



Monoclonal antibody-mediated clearance of rabies virus from the central nervous system

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Human-Animal Interface



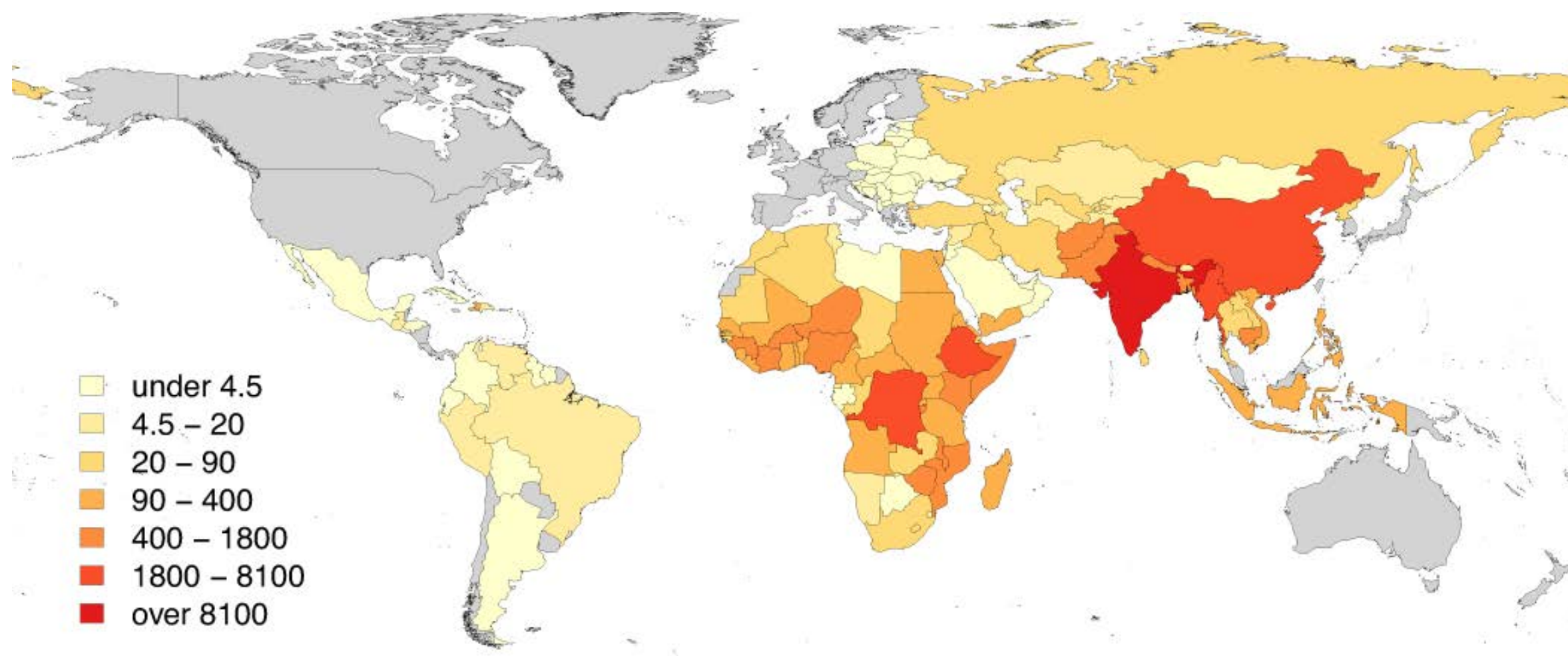
Outline

- Introduction
- Selection of the mAb cocktail
- Post-exposure prophylaxis – PEP
- Late PEP in vivo experiments
- Conclusions and ongoing evaluations

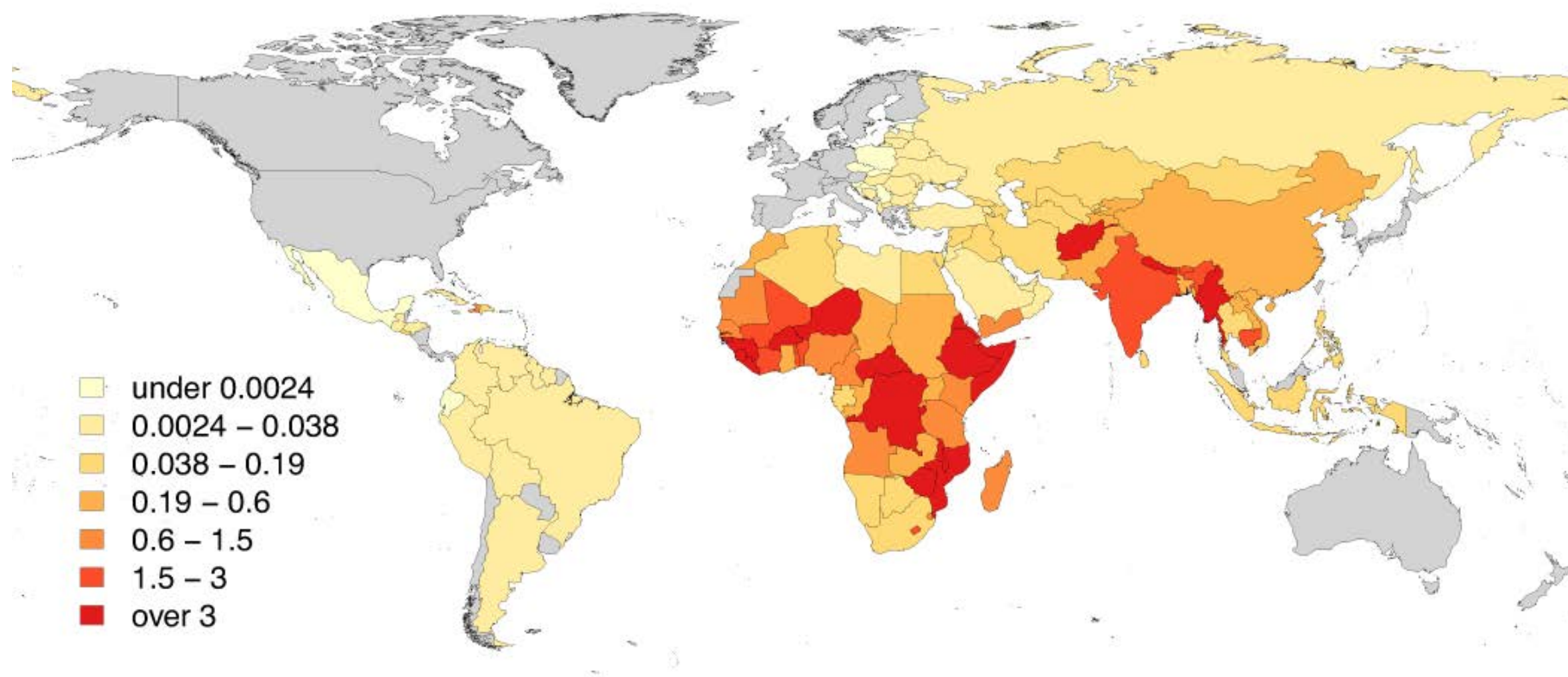


Rabies: the key-facts

- Rabies virus has a fatality rate close to 100%
- Approximately 17 million people are treated following a bite from an infected animal (mostly dogs)
- Vaccination and post-exposure prophylaxis (PEP) are effective, but there is no cure for the symptomatic infection



