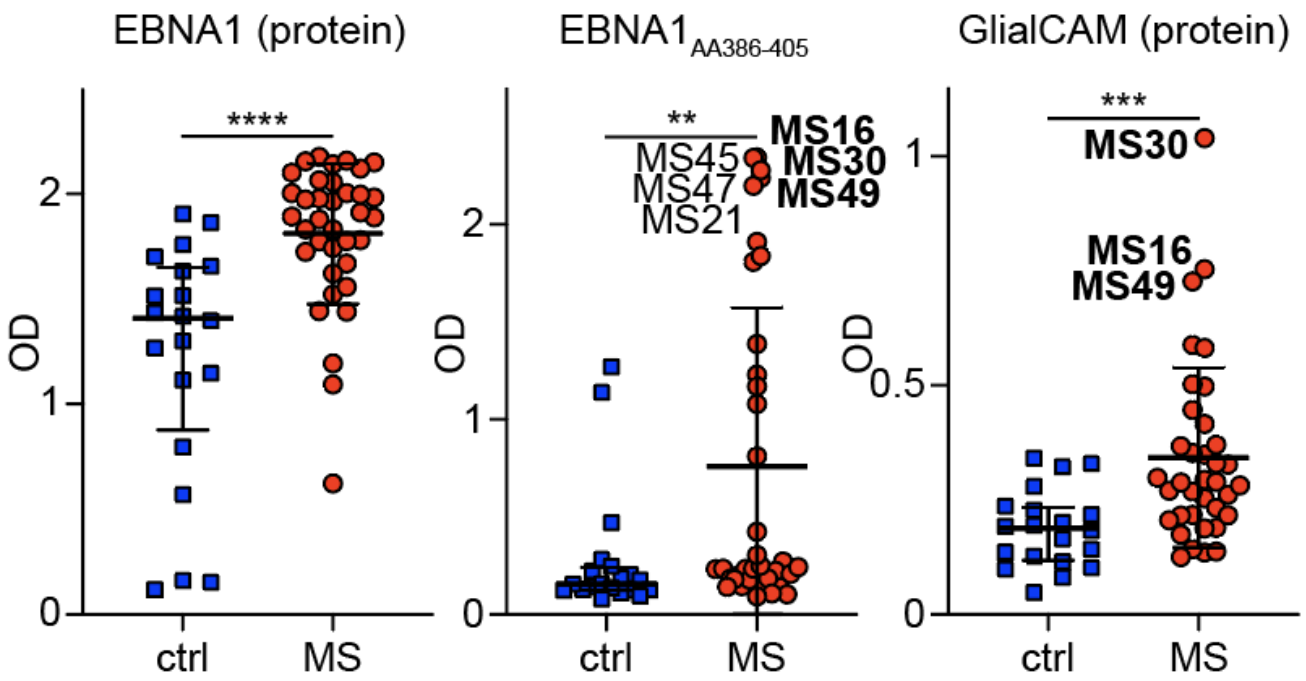
Lanz et al., *Nature*, 2022

Anti-EBNA1/GlialCAM Antibodies in a Subset of MS Patients



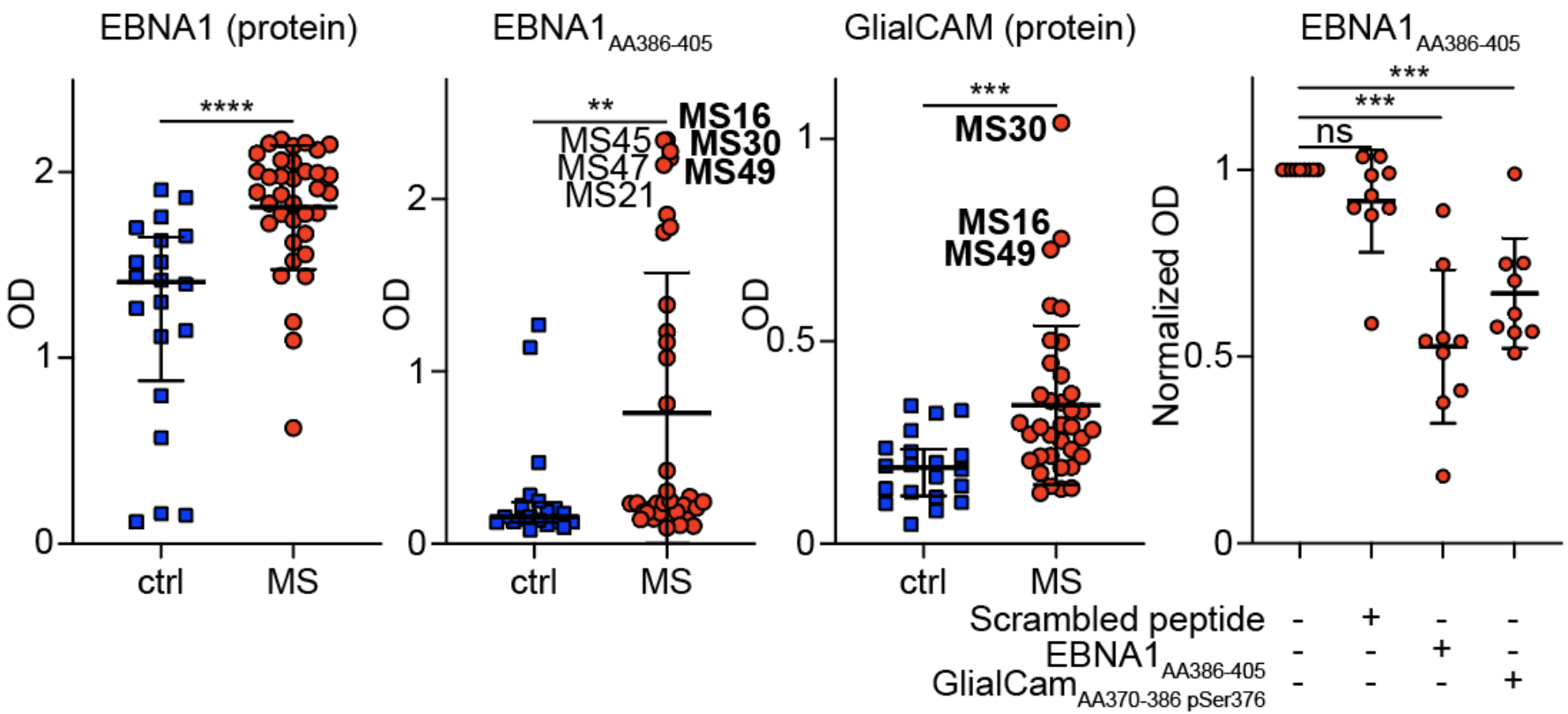
Lanz et al., *Nature*, 2022

