Immune responses in Lassa Fever survivors

Critical research for priority pathogens with epidemic potential
Online Meeting 18-01-2024
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Lassa Virus as a prototype Arenavirus

Lassa virus and fever
- Ambisense RNA virus
- Arenaviridae family
- 2 Genome segments, 4 proteins
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** 1,270 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**

**Kinetic of anti-NP IgM**

![Graph showing the kinetic of anti-NP IgM](image-url)
Kinetic of anti-NP IgG

Kinetic of anti-preGP/GP IgG
Kinetic of anti-preGP/GP IgG

Anti-preGP IgG

Anti-GP IgG

Kinetic of neutralizing antibodies
Kinetic of neutralizing antibodies

- FU1, FU2, FU3, FU4
- Modified from Ibukun, 2020

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
T cell recognition of viral peptides

Summary: Immune responses in Lassa Fever survivors

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<th>NP</th>
<th>GPC</th>
<th>Neutralisation</th>
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<td></td>
<td>Very early (during viremic phase)</td>
<td>++</td>
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<td>Low titer, high variation</td>
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<td>Late (&gt;3 month post infection)</td>
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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

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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