

CoP SAP 6.2

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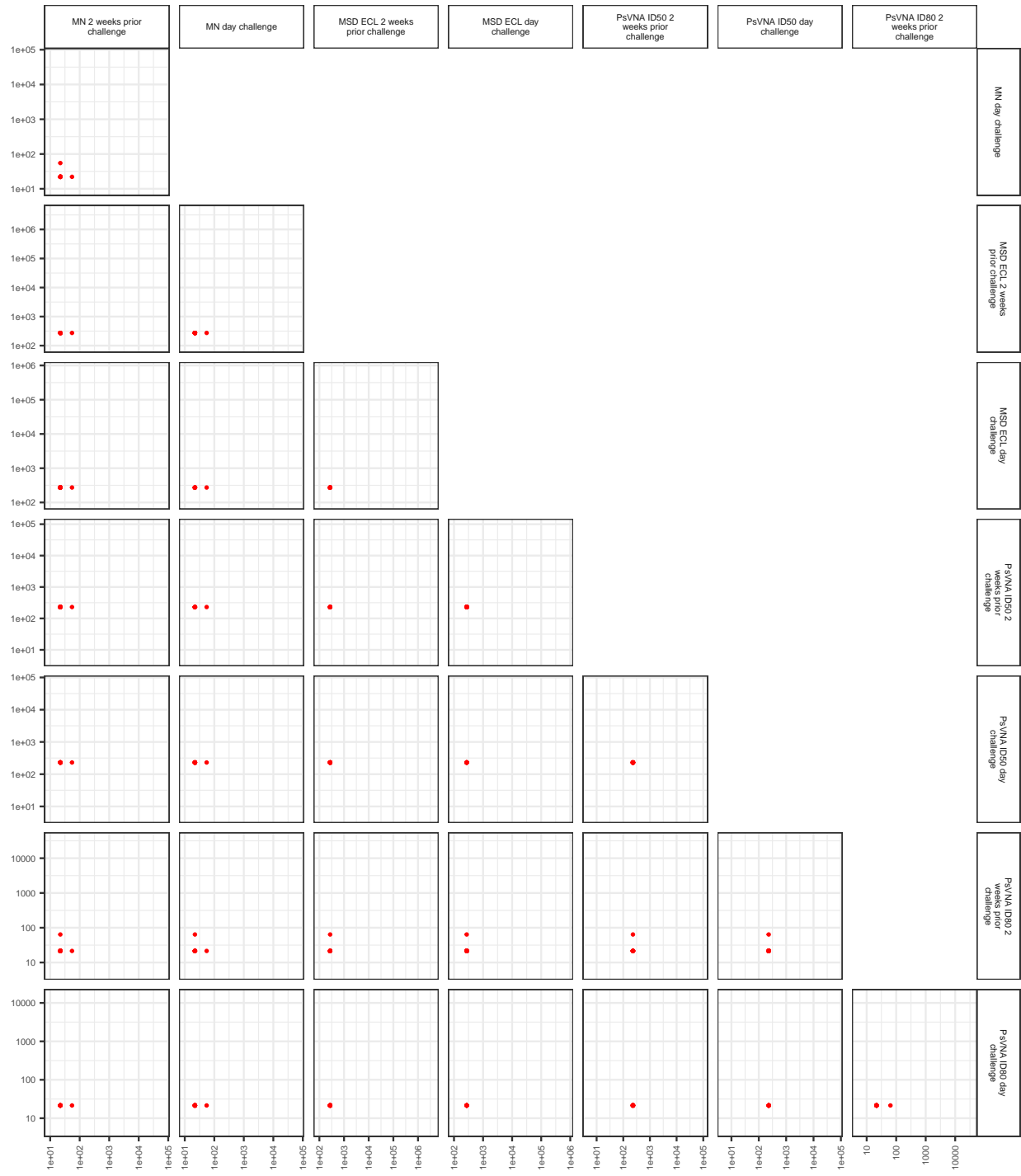
6.2 Graphical Exploration of Virus-Specific Antibodies and Viral Load

Virus-Specific Antibodies

Plots

Scatter plots of pairs of virus-specific antibodies will be generated to determine how well they correlate. All arms (different vaccine products, different dilutions, and controls) will be included on the same figure with different colors for dose groups and different panels for vaccine product.

