Immune responses in Lassa Fever survivors

Critical research for priority pathogens with epidemic potential
Online Meeting 18-01-2024
Lisa Oestereich, Department of Virology

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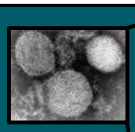
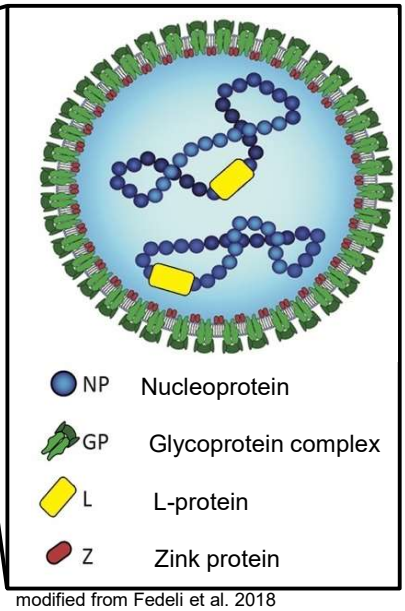
Lassa Virus as a prototype Arenavirus

Lassa virus and fever
- Ambisense RNA virus
- *Arenaviridae* family
- 2 Genome segments, 4 proteins





modified from Fedeli et al. 2018

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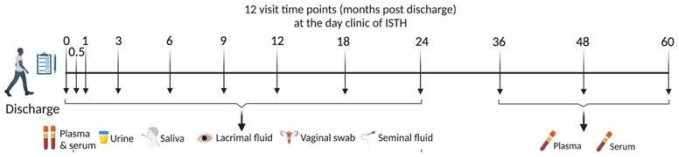
Lassa Virus

Lassa virus and fever

- Estimated 300.000 cases; 5.000 deaths annually
- Many asymptomatic cases; symptoms range from mild flu-like presentation to hemorrhage and fatal shock
- Endemic in West Africa, seasonal; especially in Nigeria
- **2019** Nigerian outbreak: >810 cases and >167 deaths
- **2023** 1270 laboratory-confirmed cases from 28 of 36 states; 18 % case fatality rate

Clinical studies at ISTH, Nigeria

- Pathogenesis study linking laboratory data with clinical data
- **Follow-up of Lassa Fever survivors**



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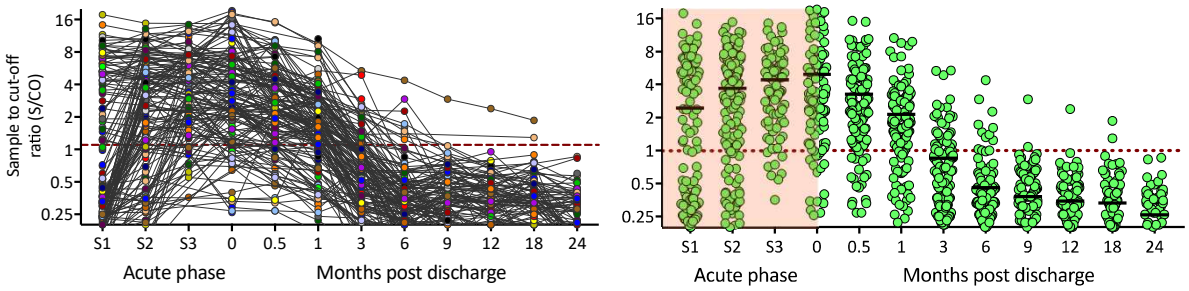
Kinetic of anti-NP IgM



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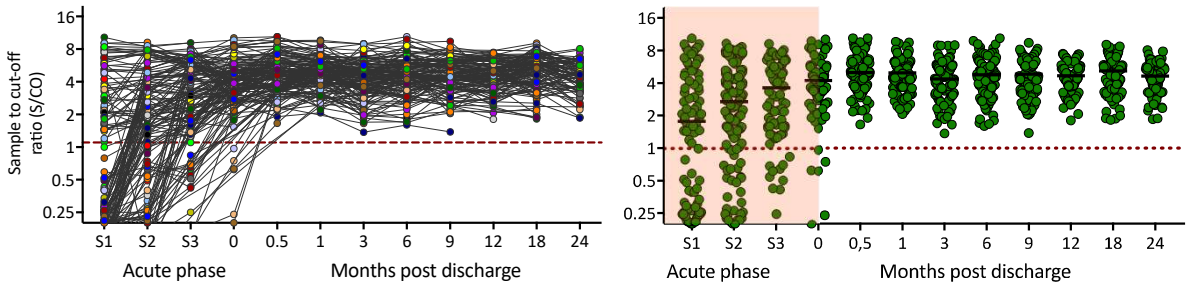
Kinetic of anti-NP IgG