→ *Human rabies deaths*



→ *Per capita deaths*



Research Article

Transparent Process

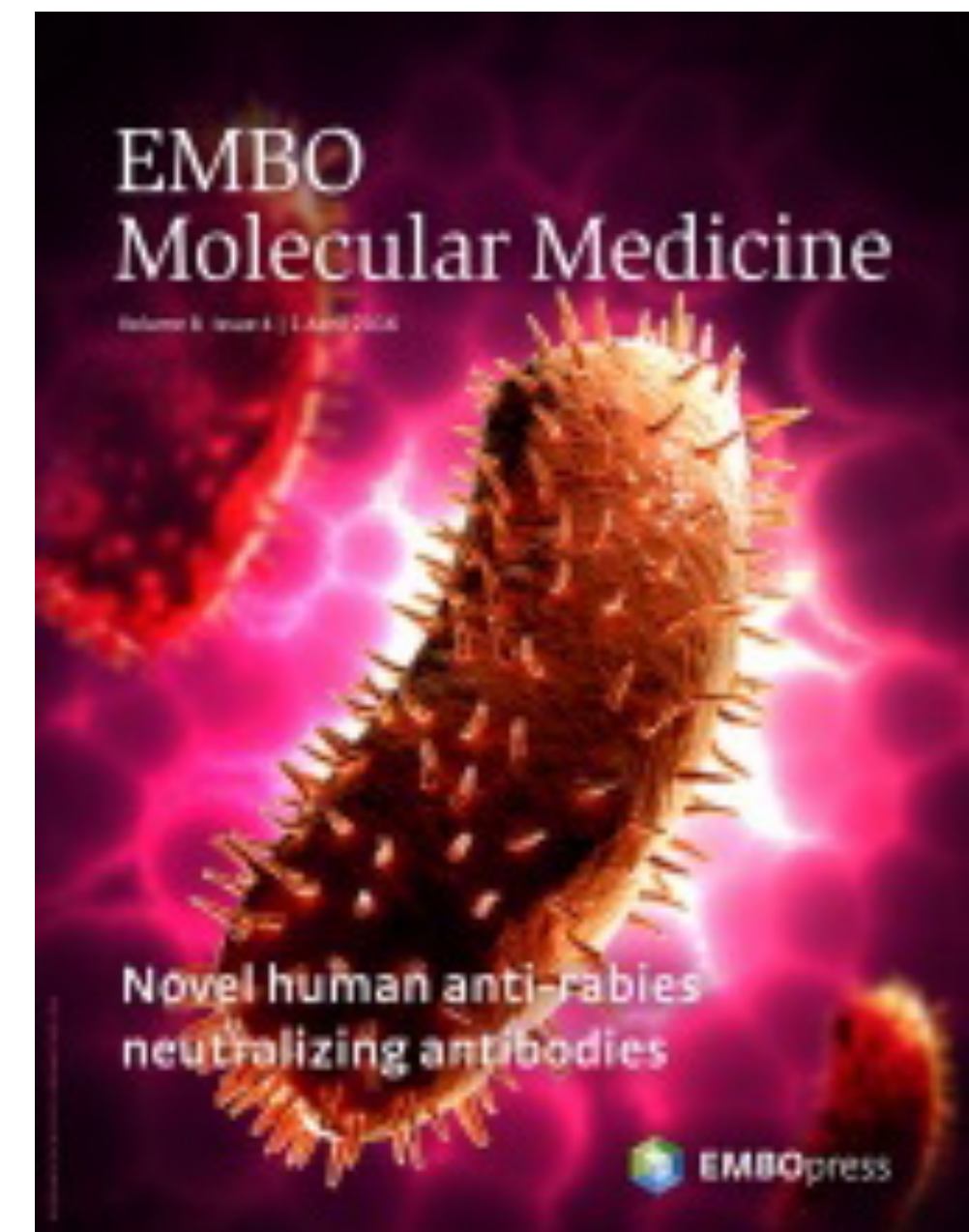
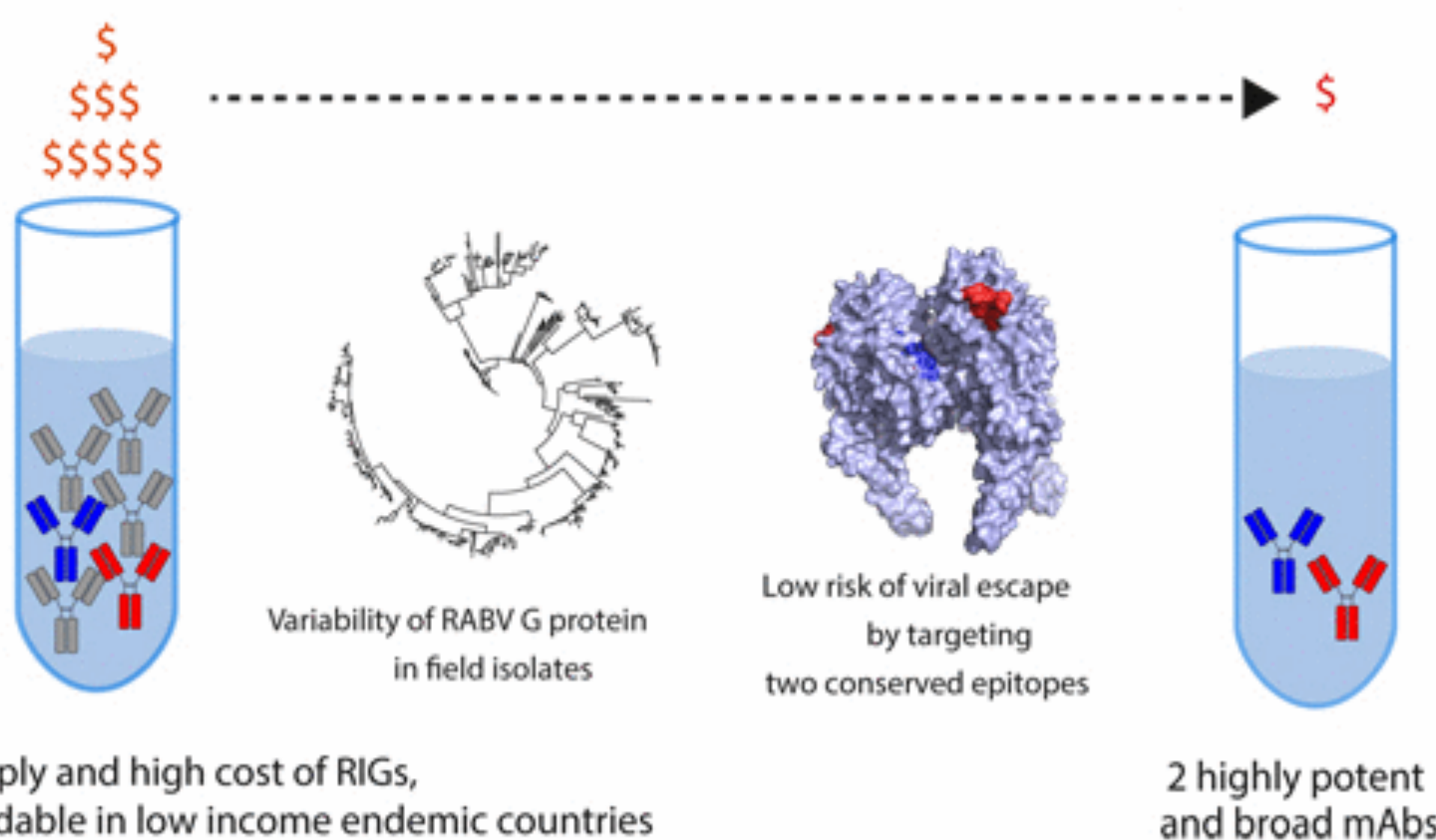
Source Data