Placebo



Dose Group • 5A

Figure 6.2.1

Sanofi

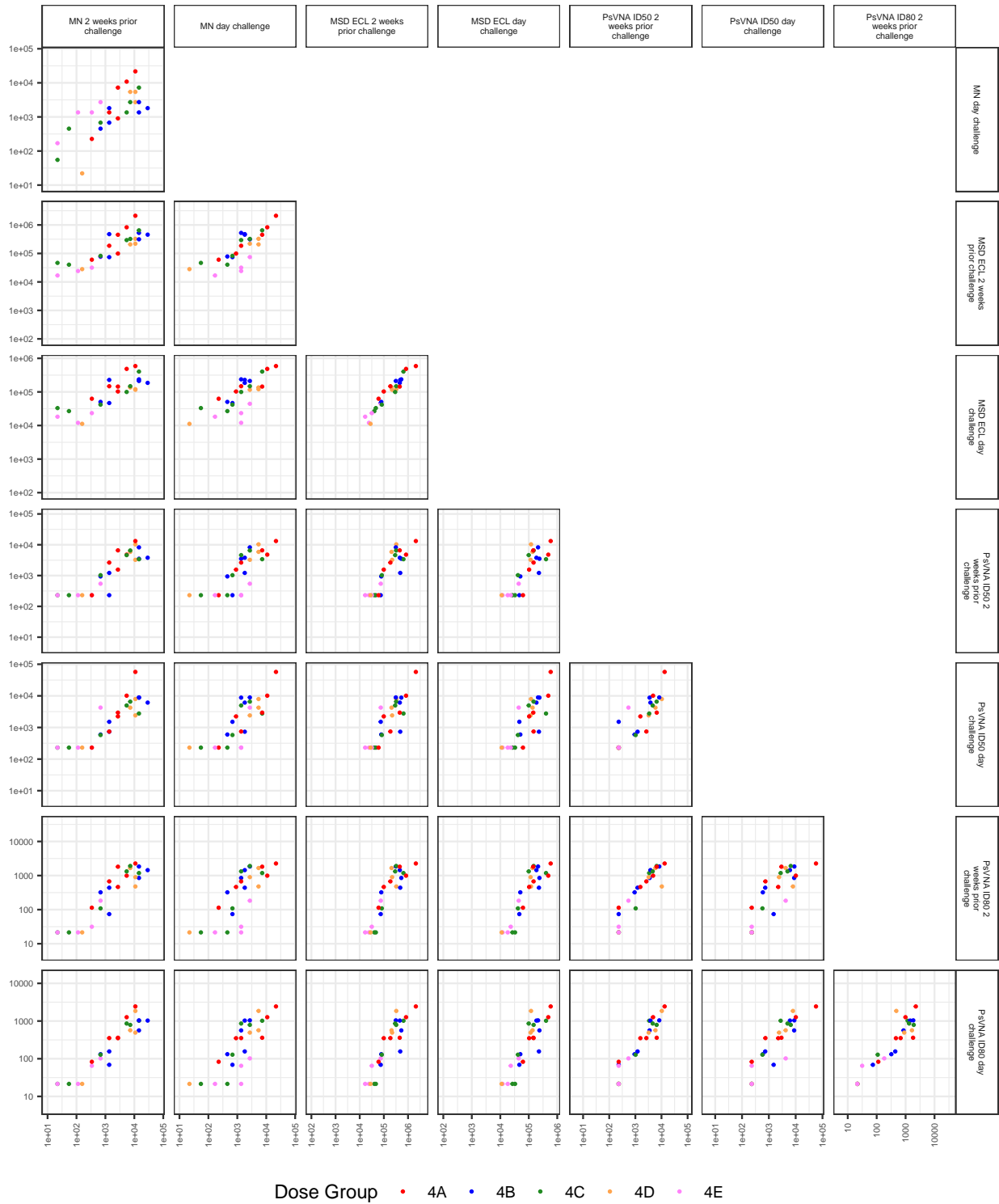


Figure 6.2.2

Moderna

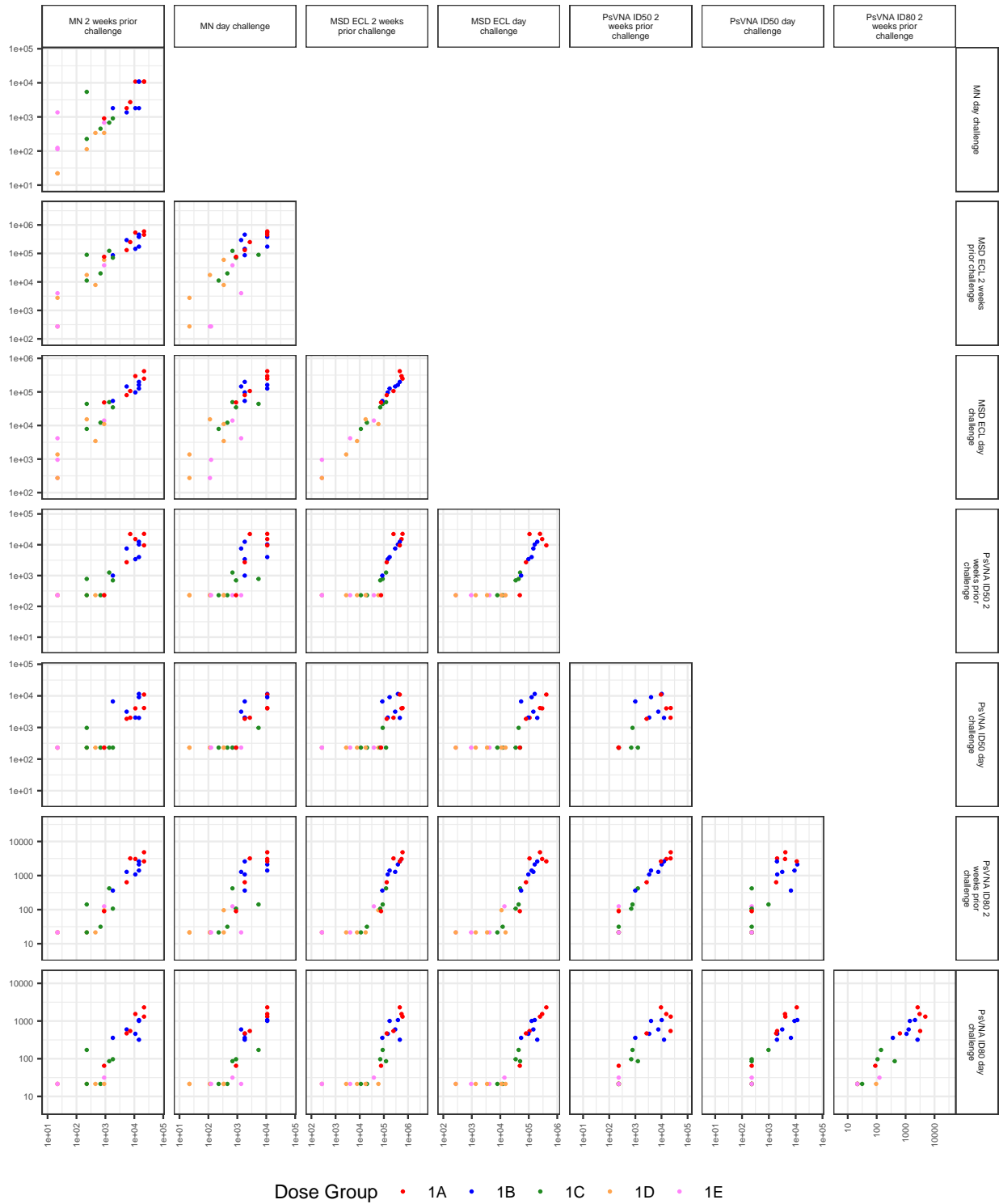


Figure 6.2.3

Janssen

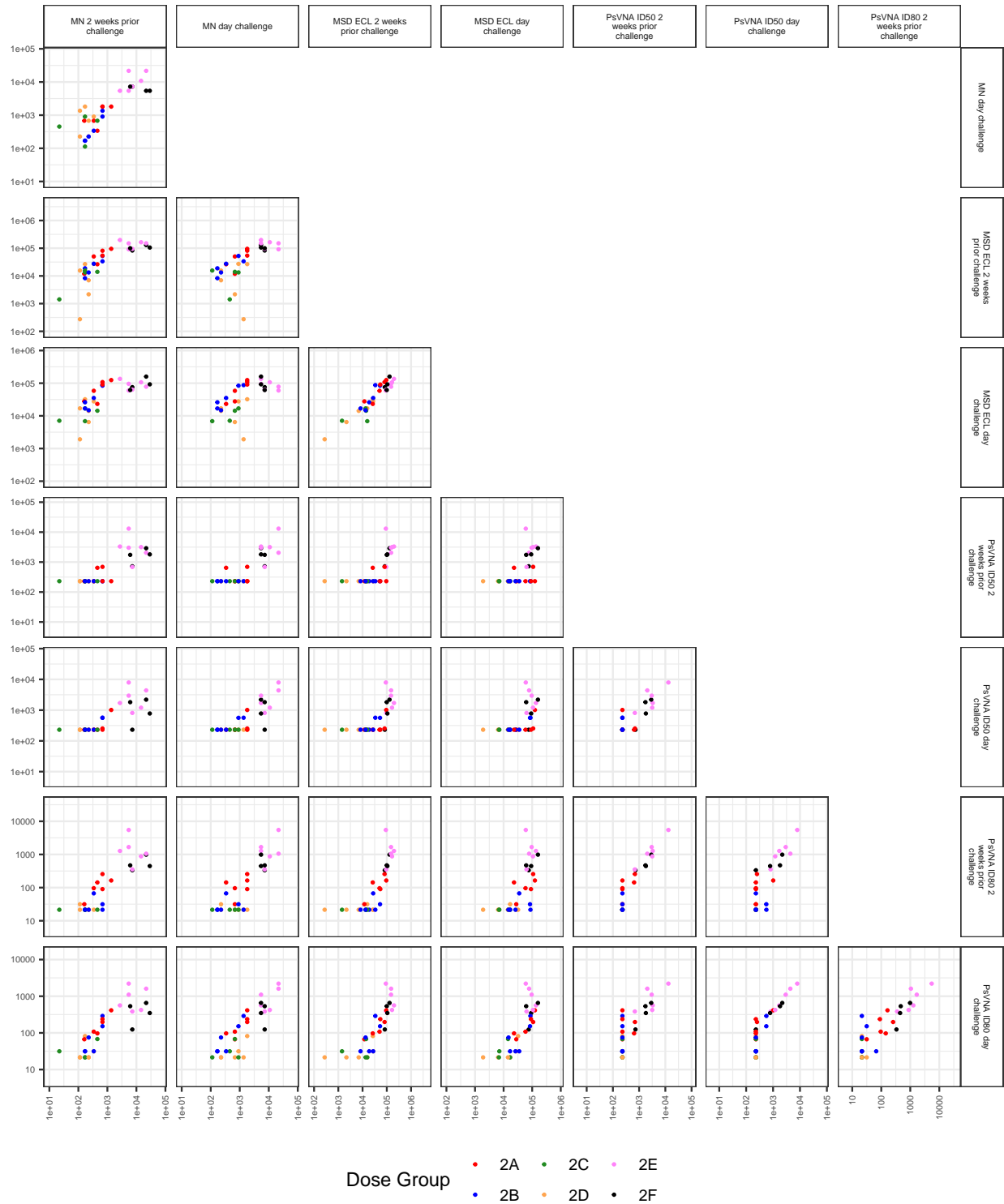


Figure 6.2.4

Novavax



Figure 6.2.5

Correlations

Simple statistics will be performed independent of the vaccine product. For example, the Spearman correlation between each pair of virus-specific antibodies will be calculated. Spearman (i.e., rank) correlations with confidence intervals will be generated; confidence intervals for the Spearman's correlation