Anti-EBNA1/GlialCAM Antibodies in a Subset of MS Patients



Lanz et al., *Nature*, 2022

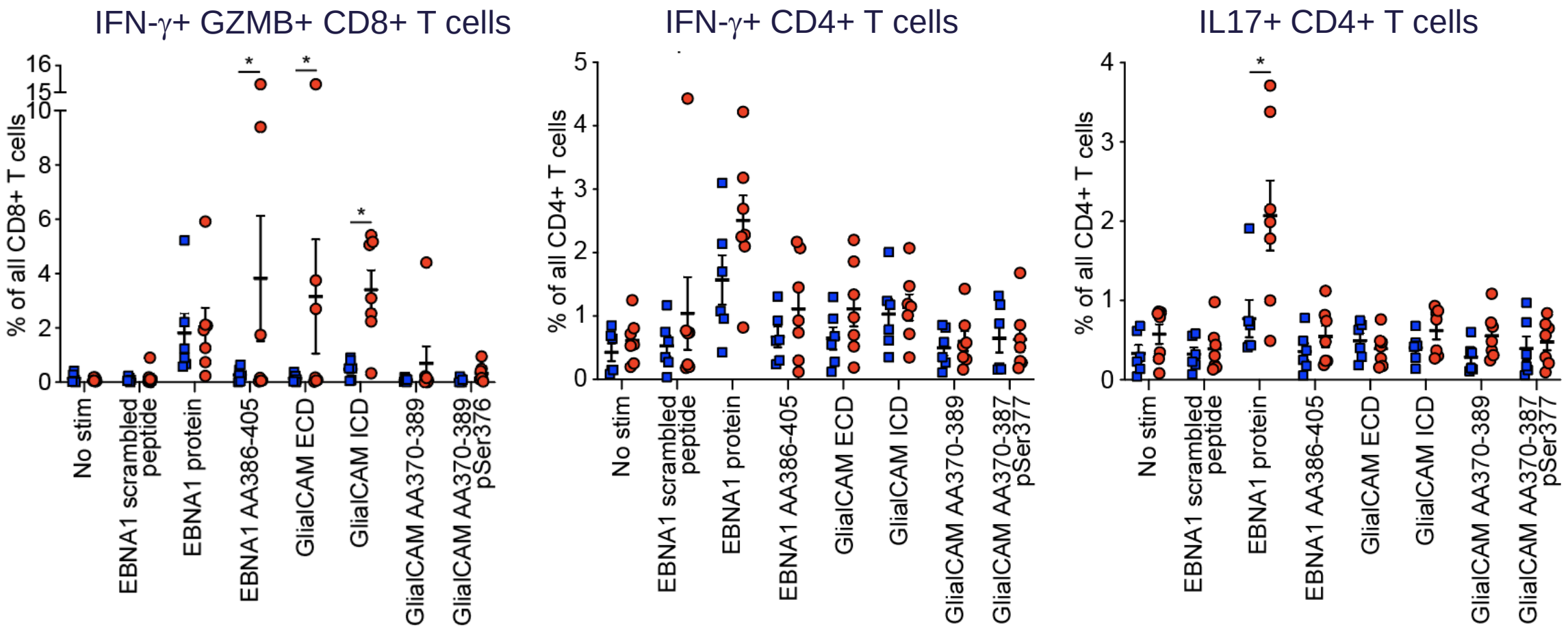
Anti-EBNA1/GlialCAM Antibodies in a Subset of MS Patients



