

A novel proposal: antibody treatment for AFM

Matthew R. Vogt, M.D., Ph.D.

Clinical Fellow in Pediatric Infectious Diseases

Laboratory of James E. Crowe, Jr., M.D.

Vanderbilt University Medical Center

Soon-to-be Assistant Professor of Pediatrics and Microbiology & Immunology

University of North Carolina at Chapel Hill

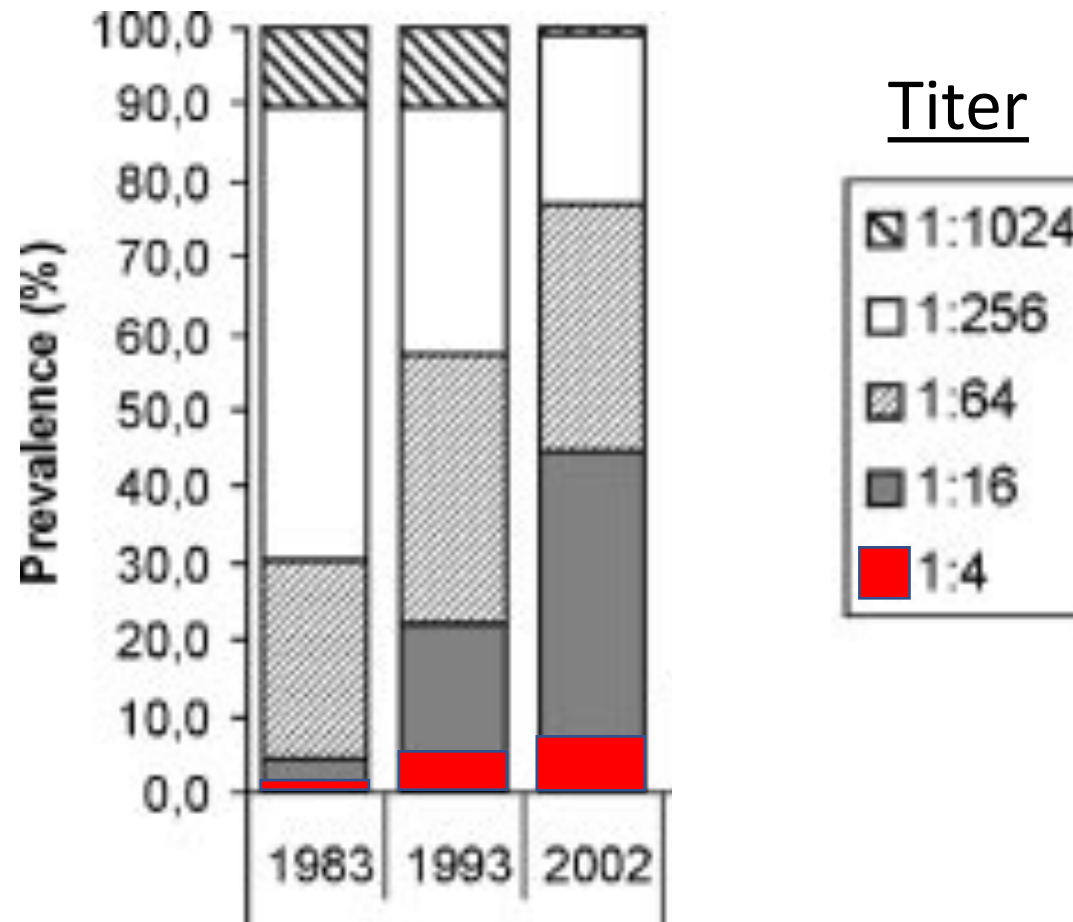
I have no financial relationships to disclose.

I am co-inventor on a pending patent for
EV-D68-binding human monoclonal antibodies.

Outline

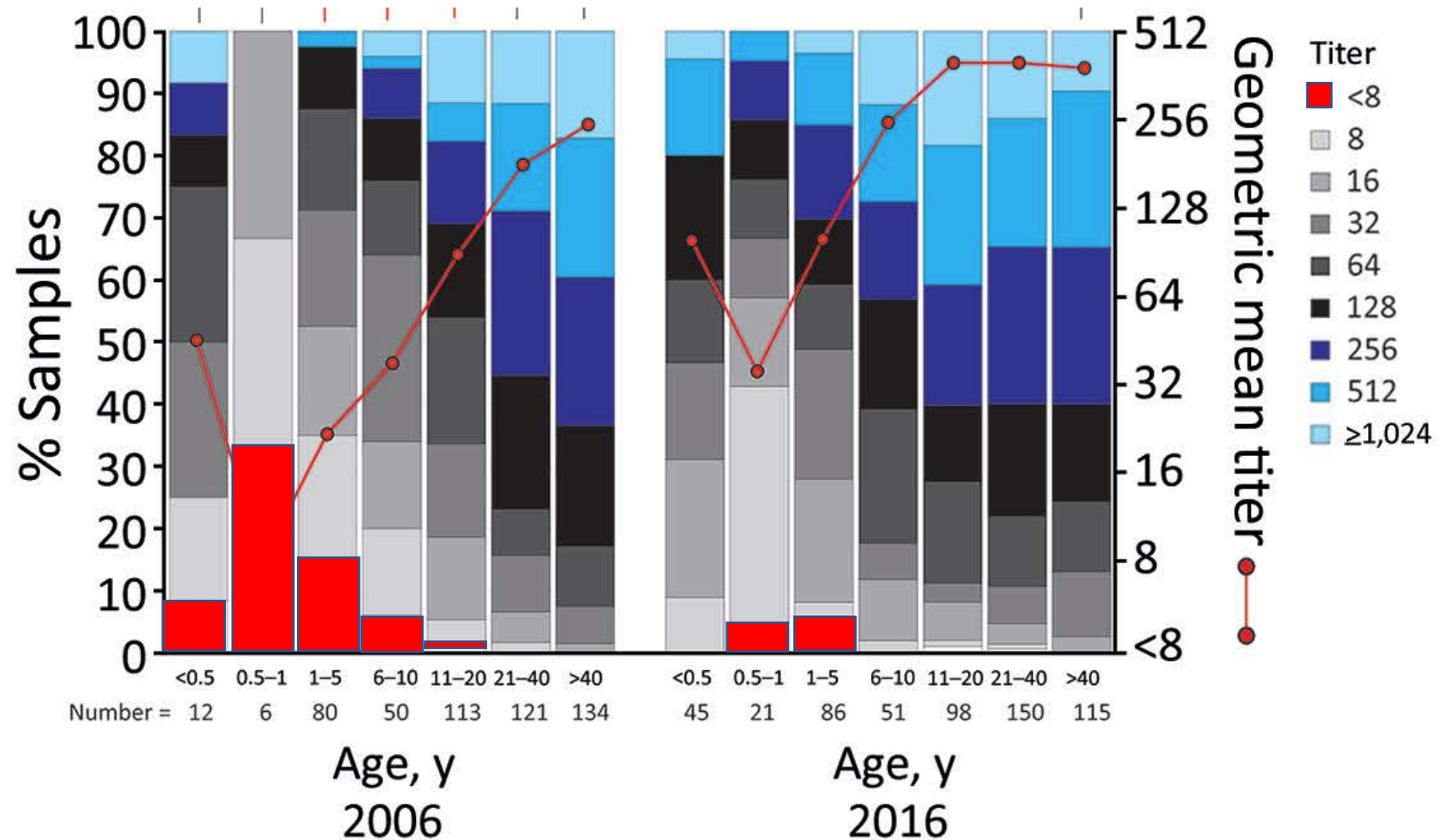
- Review EV-D68 seroepidemiology
 - Adults – near universal seroprevalence
 - Children – nadir in early years of life
- Human monoclonal antibodies (mAbs) *in vitro*
 - Neutralize with variable cross-reactivity
- Human mAb *in vivo*
 - Highly efficacious
- MAb development for use in humans