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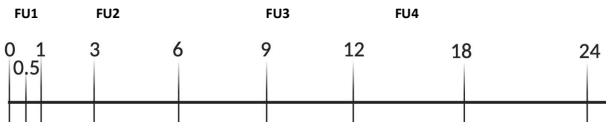
Kinetic of anti-preGP/GP IgG



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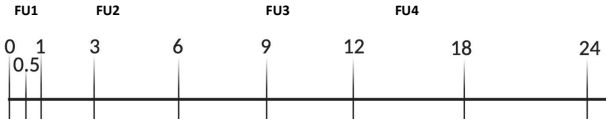
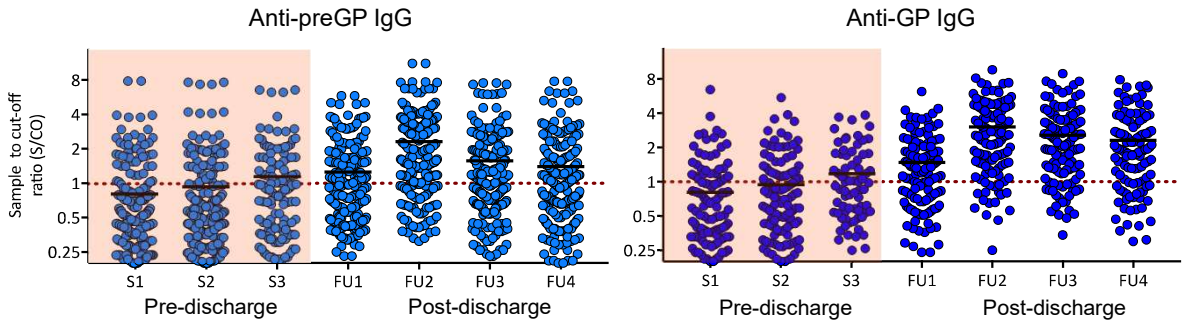
Kinetic of anti-preGP/GP IgG





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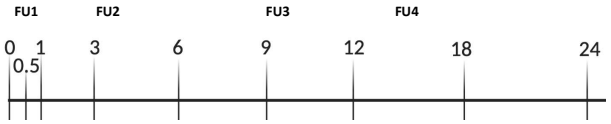
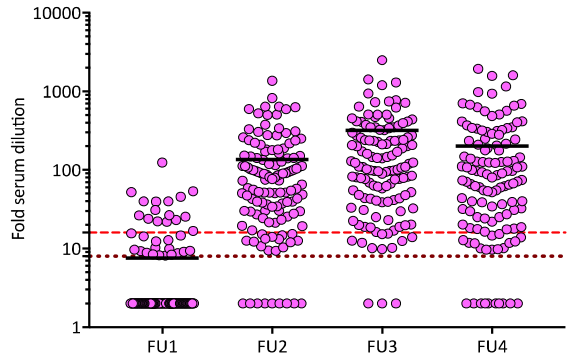
Kinetic of neutralizing antibodies





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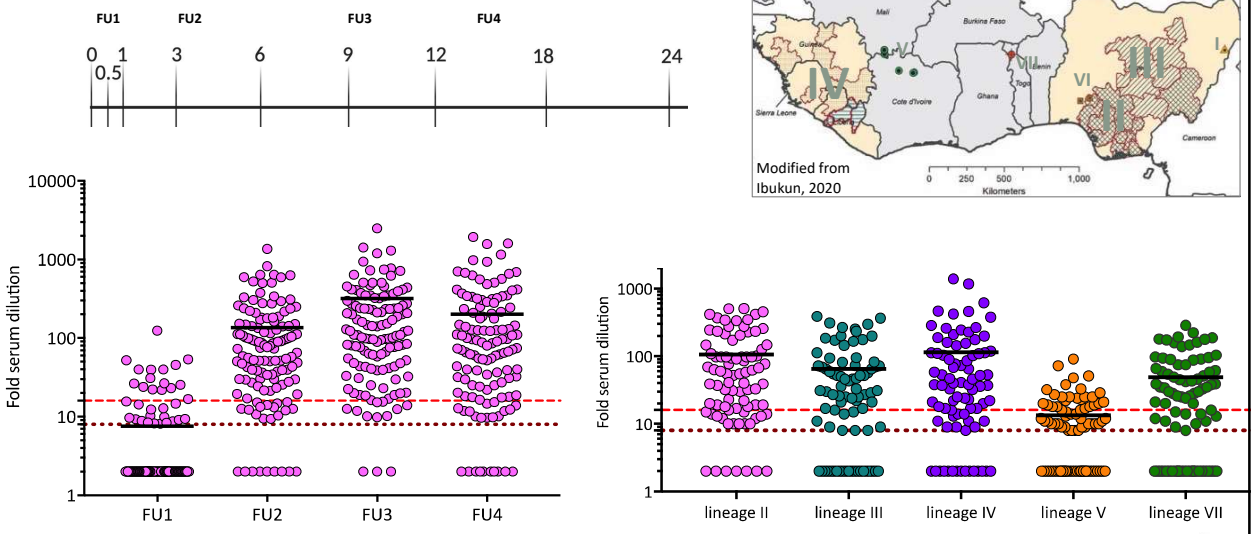
Kinetic of neutralizing antibodies