Lanz et al., *Nature*, 2022

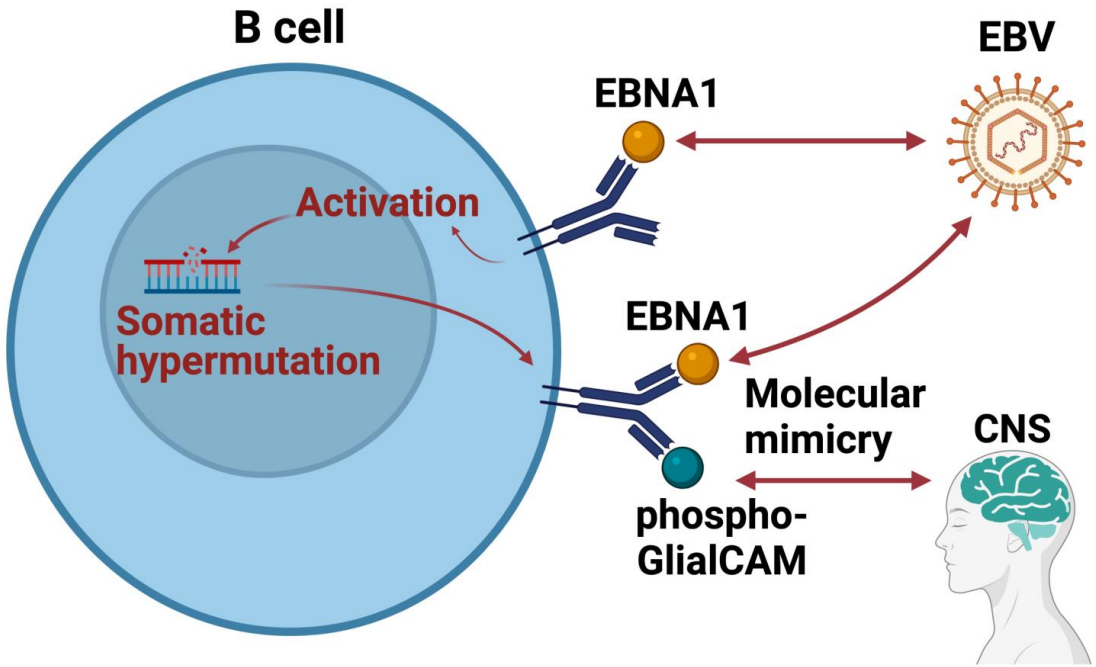
Anti-EBNA1/GlialCAM T cells in MS

Healthy controls
MS patients



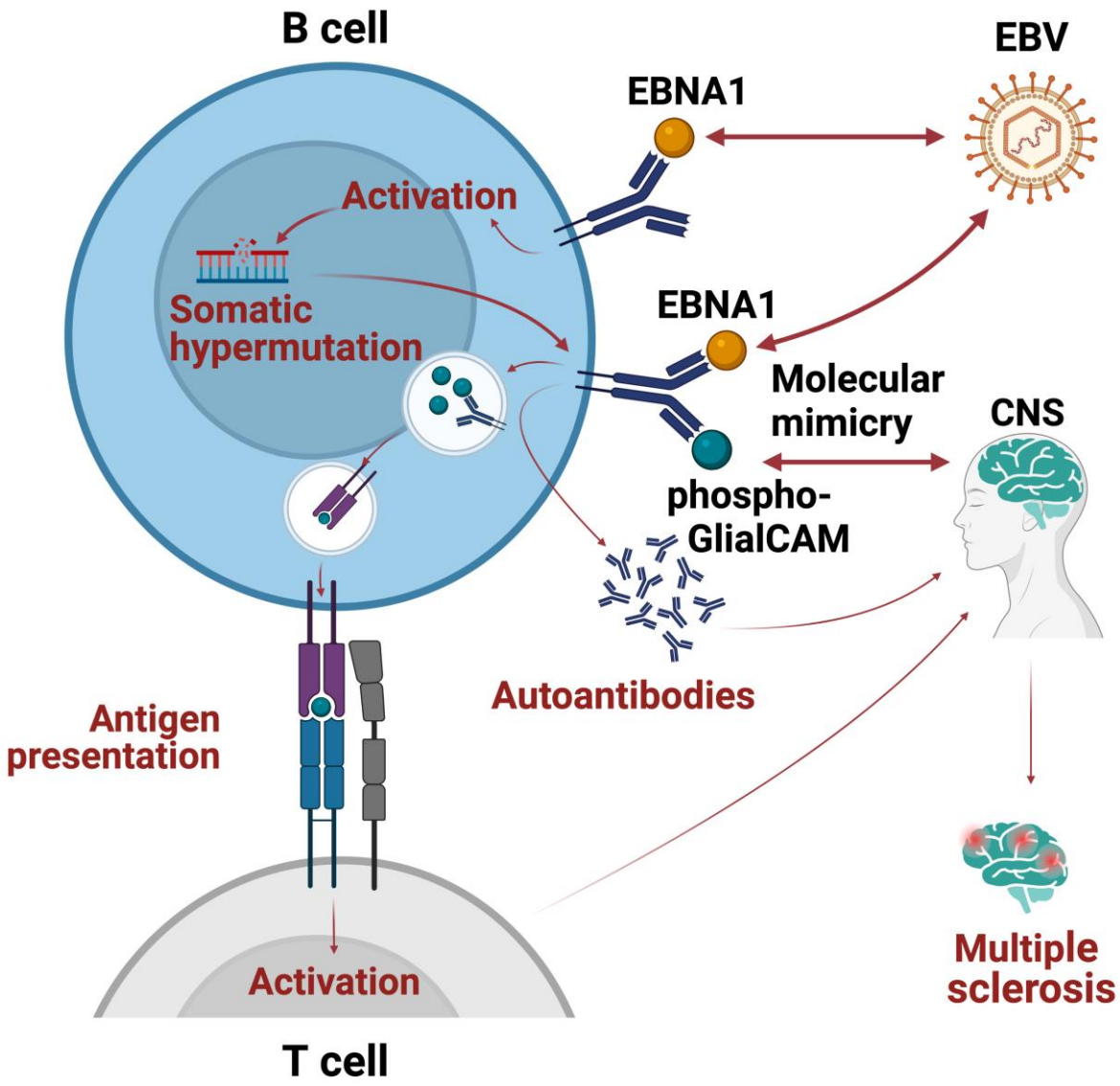
Lanz et al., *Nature*, 2022

Pathomechanism: Molecular Mimicry between EBNA1 and GlialCAM