Finland, 1983, 1993, & 2002

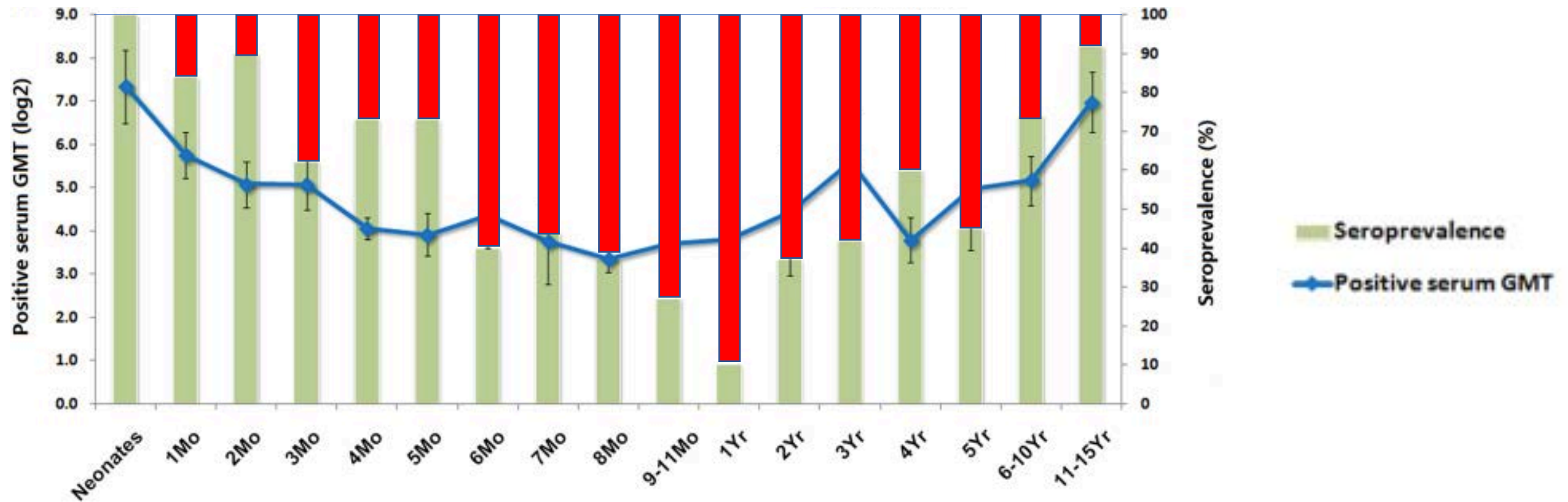


- Pregnant (adult) women

United Kingdom, 2006 & 2016



China, 2010



Seroepidemiology conclusions

- Nearly all adults have EV-D68 neutralizing antibodies
 - Across time
 - Across the world
- Newborns have neutralizing antibodies
- Neutralization titers nadir in early years of childhood
 - Similar age window as AFM

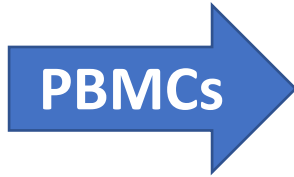
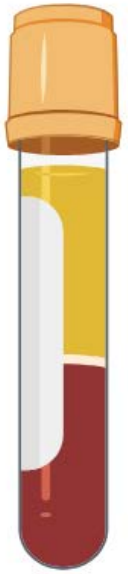
Hypothesis

Antibody protects from AFM, but not mucosal disease

Aims

- 1) Catalog the different classes of EV-D68 binding antibodies that humans make**
- 2) Determine how antibodies modify EV-D68 pathogenesis**

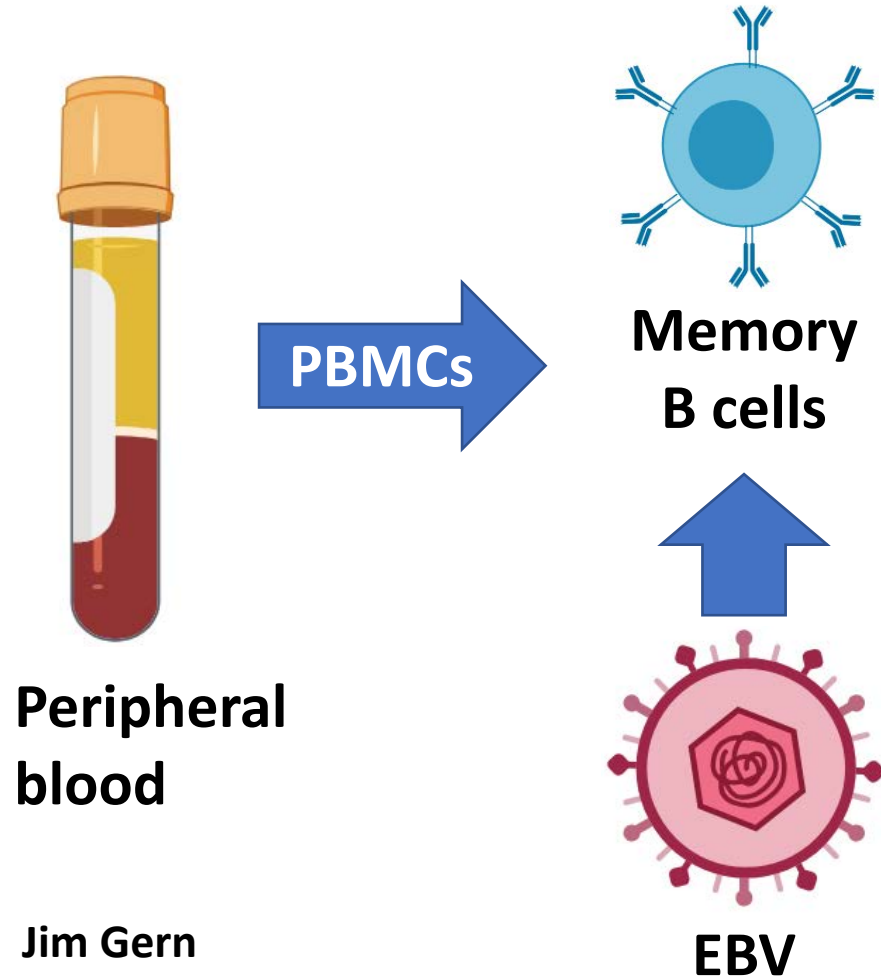
62 human monoclonal antibodies (mAbs) isolated