Open Access

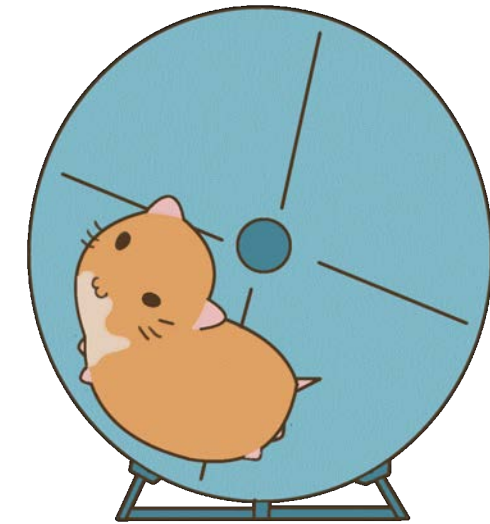
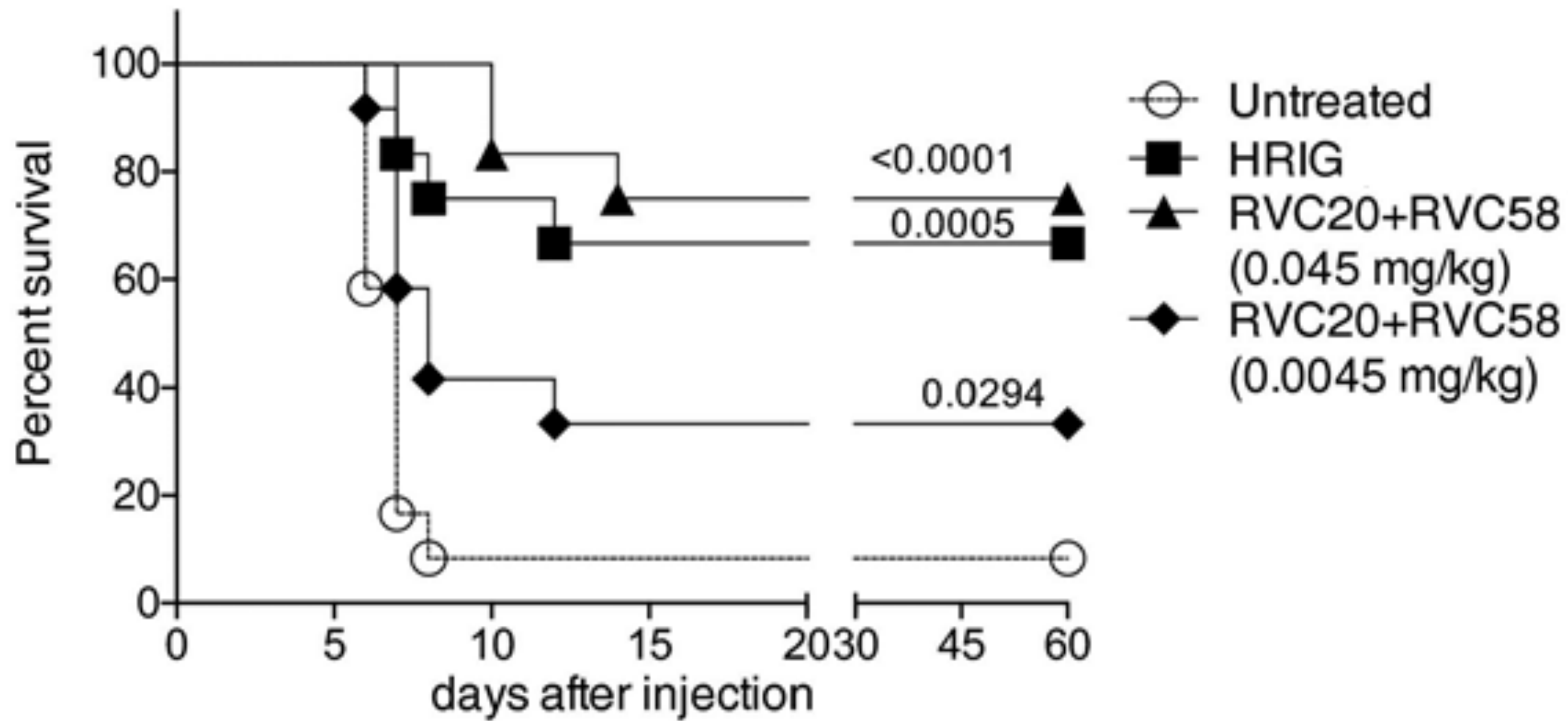
Development of broad-spectrum human monoclonal antibodies for rabies post-exposure prophylaxis

Paola De Benedictis, Andrea Minola, Elena Rota Nodari, Roberta Aiello, Barbara Zecchin, Angela Salomoni, Mathilde Foglierini, Gloria Agatic, Fabrizia Vanzetta, Rachel Lavenir, Anthony Lepelletier, Emma Bentley, Robin Weiss, Giovanni Cattoli, Ilaria Capua, Federica Sallusto, Edward Wright, Antonio Lanzavecchia, Hervé Bourhy, Davide Corti

Bite by a rabid animal → Vaccination + RIGs administration

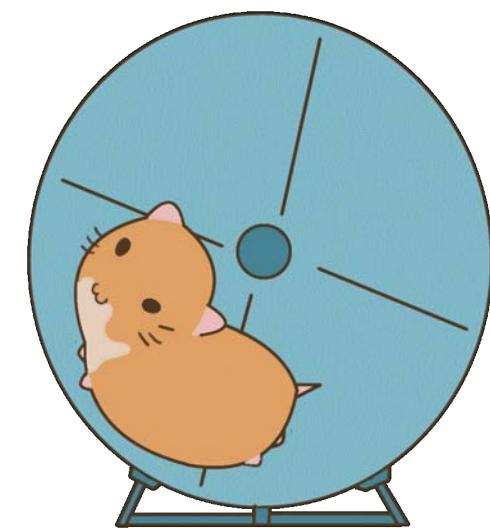
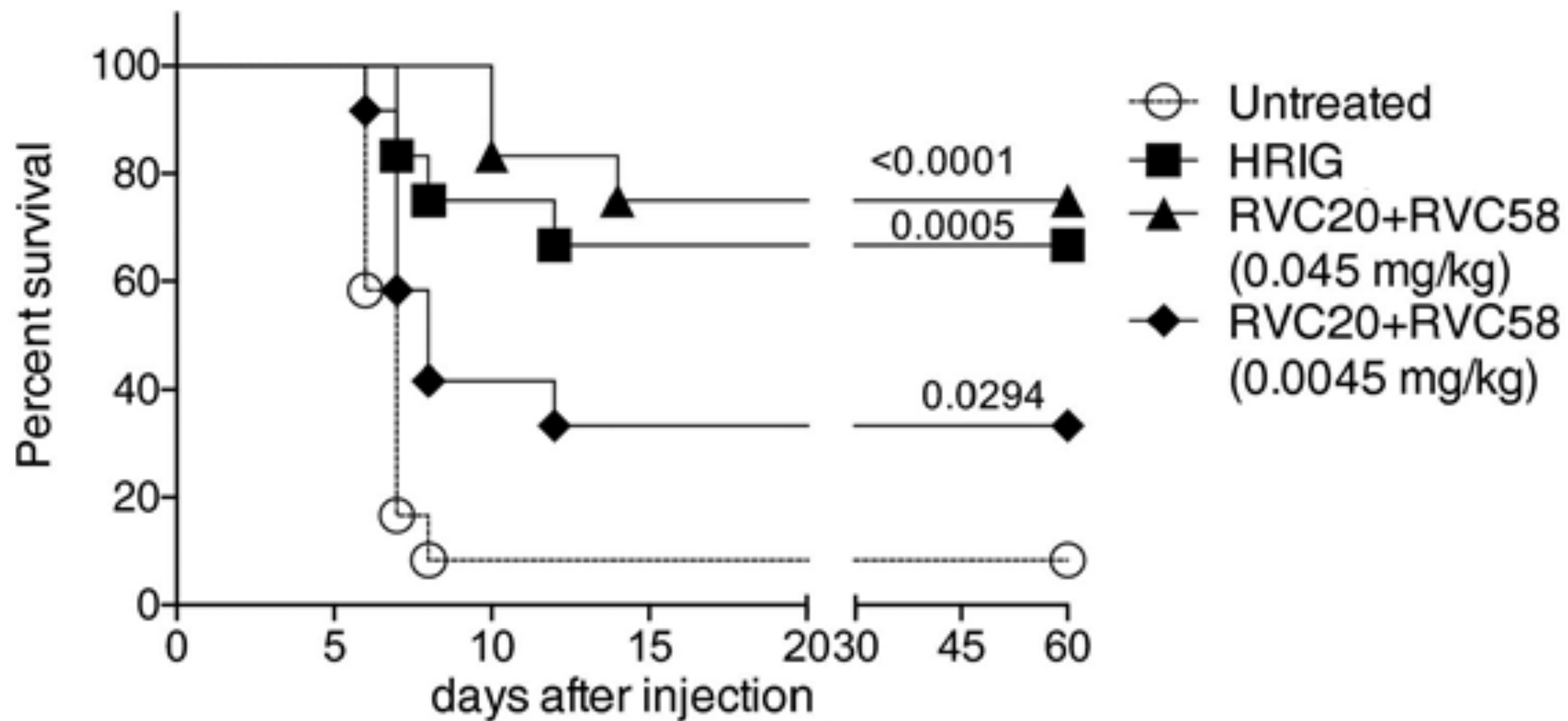


