# Infant HIV vaccination: relationship to childhood vaccines and maternal antibodies

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## INTRODUCTION

- An infant HIV vaccine could prevent the 150,000 new annual pediatric HIV infections.
- Previous research has demonstrated that vaccine co-administration can interfere with elicited immune responses, therefore it is important to understand how an infant HIV vaccine would interact with WHO recommended pediatric vaccines.
- It is unknown whether maternal antibodies disrupt infant HIV vaccine-elicited responses.

### STUDY AIMS

1. Develop a high-throughput, sample-saving tool to measure antibody responses elicited by common childhood vaccines.
2. Assess whether infant HIV vaccines from Pediatric AIDS Clinical Trials Group (PACTG) protocols 230 and 326 influenced common pediatric vaccine antibody levels.
3. Evaluate the impact of maternal antibodies on infant HIV vaccine-elicited responses.

## METHODS

Table 1. Pediatric vaccine multiplex assay (PVMA) antigens and standards.

| Vaccine | Vaccine Antigen | WHO International Standard |
|---|---|---|
| HepB | Recombinant HepB Surface Antigen (Adw) | Anti-HepB Surface Antigen Immunoglobulin |
| HiB | HbO-HA | Anti-HiB Reference Serum |
| Pertussis | Pertussis Toxin | Pertussis Antiserum |
| Tetanus | Tetanus Toxoid | Tetanus Immunoglobulin |
| Diphtheria | Diphtheria Toxin | Diphtheria Antitoxin IgG |
| Rubella | Rubella Virus Capsid Protein | Anti-Rubella Immunoglobulin |
| RSV | DS-Cav1 (RSV F Protein) | Synagis (mAb not WHO IS) |