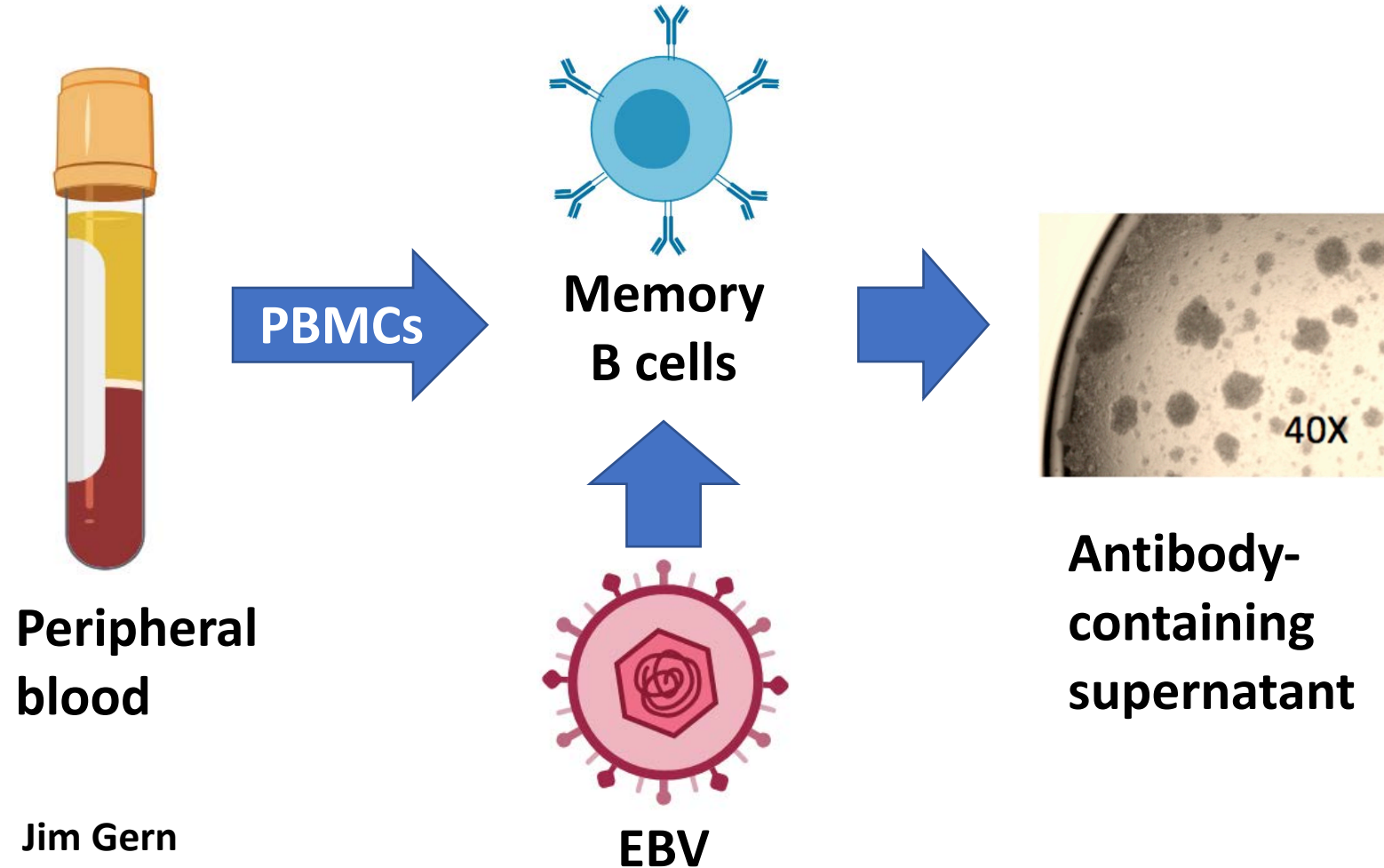
**Peripheral
blood**

Jim Gern

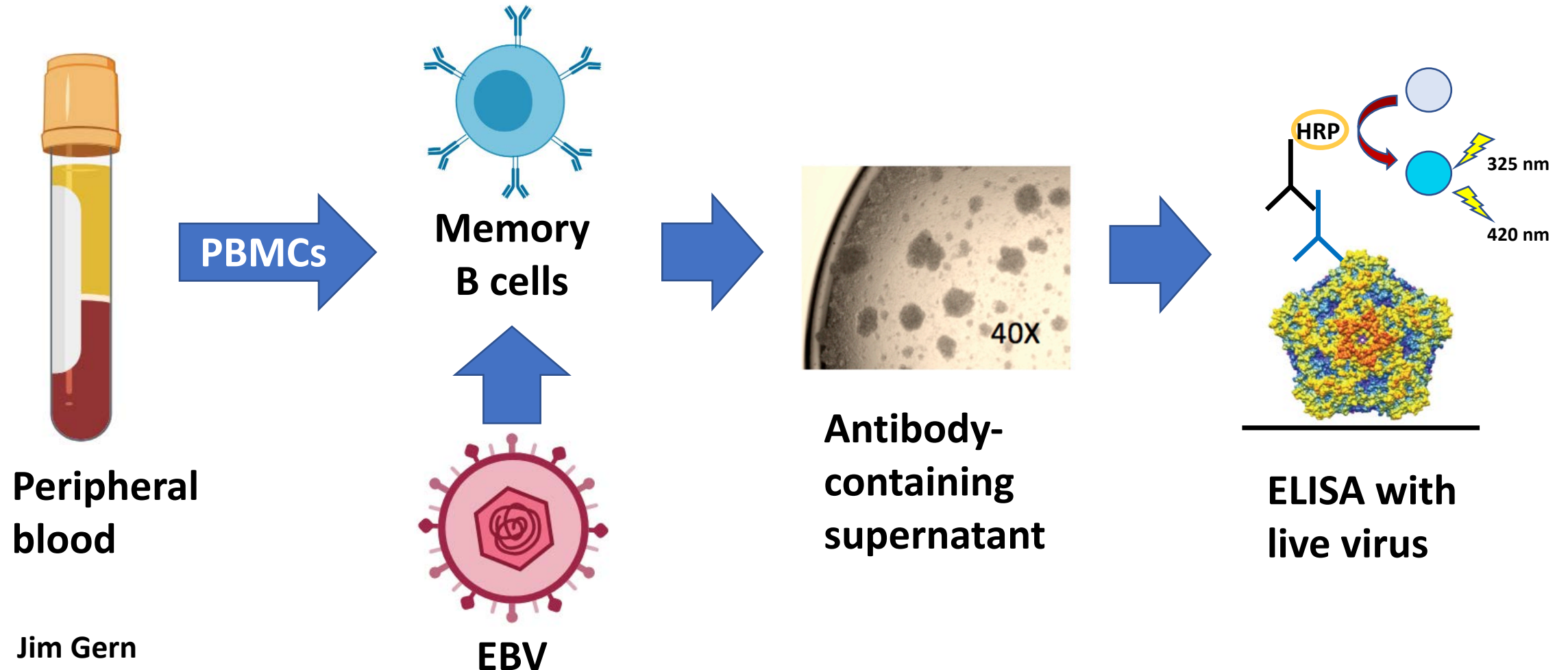
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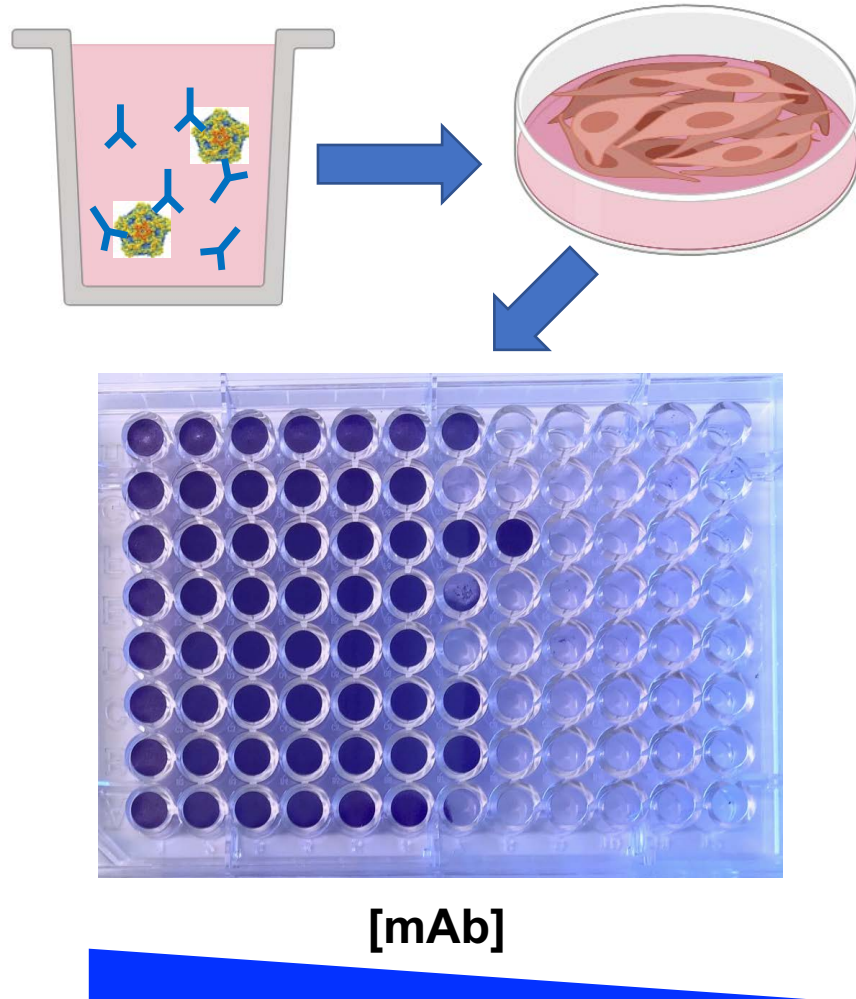