coefficient are calculated by using the ranks in a Pearson's correlation, which generally performs well (Caruso and Cliff, 1997). As there were not many ties, nonparametric bootstrap as a sensitivity analysis was not done.

Table 6.2.1: Spearman Correlations of Virus-Specific Antibodies

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
log MN 2 weeks prior challenge	-	-	-	-	-	-	-	-
log MN day challenge	0.89 (0.85, 0.92)	-	-	-	-	-	-	-
log MSD ECL 2 weeks prior challenge	0.93 (0.9, 0.95)	0.89 (0.84, 0.92)	-	-	-	-	-	-
log MSD ECL day challenge	0.91 (0.88, 0.94)	0.89 (0.84, 0.92)	0.98 (0.97, 0.98)	-	-	-	-	-
log PsVNA ID50 2 weeks prior challenge	0.89 (0.85, 0.92)	0.86 (0.8, 0.9)	0.91 (0.88, 0.94)	0.89 (0.84, 0.92)	-	-	-	-
log PsVNA ID50 day challenge	0.88 (0.83, 0.91)	0.86 (0.81, 0.9)	0.9 (0.86, 0.93)	0.89 (0.85, 0.92)	0.93 (0.9, 0.95)	-	-	-
log PsVNA ID80 2 weeks prior challenge	0.92 (0.89, 0.94)	0.87 (0.83, 0.91)	0.93 (0.9, 0.95)	0.91 (0.88, 0.94)	0.96 (0.94, 0.97)	0.92 (0.89, 0.94)	-	-
log PsVNA ID80 day challenge	0.93 (0.9, 0.95)	0.91 (0.88, 0.94)	0.93 (0.9, 0.95)	0.94 (0.91, 0.96)	0.93 (0.91, 0.95)	0.94 (0.92, 0.96)	0.95 (0.92, 0.96)	-