PEP experiments



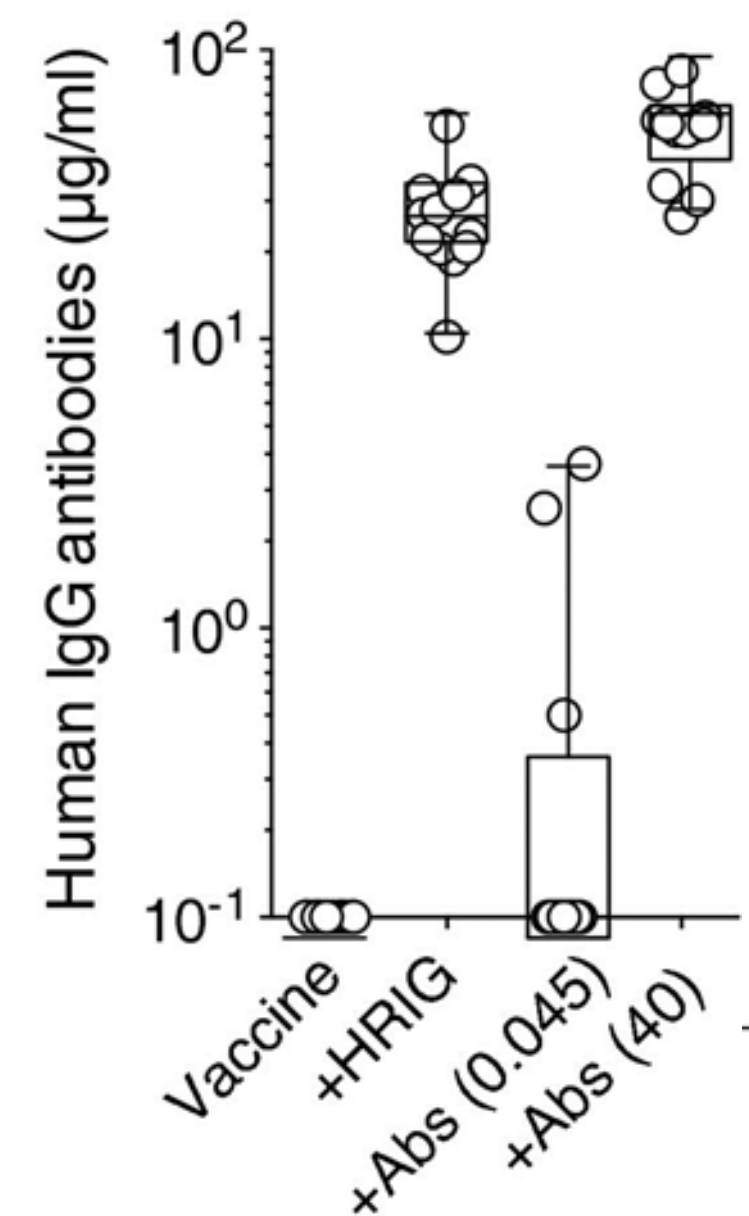
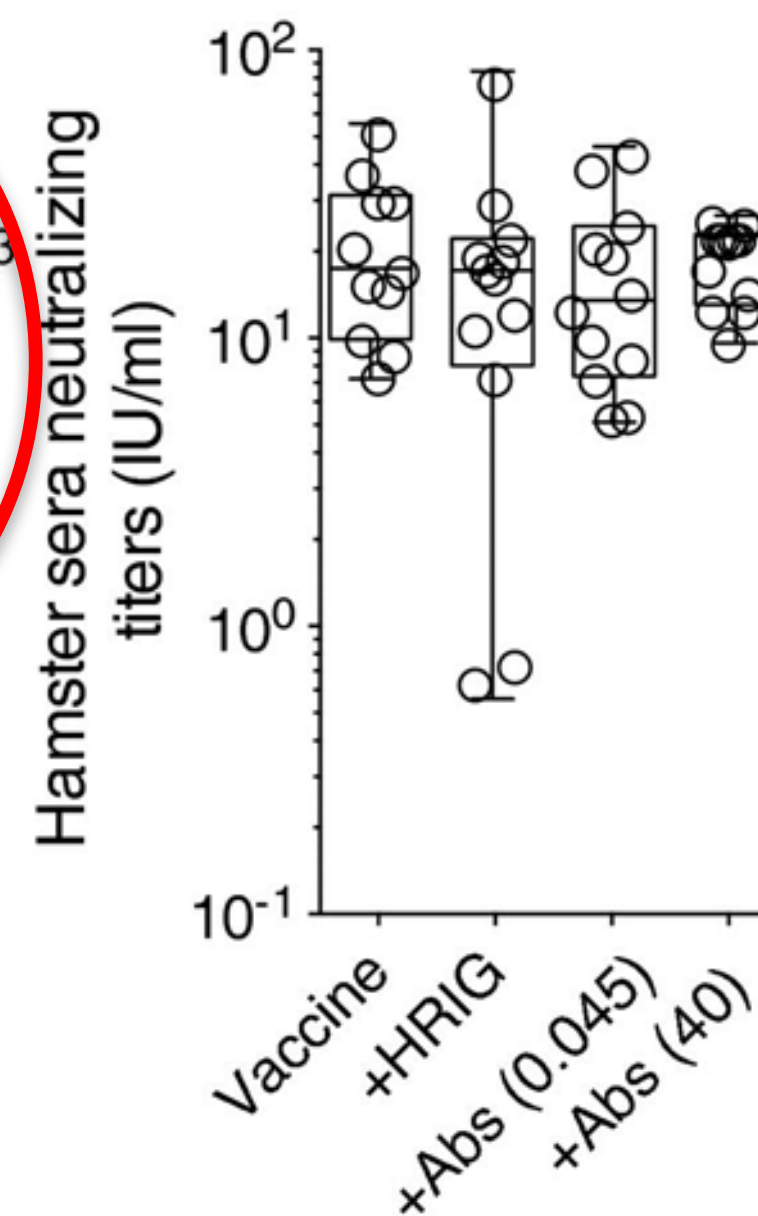
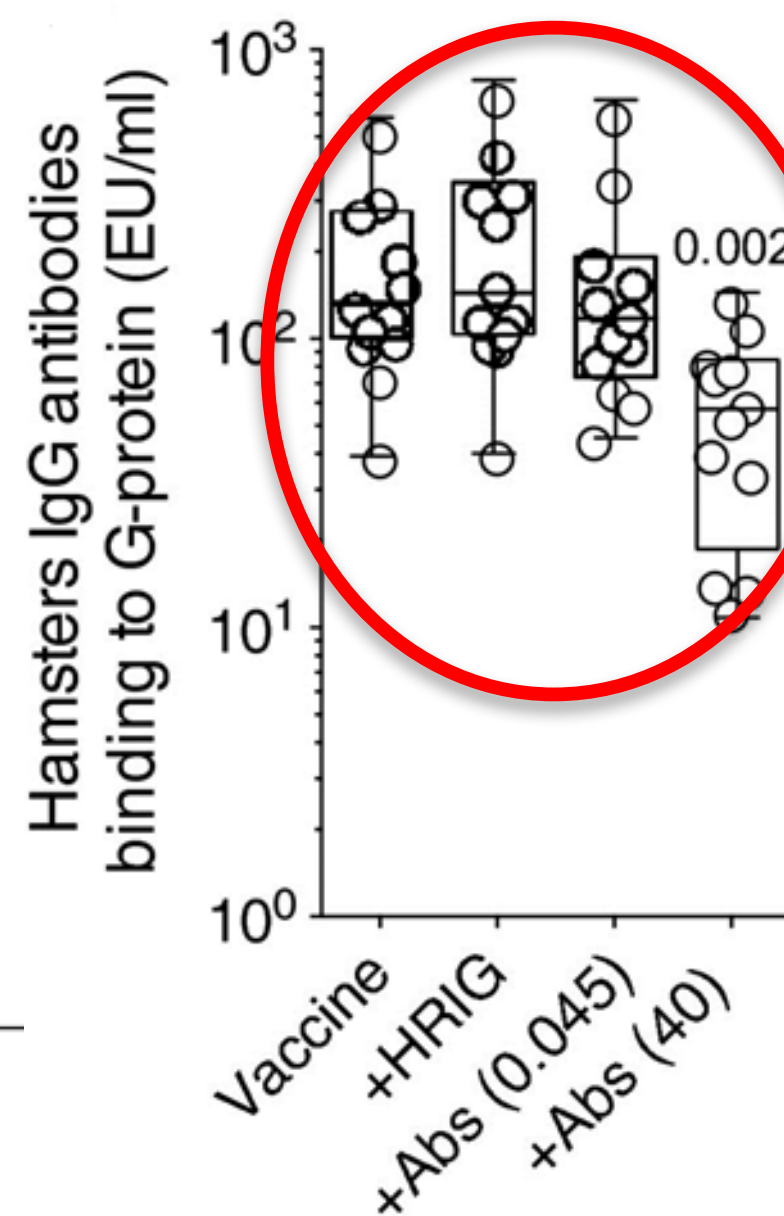
The cocktail protects Syrian hamsters from a lethal RABV challenge