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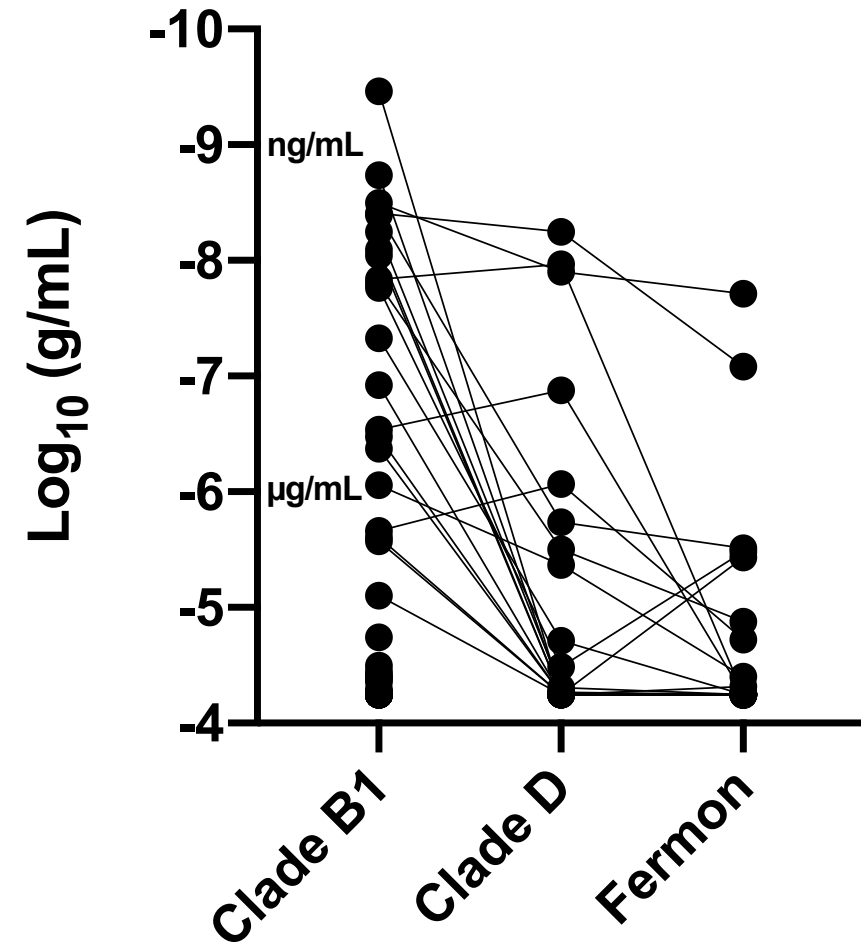
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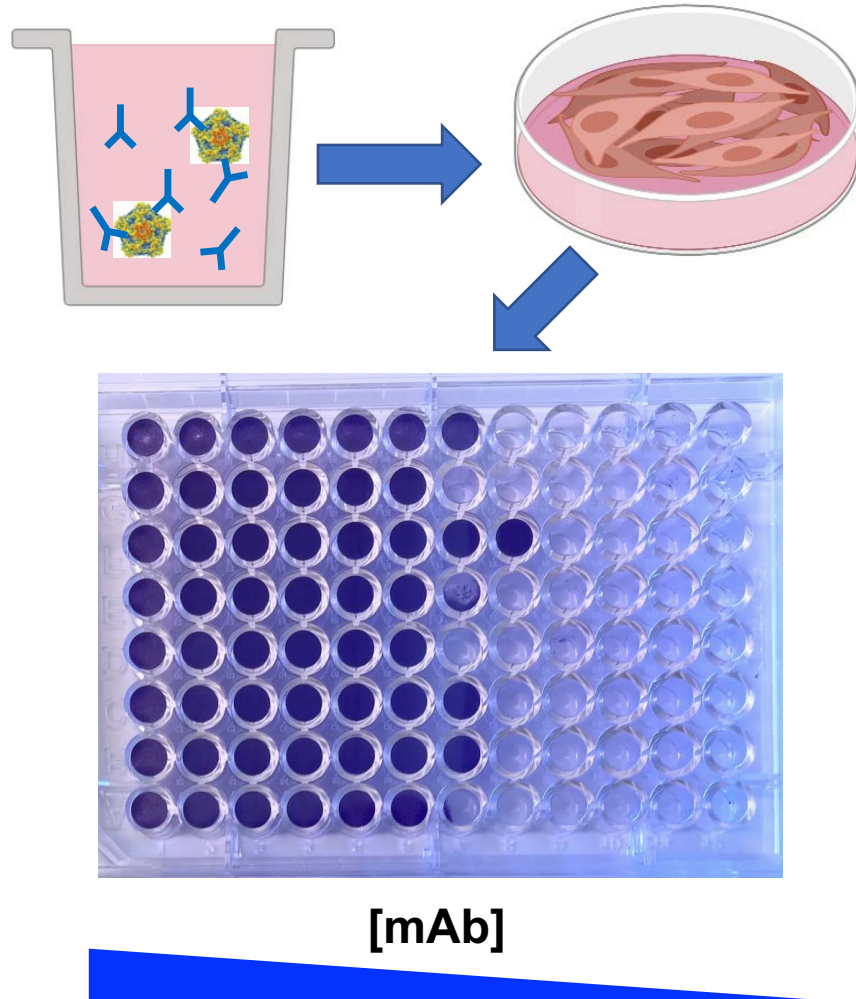
Some mAbs neutralize EV-D68 quite potently