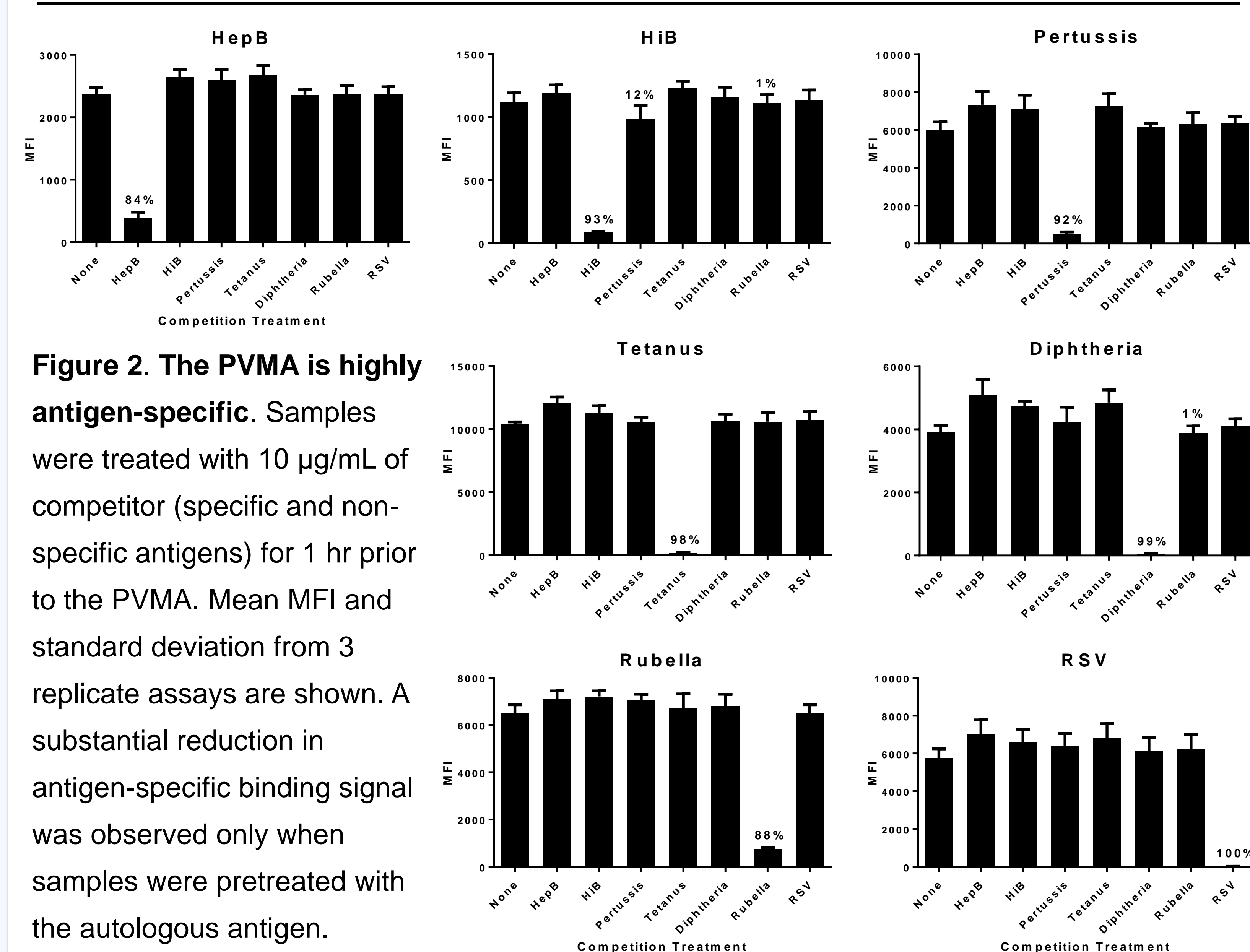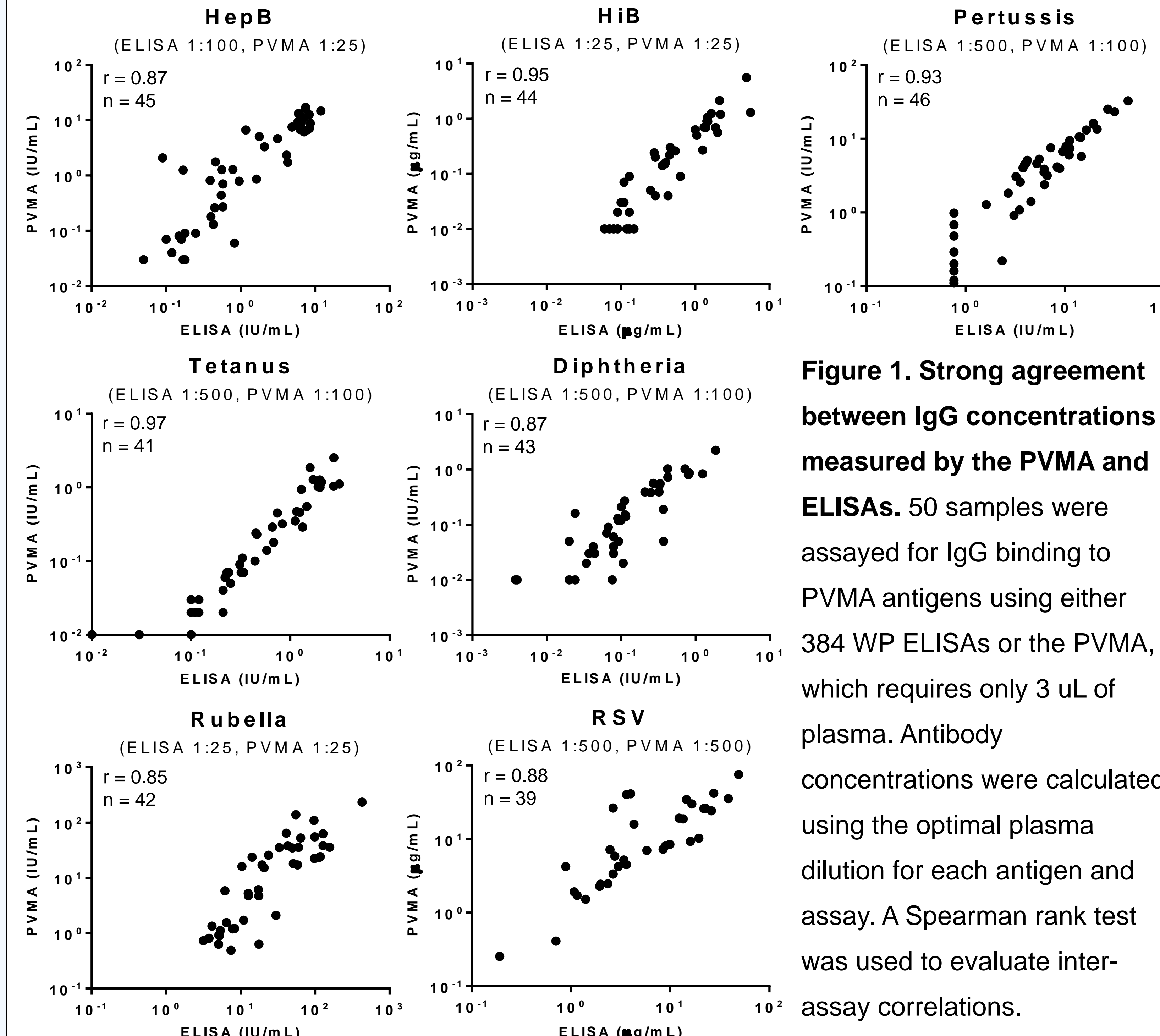- **Aim 1**: IgG against the PVMA antigens was measured by the PVMA and 384 WP ELISAs in 50 plasma samples. Assay results were compared to evaluate PVMA accuracy and sensitivity. PVMA specificity was assessed by competition-binding assays.
