IMPACT OF INTRAUTERINE HIV EXPOSURE ON INFANT ANTIVIRAL ANTIBODY REPERTOIRE

299

Rachael W Gachogo [1], Anna-Ursula Happel[1],Berenice Alinde[1,2] Clive M. Gray[1,2], Heather Jaspan[1,3,4], and Sonwabile Dzanibe[1]

[1]University of Cape Town and [2]Stellenbosch University, Cape Town, South Africa, [3]Seattle Children's Research Institute and [4]University of Washington, Seattle, Washington, USA.

1 BACKGROUND

Antibody responses to vaccines do not explain health outcome disparities observed between infants who are HIV-exposed but uninfected (iHEU) and HIV-unexposed and uninfected (iHUU). We thus investigated the effect of HIV-exposure on the infant pan-viral-specific antibody repertoires between iHEU and iHUU.

2 METHODS

IgG titers against 206 eukaryote-infecting viruses were measured using Phage Immunoprecipitation Sequencing[1] in plasma of iHEU (n=15) and iHUU (n=15) at birth and 36 weeks of life (Fig. 1). Data analysis was performed using AntiViral Antibody Response Deconvolution Algorithm (ARVARDA)[2]. High-dimensional reduction analysis and pairwise comparison was performed in R with $\alpha<0.05$.

Viral-specific antibody repertoires differed between HIV-exposed and uninfected infants and HIV-unexposed and uninfected infants at birth but converged at 36 weeks of life.

3 RESULTS

- Distinct viral antibody repertoires were observed in infants' plasma between birth and week 36 regardless of HIV exposure status (Fig. 2A).
- Viral antibody repertoires differed between iHEU and iHUU at birth but were similar at 36 weeks of life (Fig. 2B & 2C).
- At birth, iHEU had a lower antibody repertoire breadth compared to iHUU (Fig. 2D).
- Infant plasma at birth contained predominantly antibodies to herpesviruses while antibodies against enteroviruses were common at 36 weeks of life (Fig. 2E & 2F).
- At birth, mastadenovirus C and enterovirus B & C specific IgG levels were higher in iHUU compared to iHEU , while those against rhinovirus C were higher in iHUU at 36 weeks of life. HIV-specific IgG were only detected in iHEU (Fig. 2E, 2G & 2H).

4 CONCLUSIONS

Lower antibody repertoire breadth of iHEU at birth could have clinical significance including increased risk of infections. Further analysis of the maternal antibody repertoire is required to determine whether the differences observed between iHEU and iHUU at birth are as result of impeded transplacental antibody transfer or different antibody repertoire between women living with HIV and women living without HIV.

5 ADDITIONAL KEY INFORMATION

References

1. G. J. Xu et al., Science 348, aaa0698 (2015). DOI: 10.1126/science.aaa0698
2. Monaco, D. R et al., Deconvoluting virome-wide antibody epitope reactivity profiles. (2022). EBioMedicine, 75, 103747. https://doi.org/10.1016/j.ebiom.2021.103747

Author Contact Information

Rachael Gachogo:gchrac001@myuct.ac.za

Acknowledgements

This study was funded by NIH and SA-MRC.

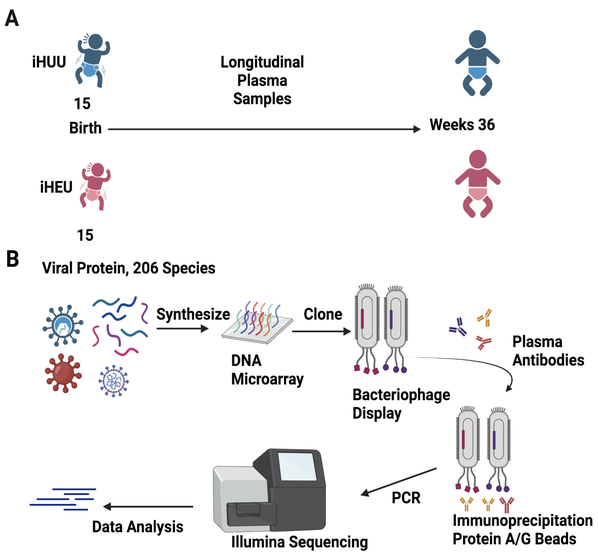

Fig.1|: Profiling infant viral specific antibody repertoires. A) Paired infant plasma samples were collected at birth and week 36. **B)** Viral-specific IgG against 206 viral species were measured using Phage Immunoprecipitation Sequencing (PhiP-Seq) – VirScan (viral epitope scanning) method.