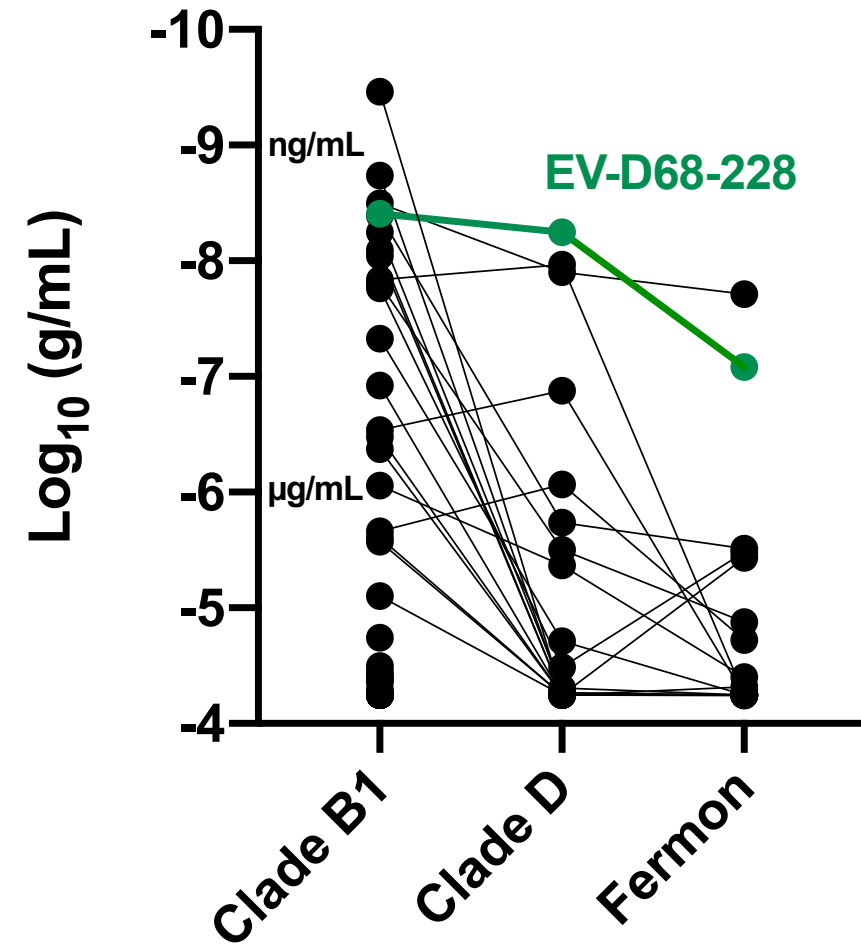
EV-D68 mAb Neutralization
IC₅₀ Values



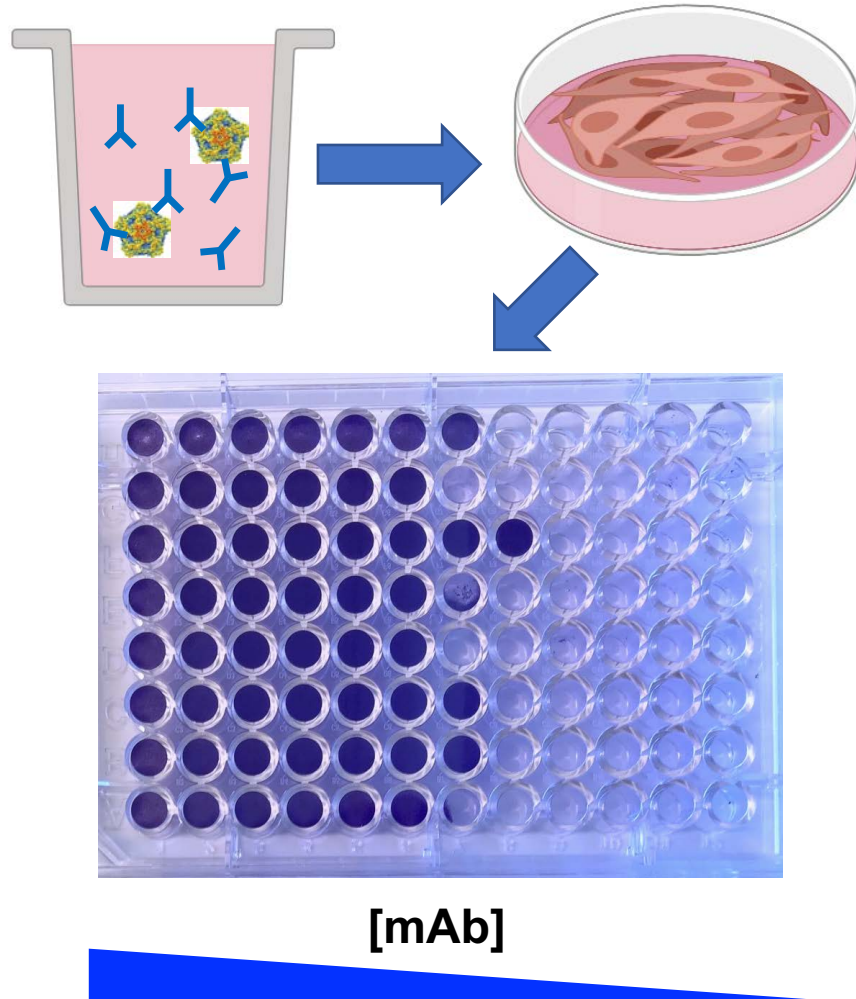
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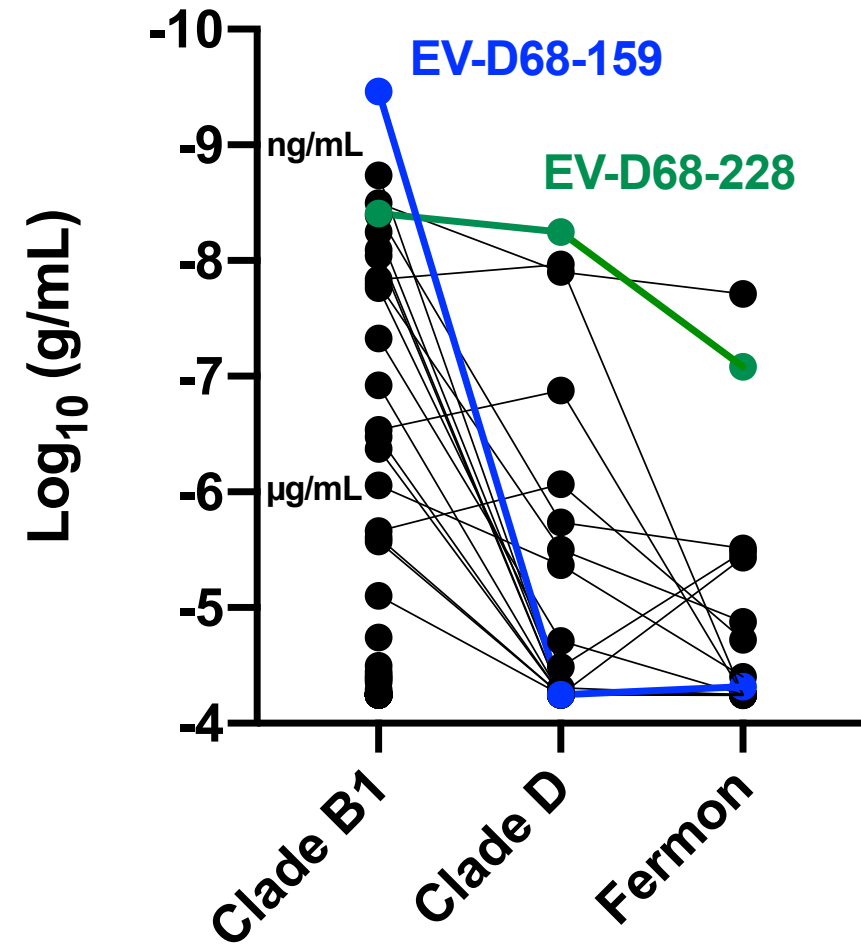
EV-D68 mAb Neutralization
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EV-D68 mAb Neutralization
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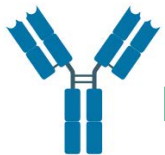
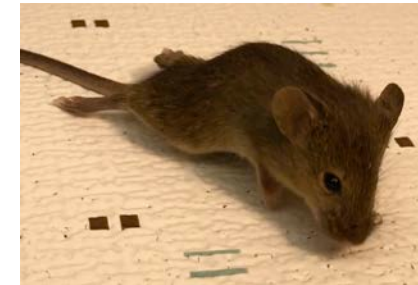
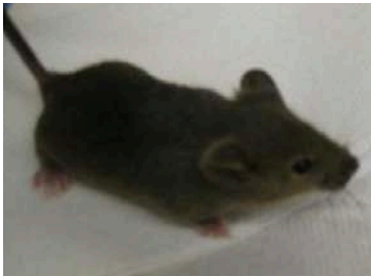