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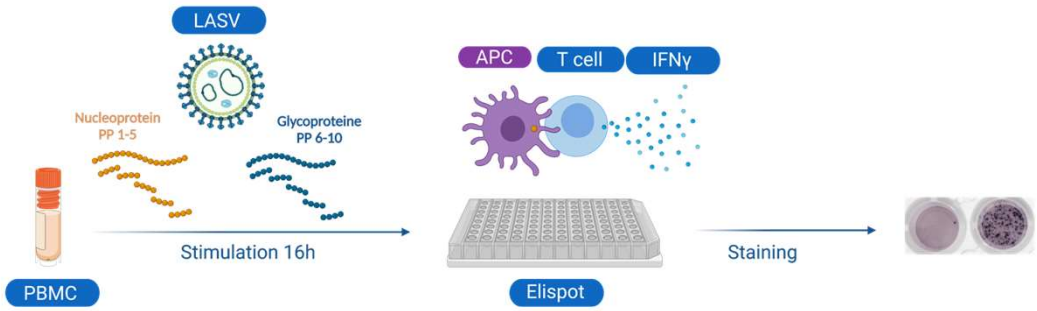
Cellular Immune responses in LF survivors – ELISpot design



- Amino acid sequence based on consensus of 2019-2020 lineage II sequences
- 15 aa peptides, overlap of 3 aa
- 5 pools of 24 – 28 peptides per pool
- 2 µg/mL of each peptide for stimulation
- 250,000 PBMC per reaction

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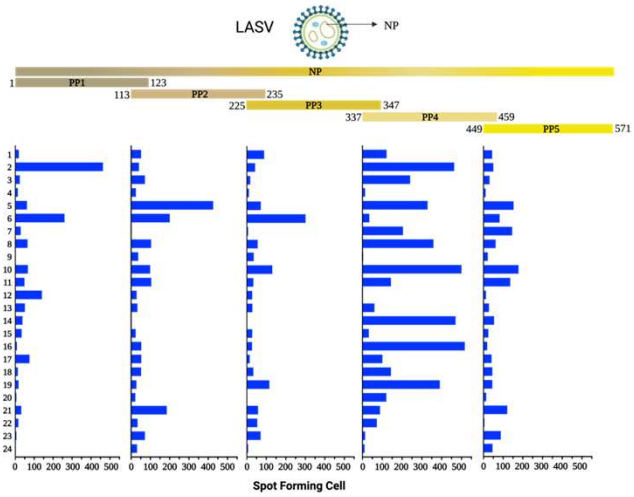
T cell recognition of viral peptides