PEP experiments



The cocktail protects Syrian hamsters from a lethal RABV challenge

The cocktail does not affect the endogenous post-vaccination antibody response.



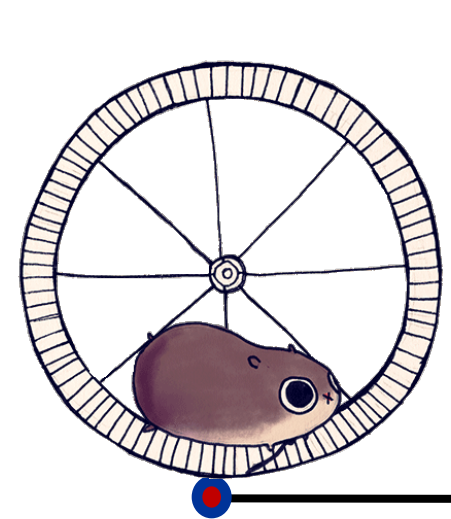


Late PEP investigations

IM challenge
CVS-11
($10^{8,76}$ MICLD₅₀/ml) **"100x"**

Standard
PEP

The dose used for this experiment
was 100 times higher than the one
used for the PEP experiment.



- 7 gg.

D0

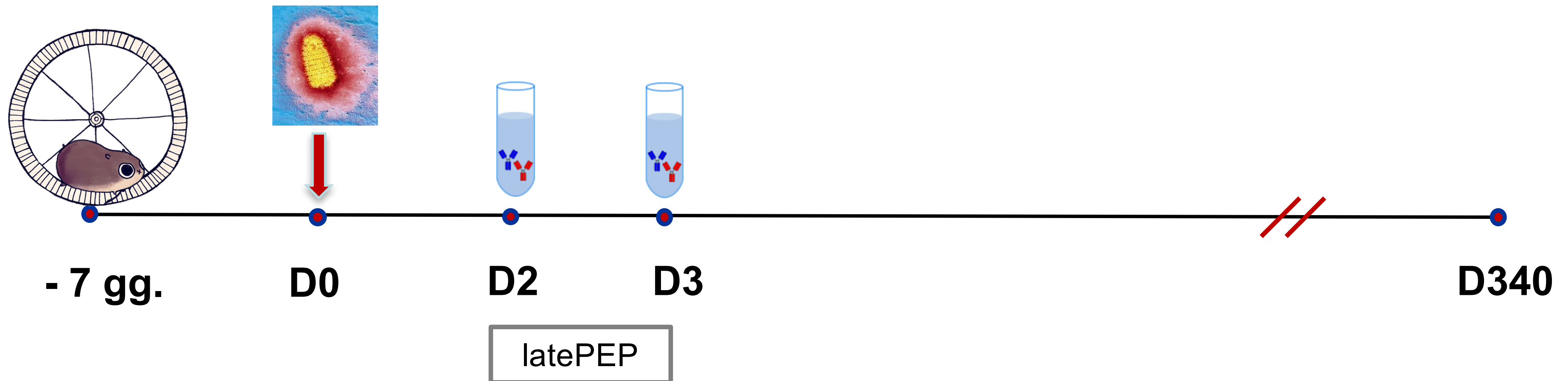
D5



Late PEP investigations

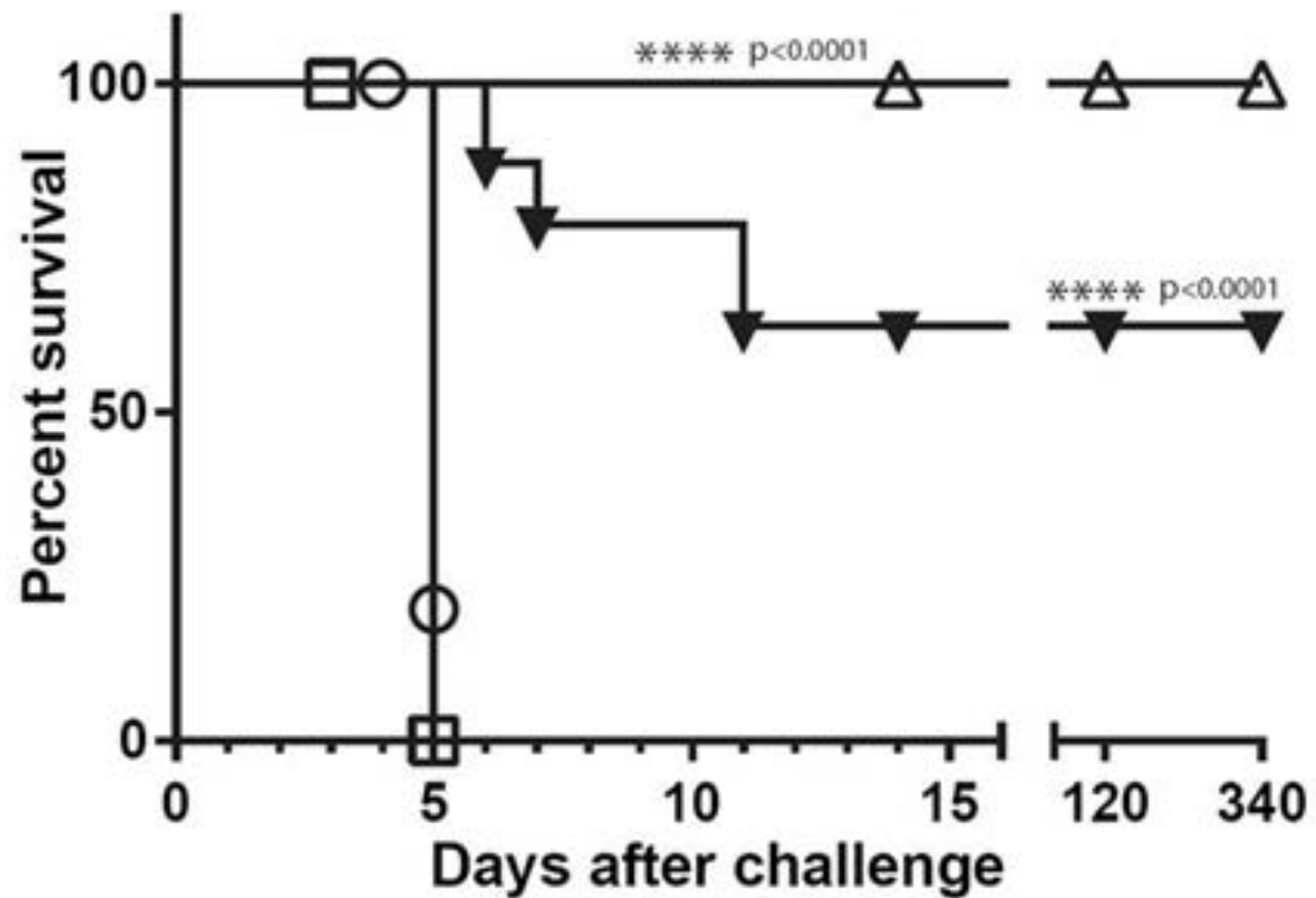
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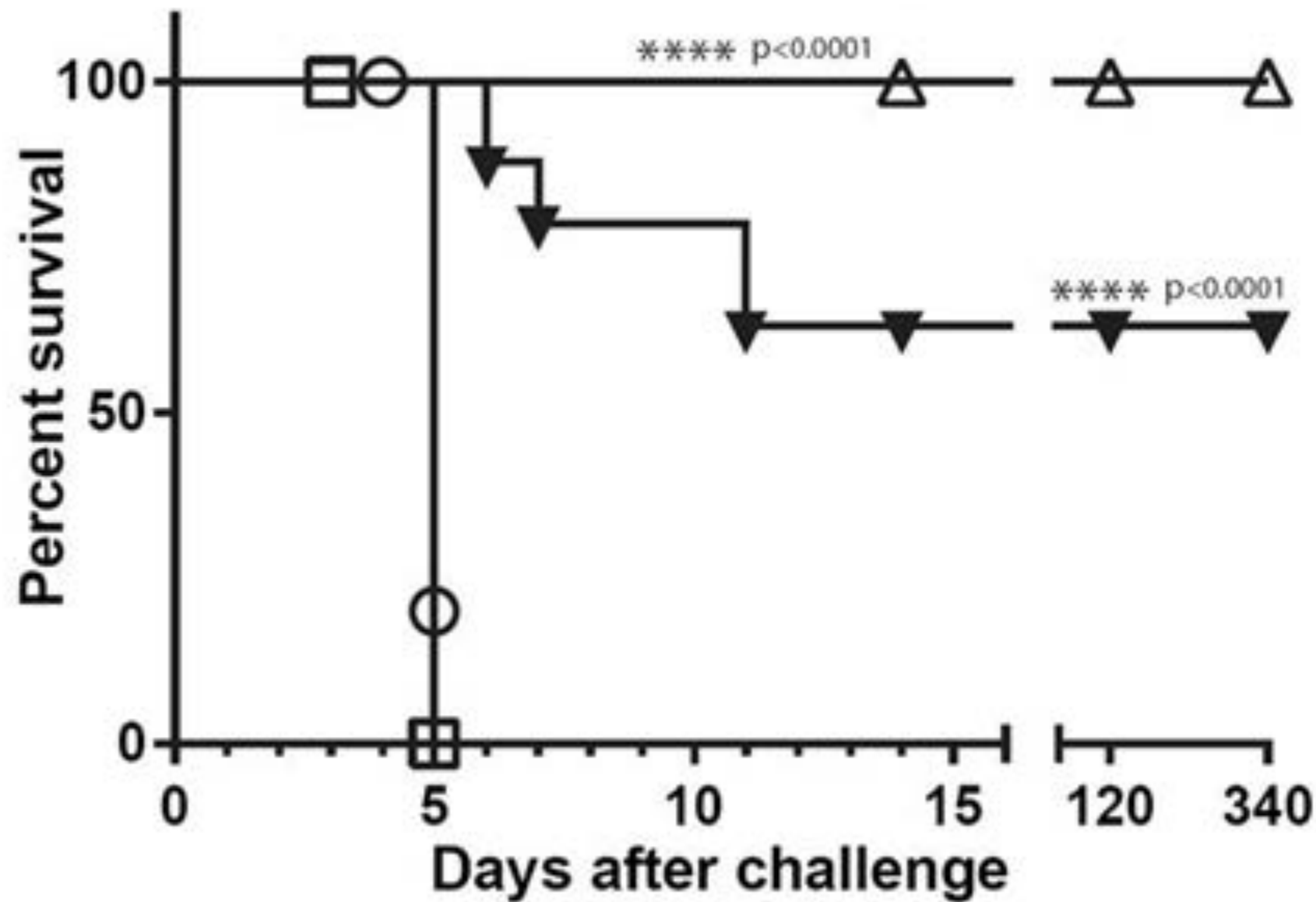
Late PEP : mAbs 40 mg/kg administered in each animal as one shot at different time points according to the group assignment.