- **Aim 2:** PACTG 230/326 infant plasma collected at 24 weeks of age was screened by the PVMA and IgG levels between HIV vaccinees and placebo recipients were compared.
- **Aim 3:** PACTG 230 vaccinee plasma from birth and two post-immunization time points was assessed for V1V2, V3, and MN gp120-specific antibodies by a multiplex assay.
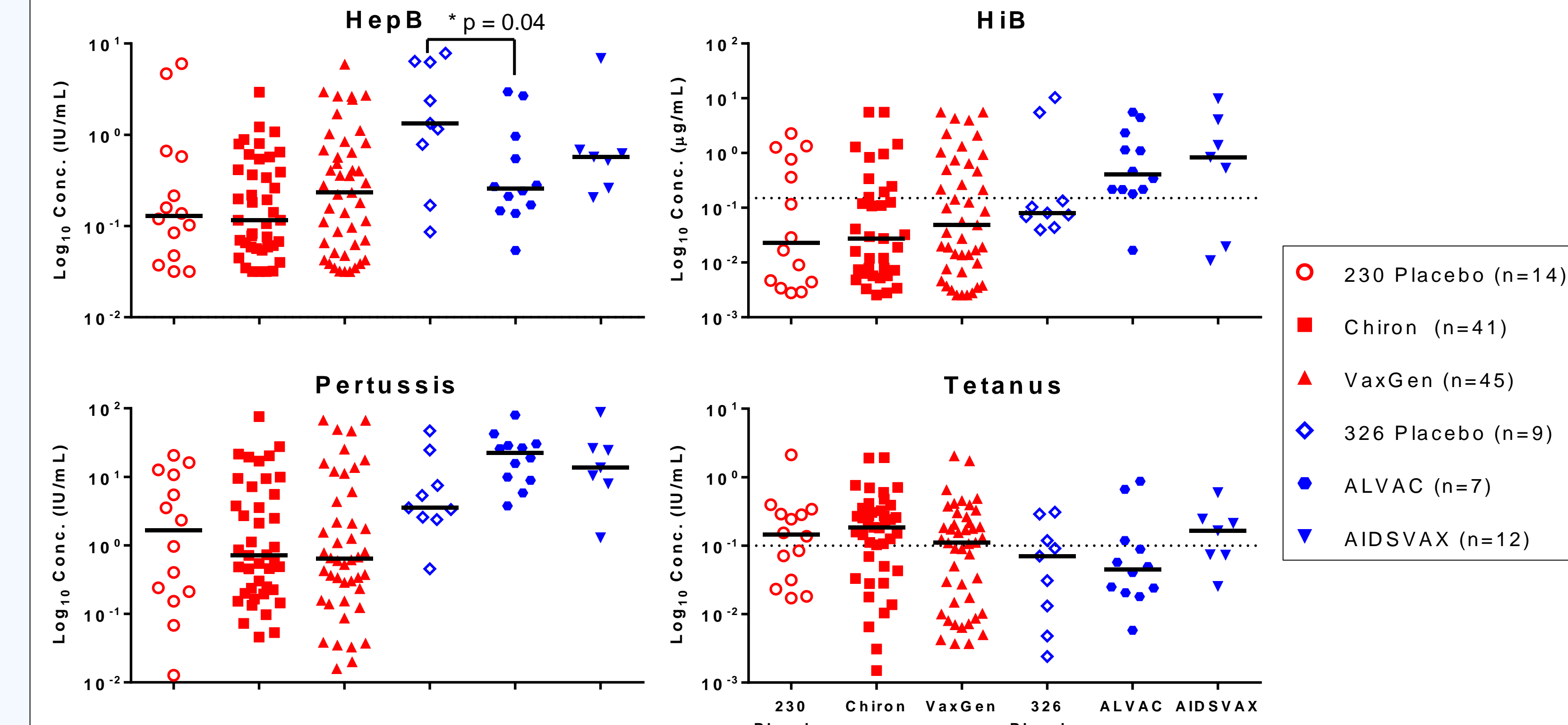
## RESULTS: AIM 1