Neurologic mouse model

Day -1

Day 0

Day 1 +



IVIG

EV-D68-228

Placebo mAb

Intraperitoneal



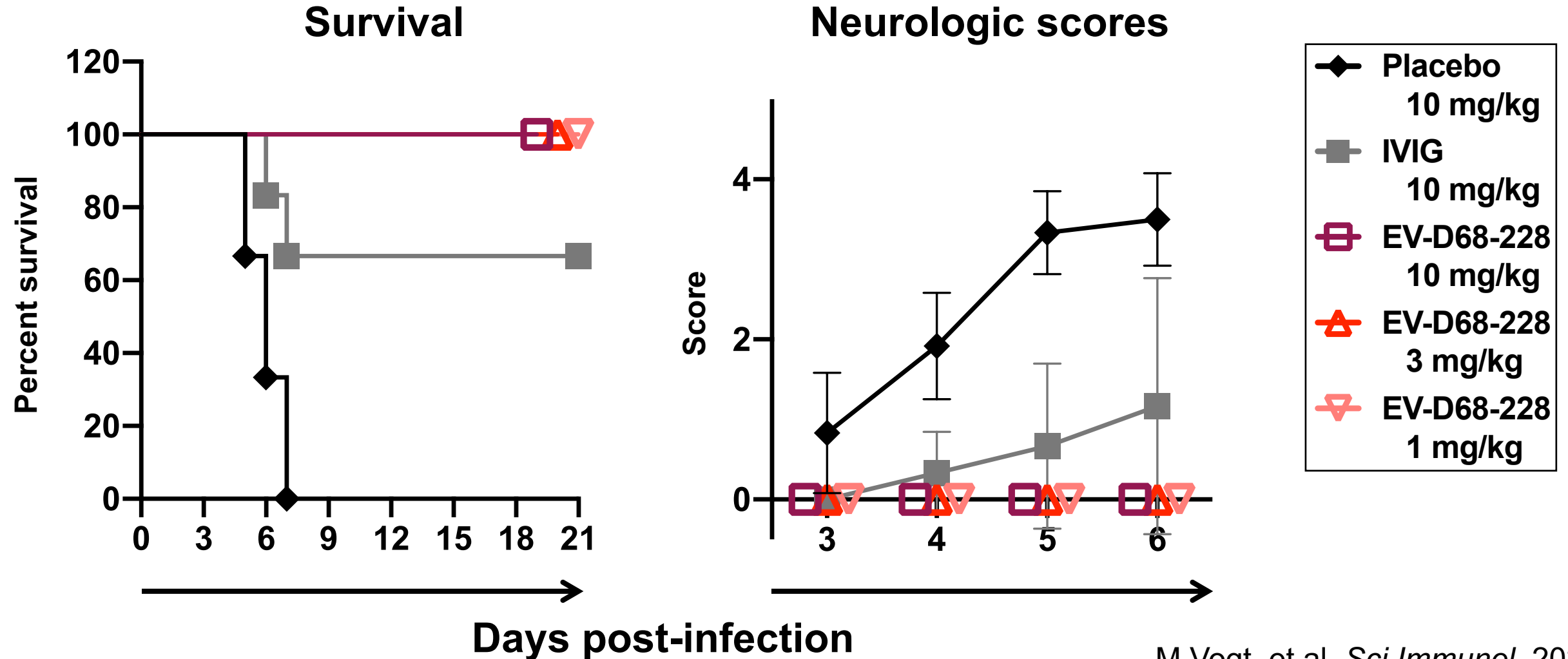
Clade B1

Intraperitoneal