Late PEP : survival and morbidity



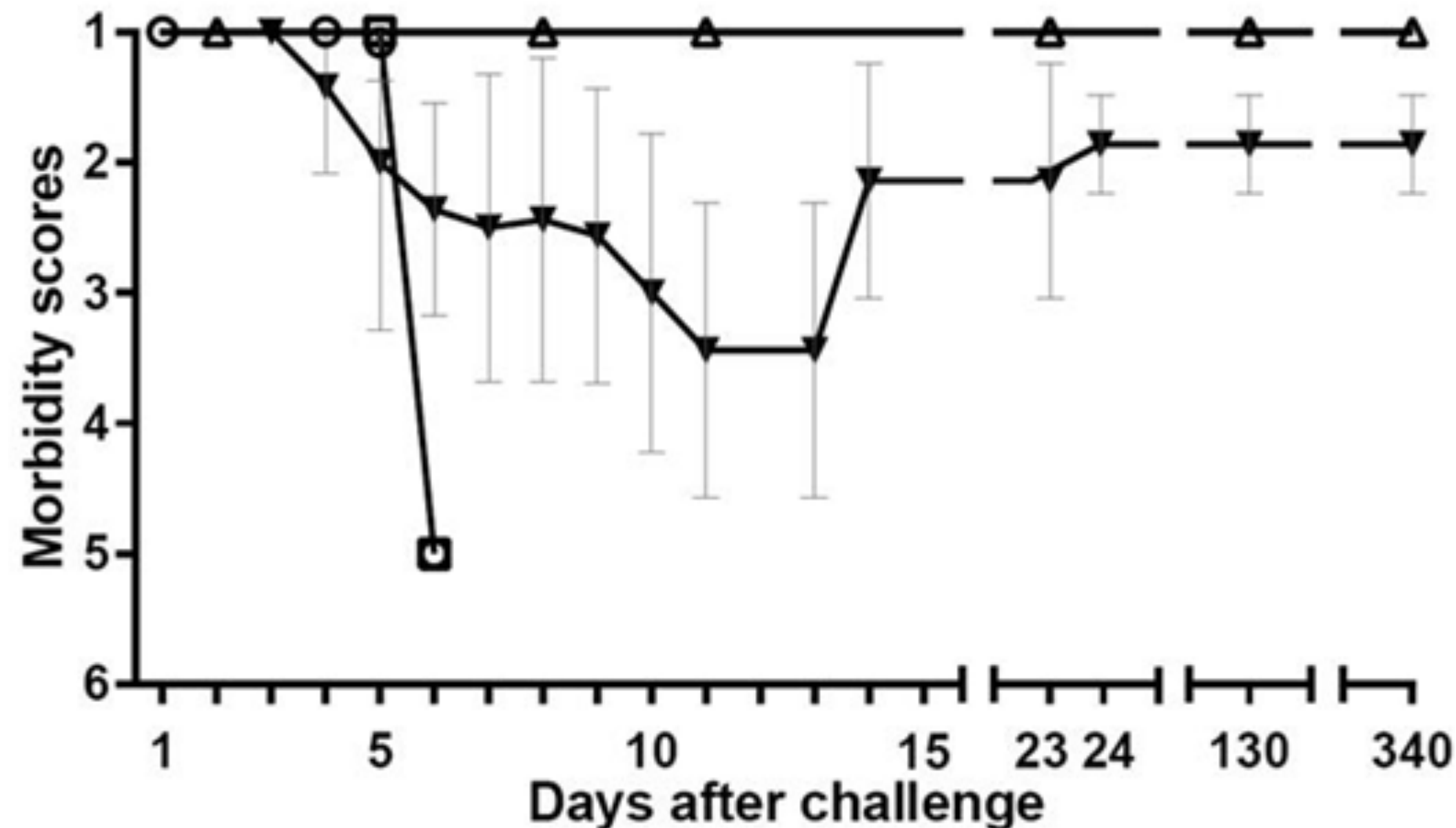
Animals treated 3 days p.i. survived in a 58.33% of cases.

Late PEP : survival and morbidity

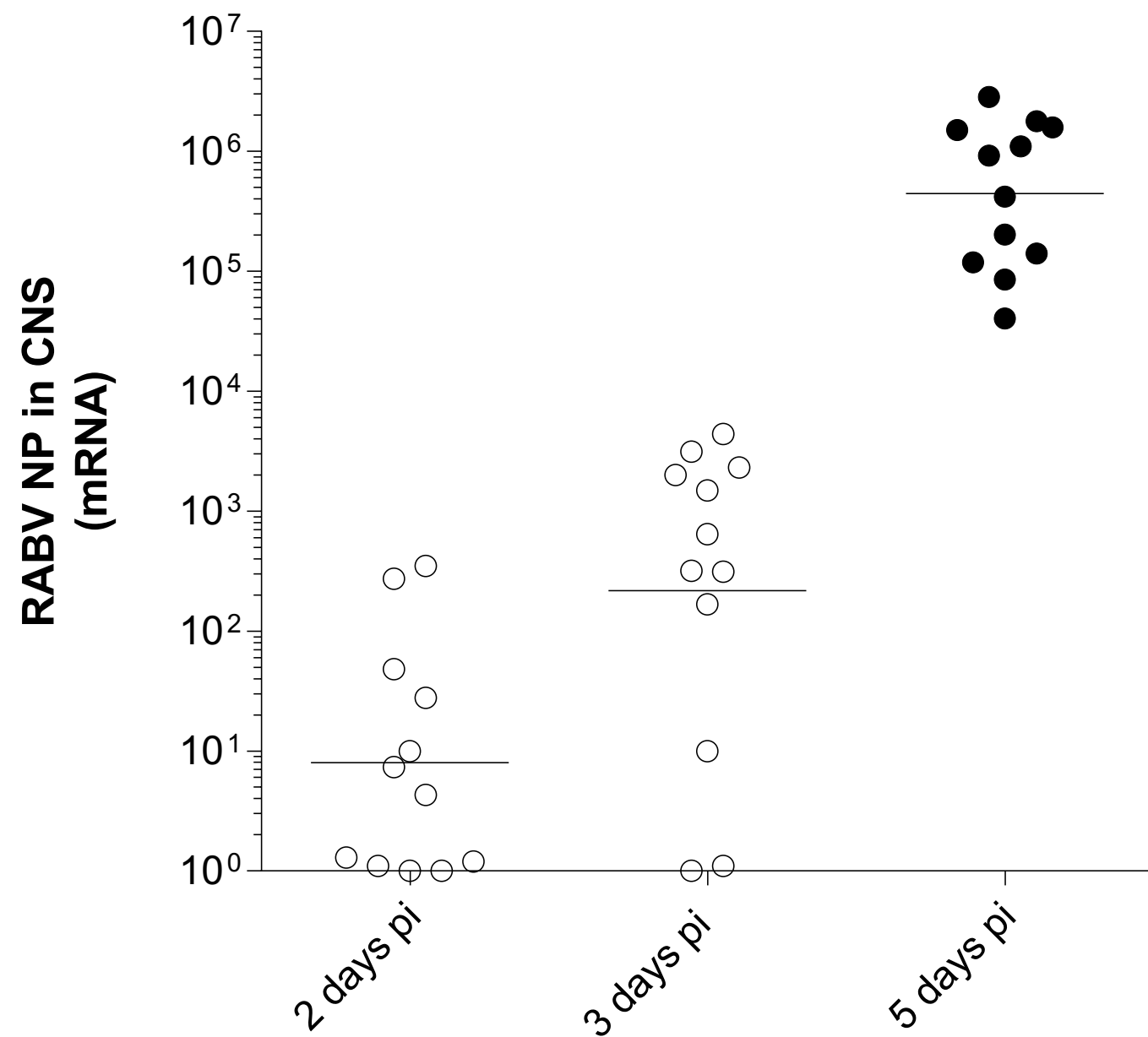


Animals treated 3 days p.i. survived in a 58.33% of cases.

Animals treated 3 days p.i. showed transient clinical signs partially recovering or stabilizing over a long observational period.