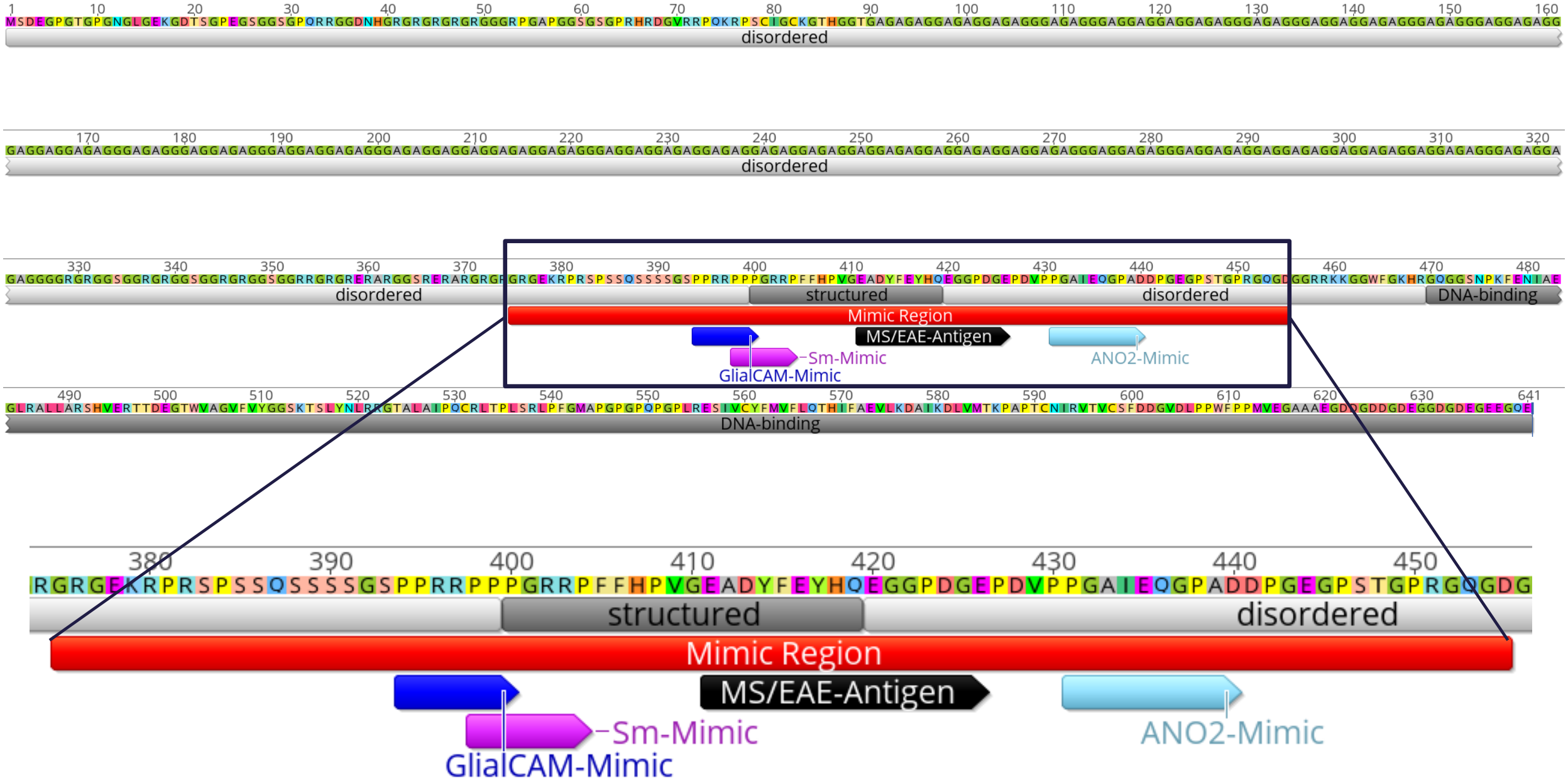
Lanz et al., *Nature*, 2022

Pathomechanism: Molecular Mimicry between EBNA1 and GlialCAM

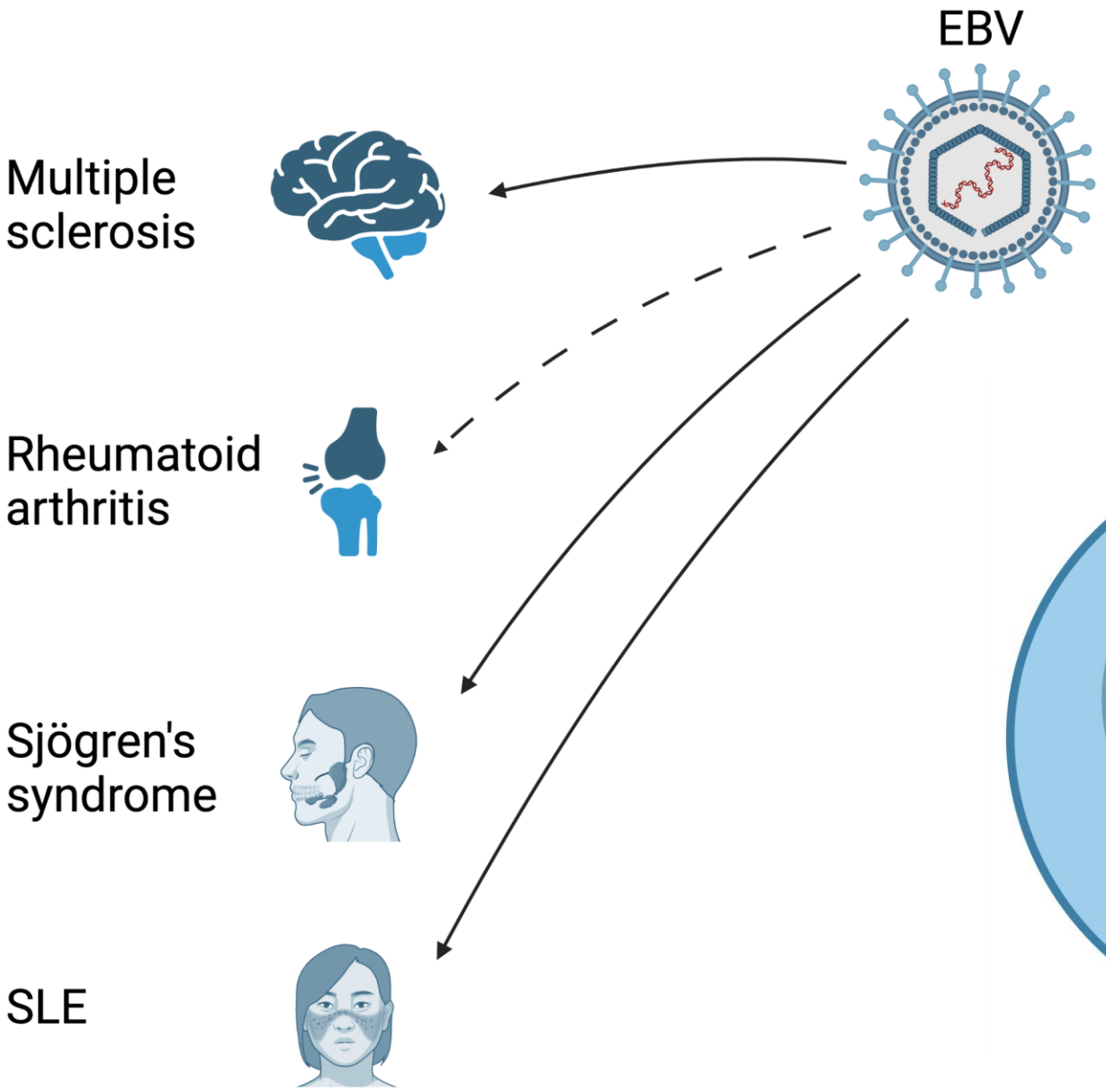


Lanz et al., *Nature*, 2022

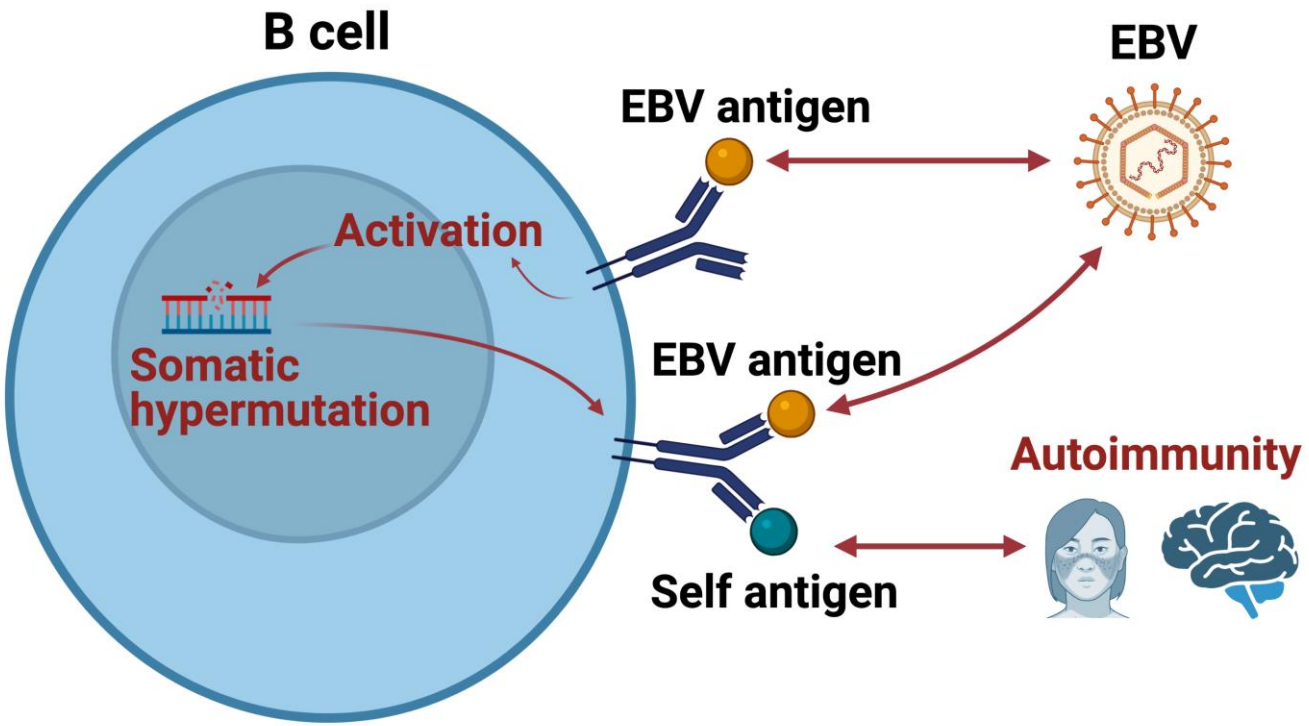
Multiple Autoimmune Mimics in a Small Region of EBNA1



Summary: Molecular Mimicry between EBV and Self Antigens



Molecular mimicry with self antigens



Acknowledgements

Robinson Lab

Tobias Lanz
Camille Brewer
Shady Younis
Jae Seung Moon
Shani Jahanbani
Orr Sharpe
Jessica Kirschmann
Alejandro Gomez
Eun Kyung Song
Heidi Wong
Qian Wang
Natalia Zamora

Collaborators

Stanford
Larry Steinman
Peggy Ho

Rockefeller
Dana Orange
Caryn Hale

U. Colorado
Michael Holers
Kevin Deane
Jennifer Seifert

UCSF
Michael Wilson
Joe DeRisi

BRI
Jane Buckner
Eddie James

NIH
Mariana Kaplan

NYU
Jill Buyon
Robert Clancy

U.S. Department of Veterans Affairs

Rheumatology Research Foundation
Advancing Treatment | Finding Cures

NIAMS
National Institute of Arthritis and Musculoskeletal and Skin Diseases