Table 2. Assay detection ranges. Lower limits of quantification from the PVMA were lower or comparable to ELISAs, which indicates that the PVMA is highly sensitive. PVMA upper limits also tended to exceed those of ELISAs, resulting in greater PVMA detection ranges.

| | Lower Limit of Quantification – Upper Limit of Quantification | | |
|---|---|---|---|
| | 384 WP ELISA | PVMA | Units |
| HepB | 0.51-123 | 1.27-25,000 | mIU/mL |
| HiB | 0.91-222 | 0.10-222 | ng/mL |
| Pertussis | 1.52-370 | 0.51-3,333 | mIU/mL |
| Tetanus | 0.05-4.1 | 0.05-111 | mIU/mL |
| Diphtheria | 0.02-5.6 | 0.01-67 | mIU/mL |
| Rubella | 34.29-25,000 | 2.54-50,000 | mIU/mL |
| RSV | 0.38-98 | 0.51-370 | ng/mL |

## RESULTS: AIM 1 CONTINUED

**HepB** (ELISA 1:100, PVMA 1:25) r = 0.87, n = 45

**HiB** (ELISA 1:25, PVMA 1:25) r = 0.95, n = 44

**Pertussis** (ELISA 1:500, PVMA 1:100) r = 0.93, n = 46

**Tetanus** (ELISA 1:500, PVMA 1:100) r = 0.97, n = 41

**Diphtheria** (ELISA 1:500, PVMA 1:100) r = 0.87, n = 43

**Rubella** (ELISA 1:25, PVMA 1:25) r = 0.85, n = 42

**RSV** (ELISA 1:500, PVMA 1:500) r = 0.88, n = 39

Figure 1. Strong agreement between IgG concentrations measured by the PVMA and ELISAs. 50 samples were assayed for IgG binding to PVMA antigens using either 384 WP ELISAs or the PVMA, which requires only 3 uL of plasma. Antibody concentrations were calculated using the optimal plasma dilution for each antigen and assay. A Spearman rank test was used to evaluate inter-assay correlations.

Figure 2. The PVMA is highly antigen-specific. Samples were treated with 10 µg/mL of competitor (specific and non-specific antigens) for 1 hr prior to the PVMA. Mean MFI and standard deviation from 3 replicate assays are shown. A substantial reduction in antigen-specific binding signal was observed only when samples were pretreated with the autologous antigen.