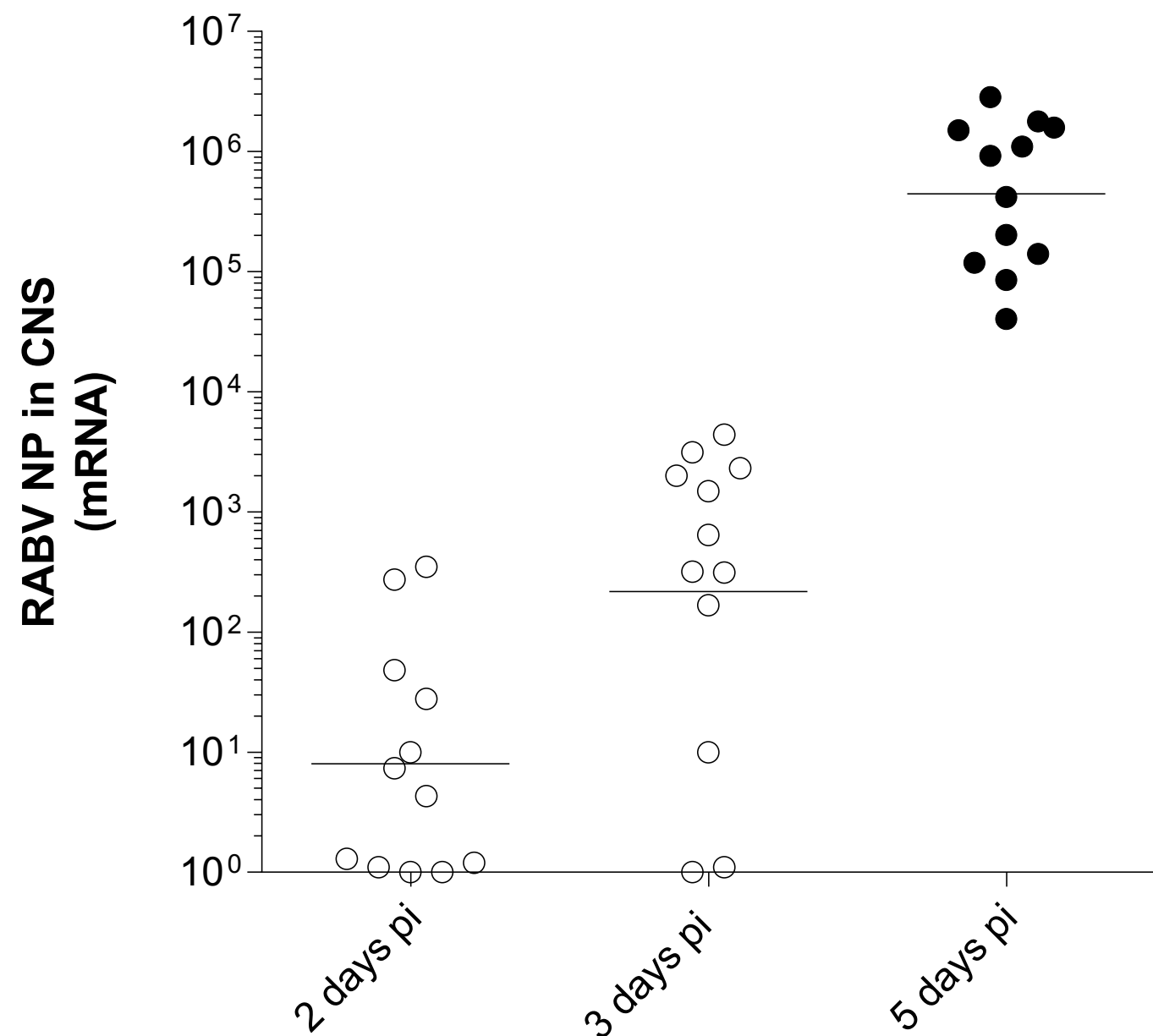


Late PEP: viral loads in treated and untreated groups



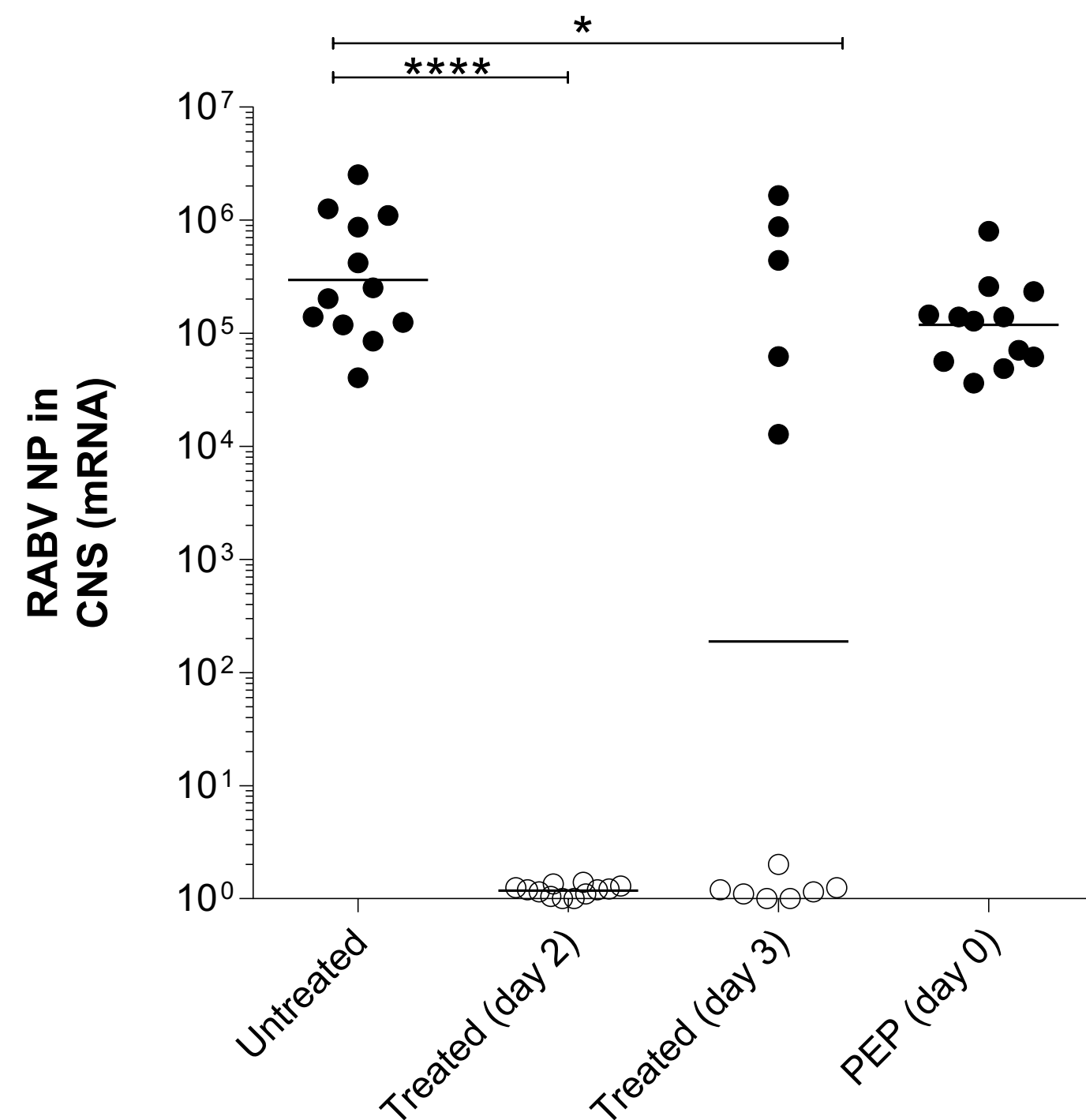
In most untreated animals virus replicates from day 2 to 3 p.i.

Late PEP: viral loads in treated and untreated groups



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Significant differences were observed in viral load between challenge and mAb-treated groups





Conclusions

- The mAb cocktail developed represents a treatment with an unprecedented breadth and potency
- It can represent a valid alternative to RIG in the frame of human rabies PEP at a considerable lower price
- It is able to treat a rabies infection, reduce the symptoms and clear the virus from the CNS



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Ongoing evaluations

- mAbs kinetics and mechanism of clearance
- Improved efficacy of alternative administration routes
- Possible synergistic effect with additional antiviral drugs



The consortium

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