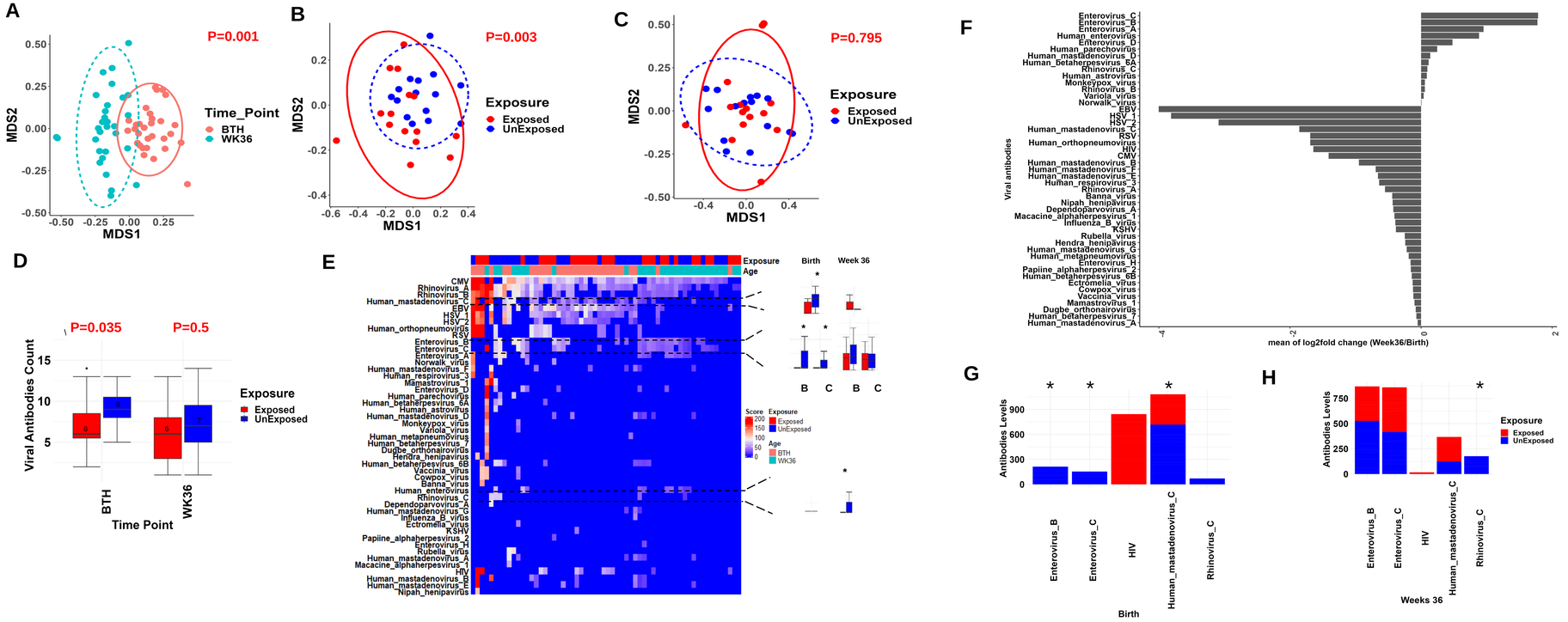

Fig.2|: Viral antibody repertoire differ between HIV-exposed uninfected infants (iHEU) and HIV-unexposed uninfected infants (iHUU) at birth but converge at 36 weeks of life A, Multidimension scaling (MDS) showing distinct clustering between infants at birth and 36 weeks by viral specific antibody titers. **B**, HIV exposure explains the differences observed in the viral antibody repertoires at birth between iHEU and iHUU. **C**, while there were no differences observed at 36 weeks of life**. D,** iHEU had fewer average number of unique viral antibodies detected per participant at birth and 36 weeks of life compared to iHUU. **E,** Antibodies against a total of forty-seven distinct viruses were detected in iHEU and iHUU at birth and 36 weeks of life. Antibodies against herpesviruses and enteroviruses dominated birth and 36 weeks repertoires, respectively. **F**, Log_2 fold change (Week36/Birth) analysis revealed waning of most viral antibodies except anti-enteroviral antibodies which increased over time. **G,** At birth iHUU had higher levels of antibodies against enterovirus B and C and mastadenovirus C compared to iHEU. HIV-specific antibodies were only detected in 10/15 of iHEU at birth. **H,** At 36 weeks of life iHUU had higher levels of rhinovirus C antibody compared to iHEU. Only 1/15 iHEU retained HIV-specific IgG**. BTH** (Birth), **WK36** (36 weeks of life)