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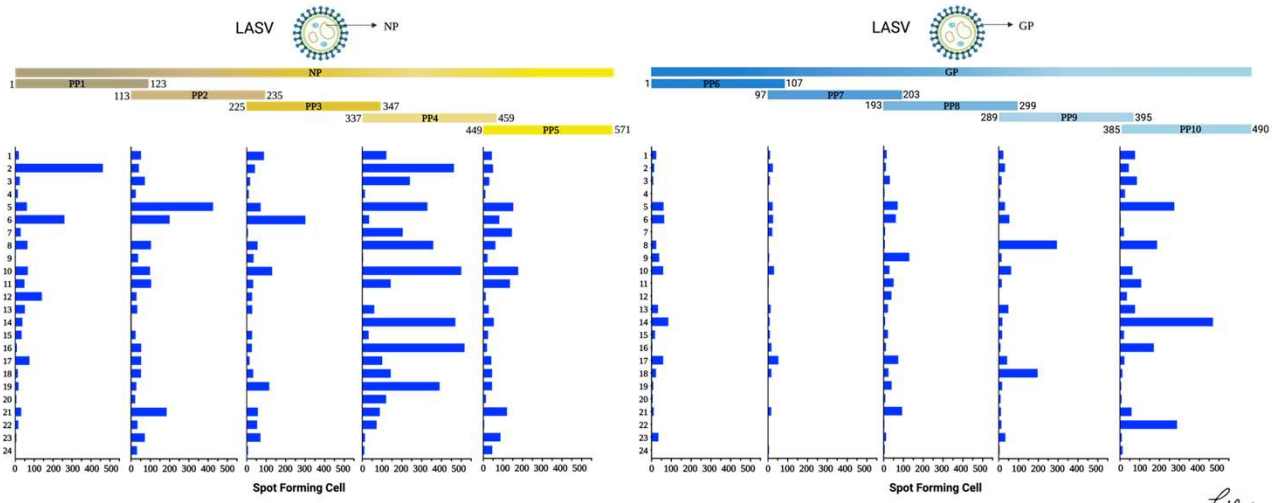
T cell recognition of viral peptides



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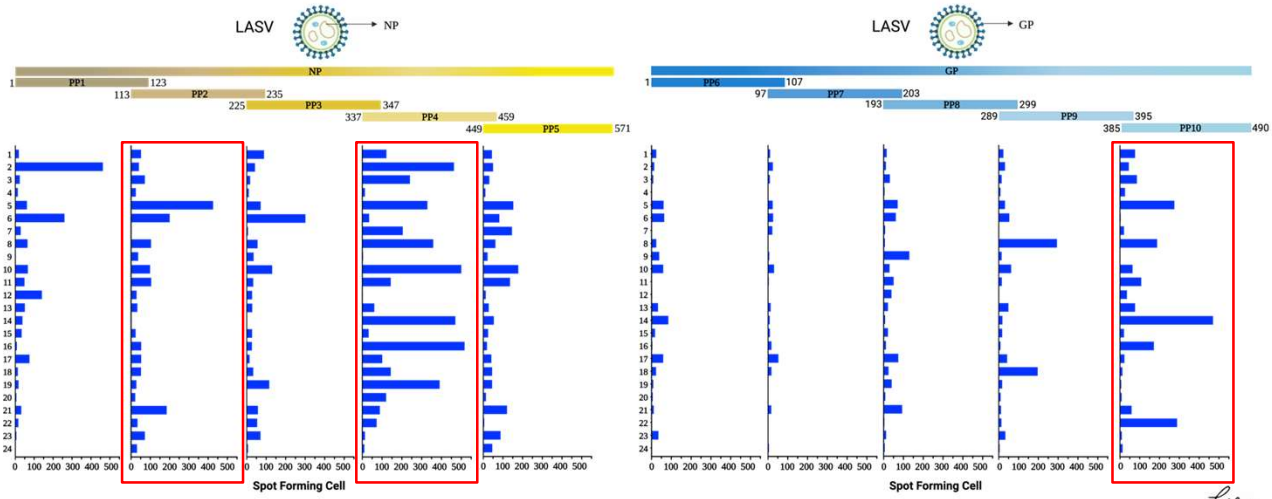
T cell recognition of viral peptides



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Summary: Immune responses in Lassa Fever survivors

NP	+++ Very early (during viremic phase)	+++
GPC	++ Later (after virus clearance)	++
Neutralisation	Low titer, high variation Late (>3 month post infection)	

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Challenges

- Most vaccines target contain GPC as an antigen
- High genetic variability of LASV strains; vaccines based on “old” lab strain
  - Crossprotection?
- Low neutralizing antibody titer and overall delayed and lower antigenicity of GPC compared to NP
- More and stronger T cells epitopes in NP compared to GPC

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Arenaviruses beyond LASV

- Mopeia and Morogoro virus infection of mice or NHP induces protective immunity (LASV challenge)
- No/low cross-reactivity of T cells between different Old World Arenaviruses
- Limited cross-reactivity of antibodies between old World Arenaviruses
- No recognition of New World Arenaviruses with Lassa Fever survivor plasma

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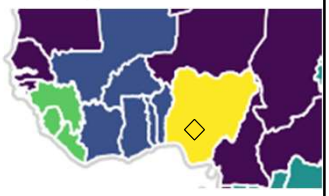

Schematic figures were created with Biorender.com

Leibniz Association

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