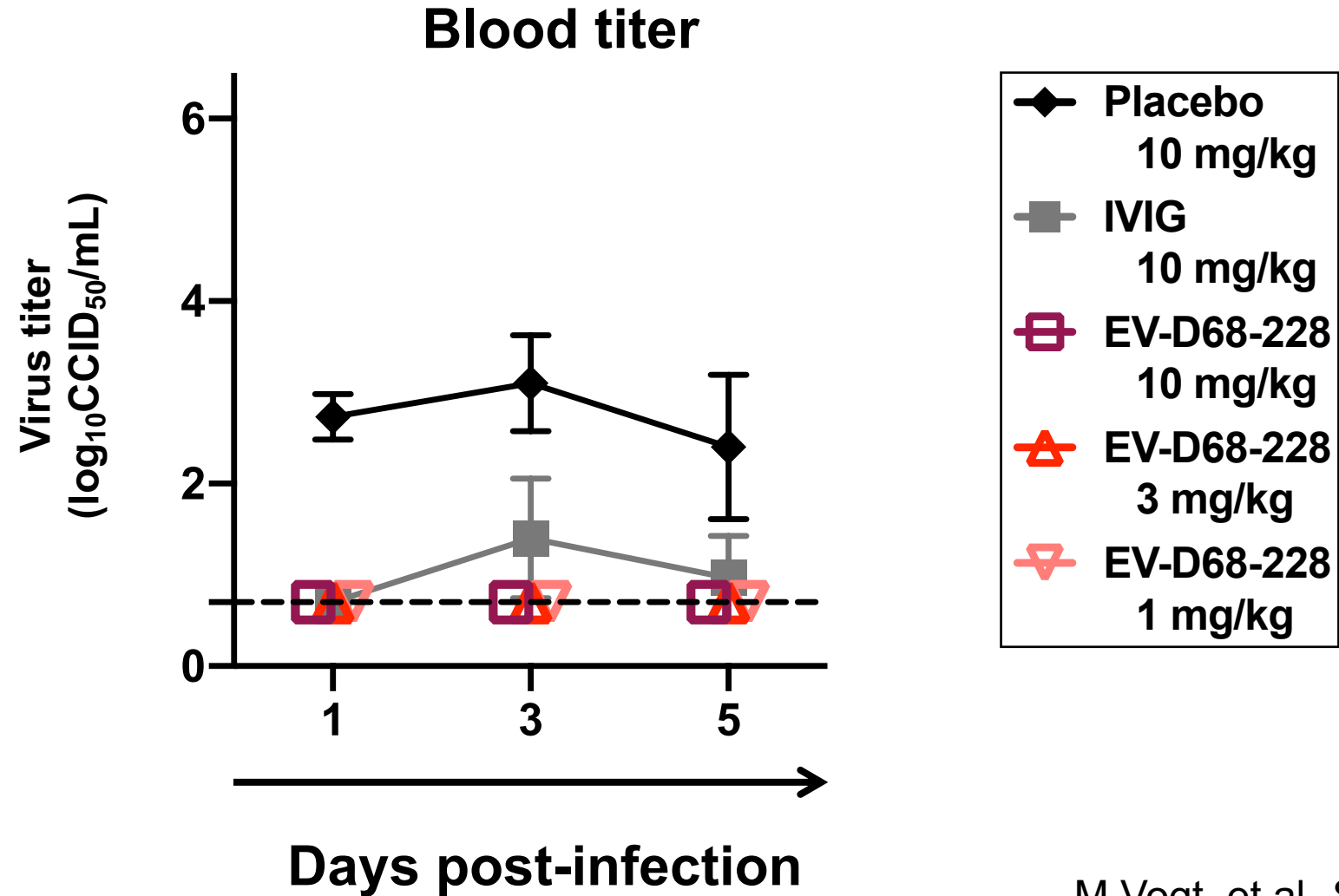


BL Hurst, et al. *Virology*. 2019

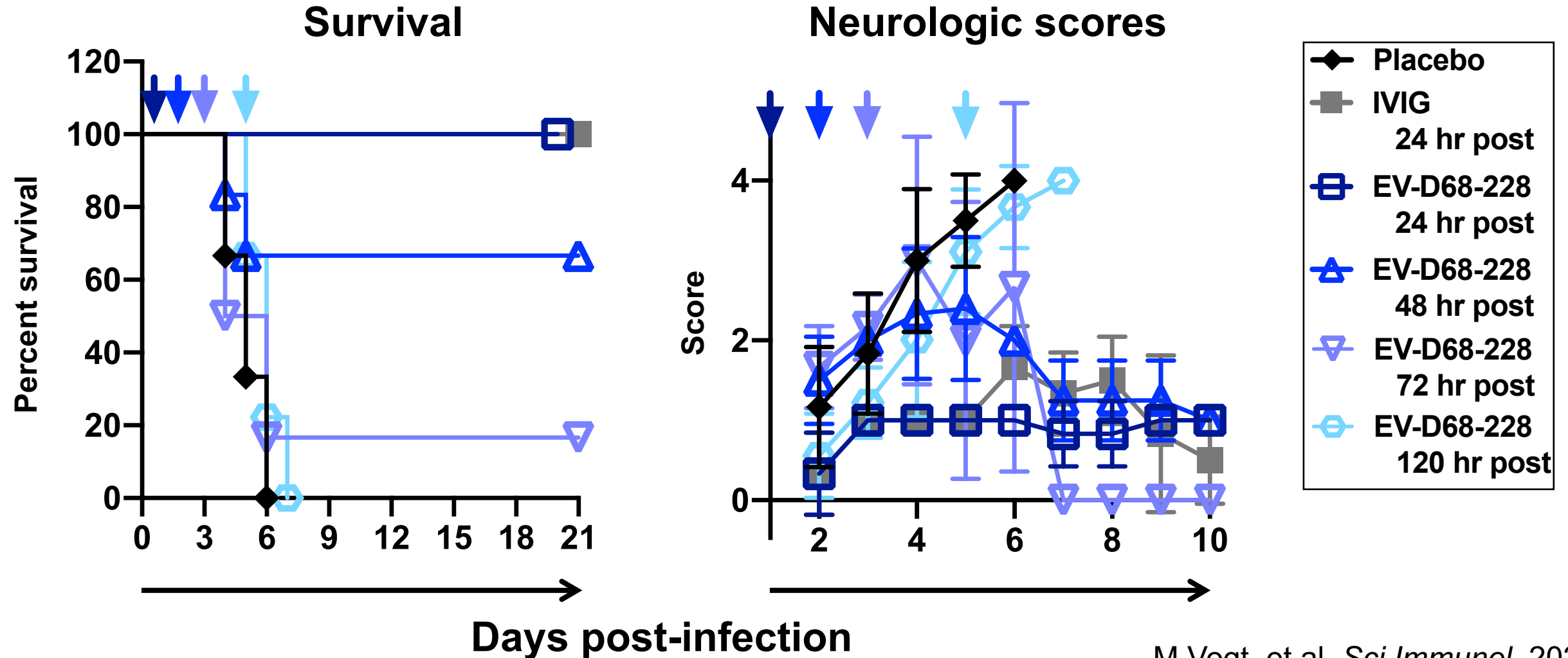
EV-D68-228 PROPHYLAXIS protects from death and disease