## RESULTS: AIM 2

HepB *p = 0.04

230 Placebo (n=14)
Chiron (n=41)
VaxGen (n=45)
326 Placebo (n=9)
ALVAC (n=7)
AIDSVAX (n=12)
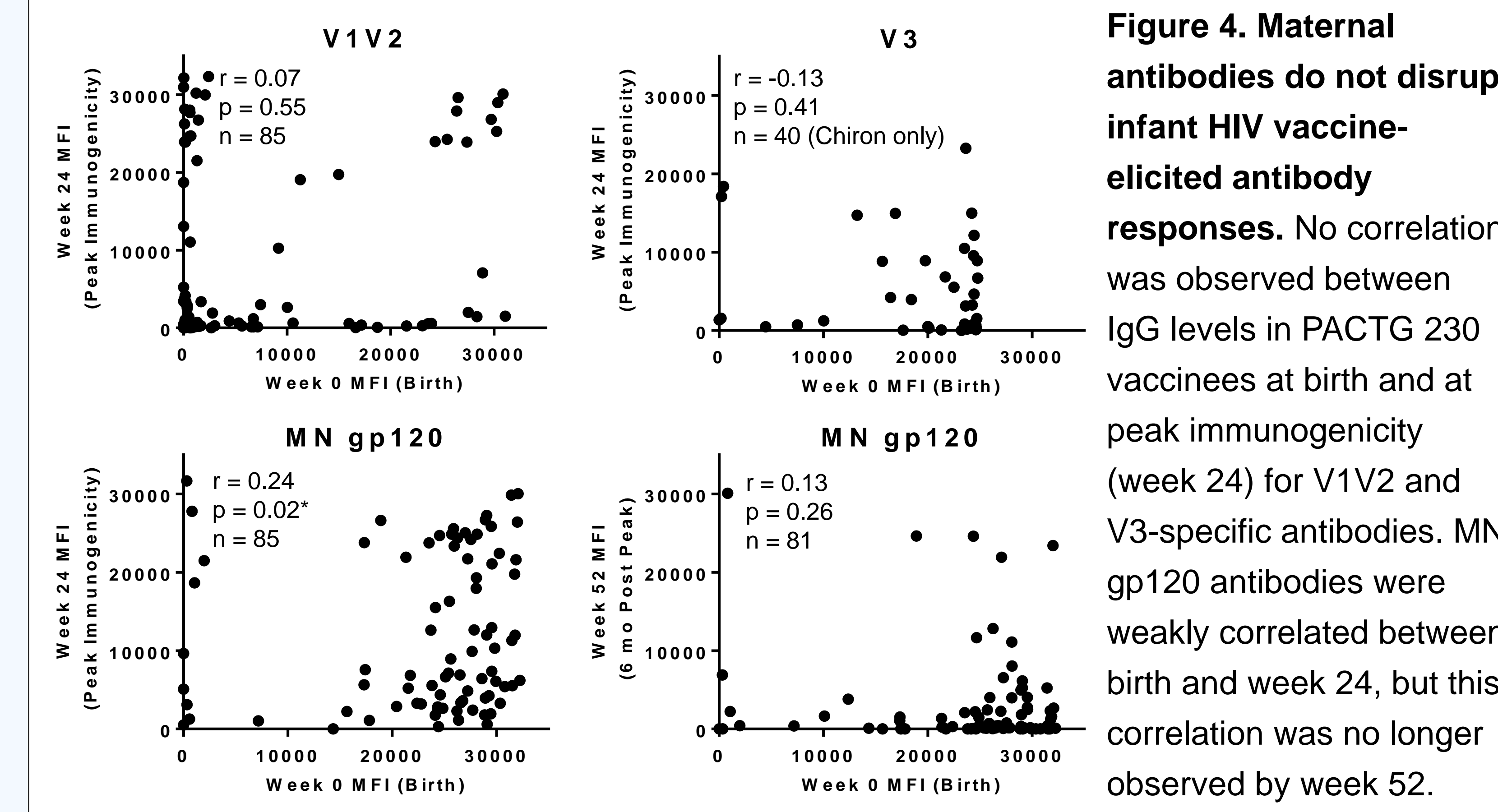
Figure 3. Infant HIV vaccines did not alter responses to common pediatric vaccines. Week 24 plasma from PACTG 230/326 was assayed by the PVMA. Solid lines indicate median values and dotted lines denote WHO IgG protective levels. P > 0.05 between placebo and vaccine groups unless otherwise noted (Wilcoxon Test).

## RESULTS: AIM 3

**V1V2** r = 0.07, p = 0.55, n = 85

**V3** r = -0.13, p = 0.41, n = 40 (Chiron only)

**MN gp120** r = 0.24, p = 0.02*, n = 85

**MN gp120** r = 0.13, p = 0.26, n = 81

Figure 4. Maternal antibodies do not disrupt infant HIV vaccine-elicited antibody responses. No correlation was observed between IgG levels in PACTG 230 vaccinees at birth and at peak immunogenicity (week 24) for V1V2 and V3-specific antibodies. MN gp120 antibodies were weakly correlated between birth and week 24, but this correlation was no longer observed by week 52.

## CONCLUSIONS AND IMPLICATIONS

- PVMA is a sample-saving (< 3 µL of sample needed), efficient tool that agrees with the conventional ELISA.
- The observation that infant HIV vaccination from PACTG 230/326 did not affect antibody responses to common childhood vaccines supports the potential of including an HIV vaccine in the infant immunization schedule.
- Maternal HIV-specific antibodies did not interfere with V1V2, V3, and MN gp120-specific antibody responses elicited by the PACTG 230 infant HIV vaccines.