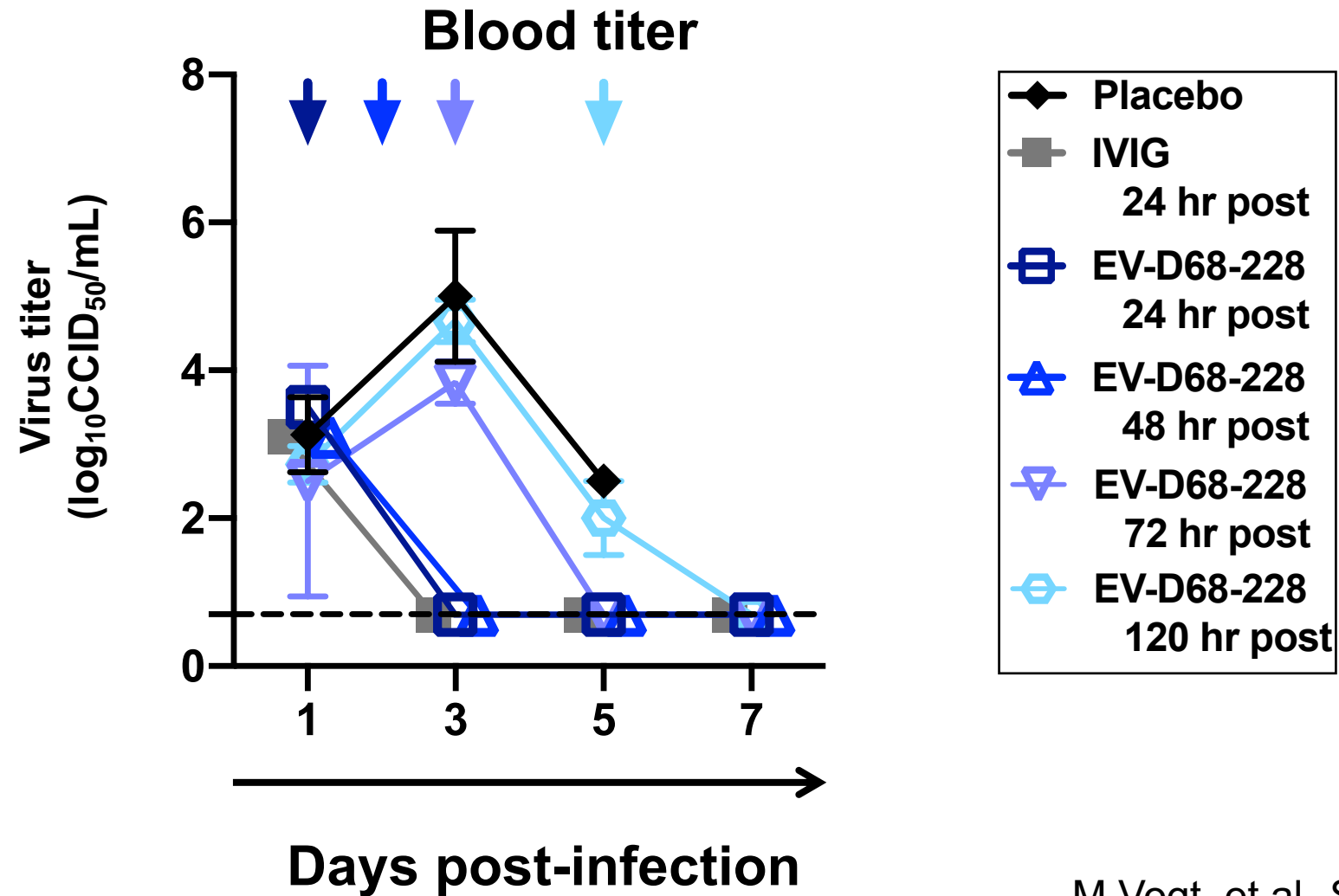
EV-D68-228 PROPHYLAXIS sterilizes the blood



EV-D68-228 TREATMENT protects from death and disease



EV-D68-228 TREATMENT reduces blood titers



EV-D68-228 human therapy development

- **Partnered with industry**
 - **Produced in plants by ZabBio and Kentucky BioProcessing**
- **Ongoing safety profiling of plant-produced mAb**
 - *In vitro* cross-reactive neutralization confirmed
 - *In vivo* protection identical
 - Safety studies being pursued
- **Could be ready for efficacy trials by 2021**



Nicotiana benthamiana

Summary and Conclusions

- **Nearly all adults have EV-D68 neutralizing antibodies**
- **Antibody naïve age cohorts overlap with AFM age cohorts**
- **EV-D68-228, a potently neutralizing, cross-reactive mAb, protects mice at both the respiratory mucosa and the CNS**
 - **Vaccines are likely to prevent AFM**
 - **We are developing EV-D68-228 for use as a human therapeutic**

Acknowledgements

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AFM: From the clinic to the bench and back to the patient



E. Ann Yeh, MD, FRCPC, Dip ABPN.

*Professor, Faculty of Medicine, University of
Toronto*

*Director, Pediatric MS and Neuroinflammatory
Disorders Program*

*Senior Associate Scientist, Division of
Neuroscience and Mental Health, SickKids
Research Institute*

The Hospital for Sick Children