Viral Load

Plots

Pairwise plots of each virus-specific antibody with each viral load measurement will be generated. Data will be plotted with different colors for dose group and different panels for vaccine product.

Placebo

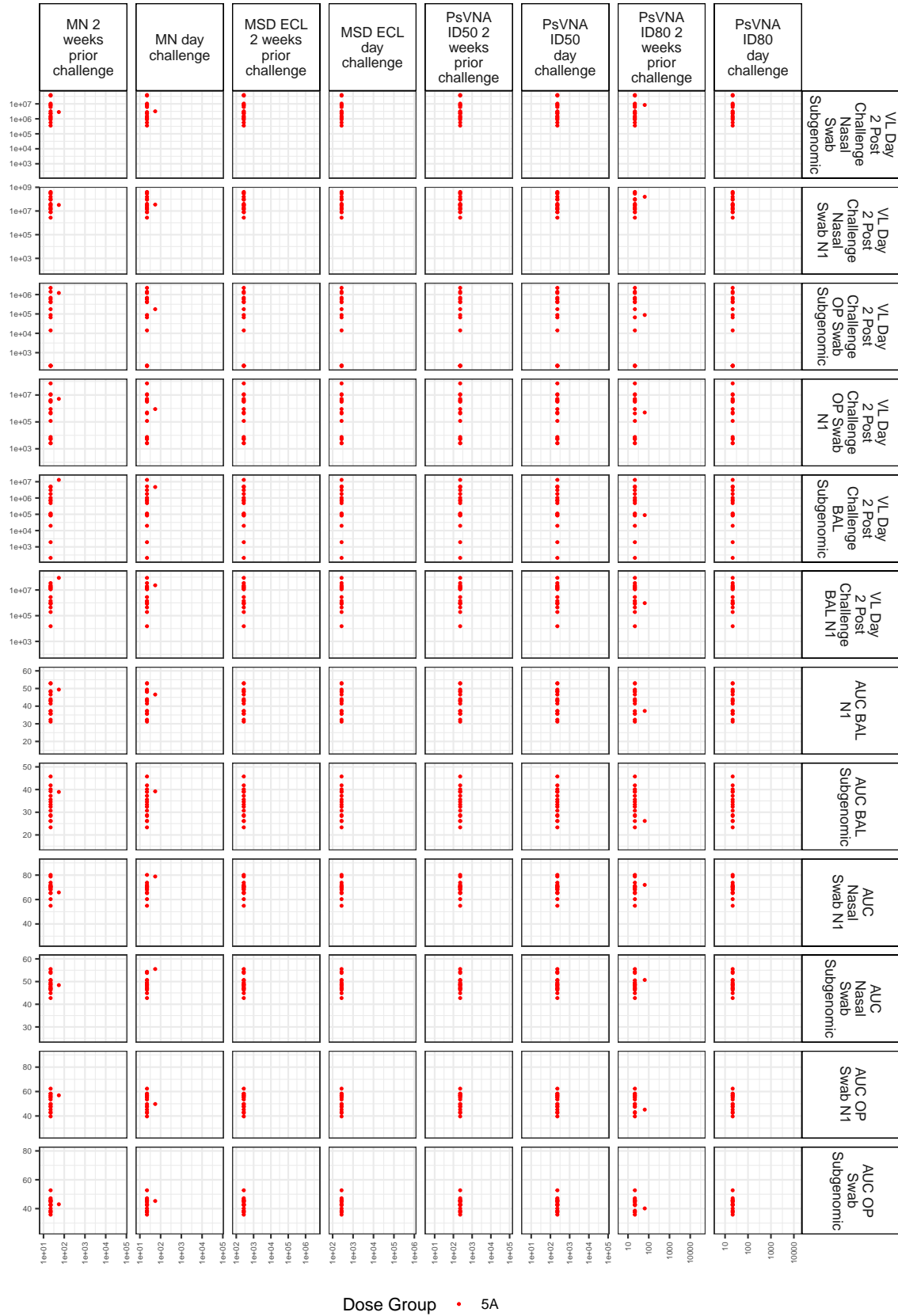


Figure 6.2.6

Sanofi

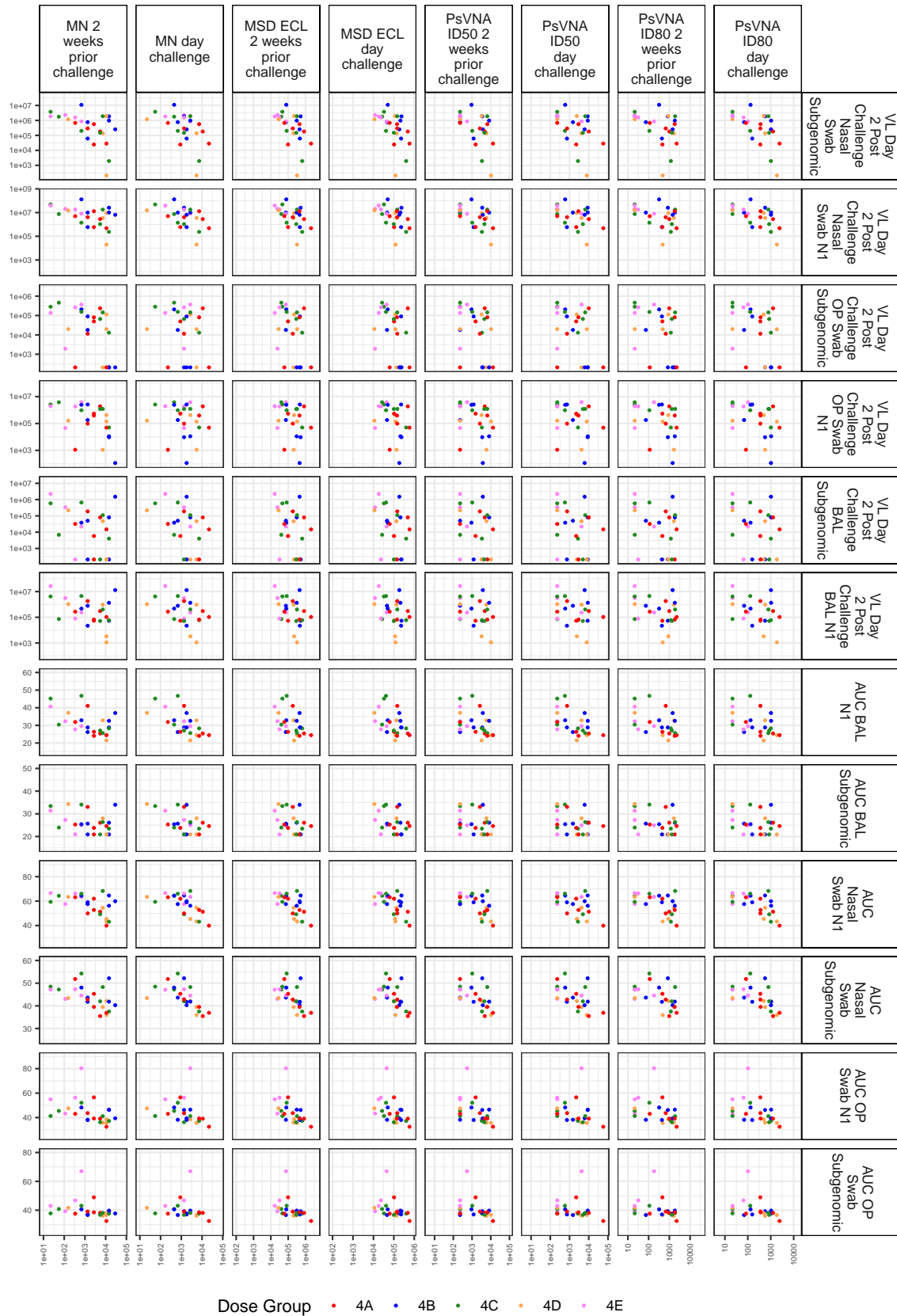


Figure 6.2.7

Moderna

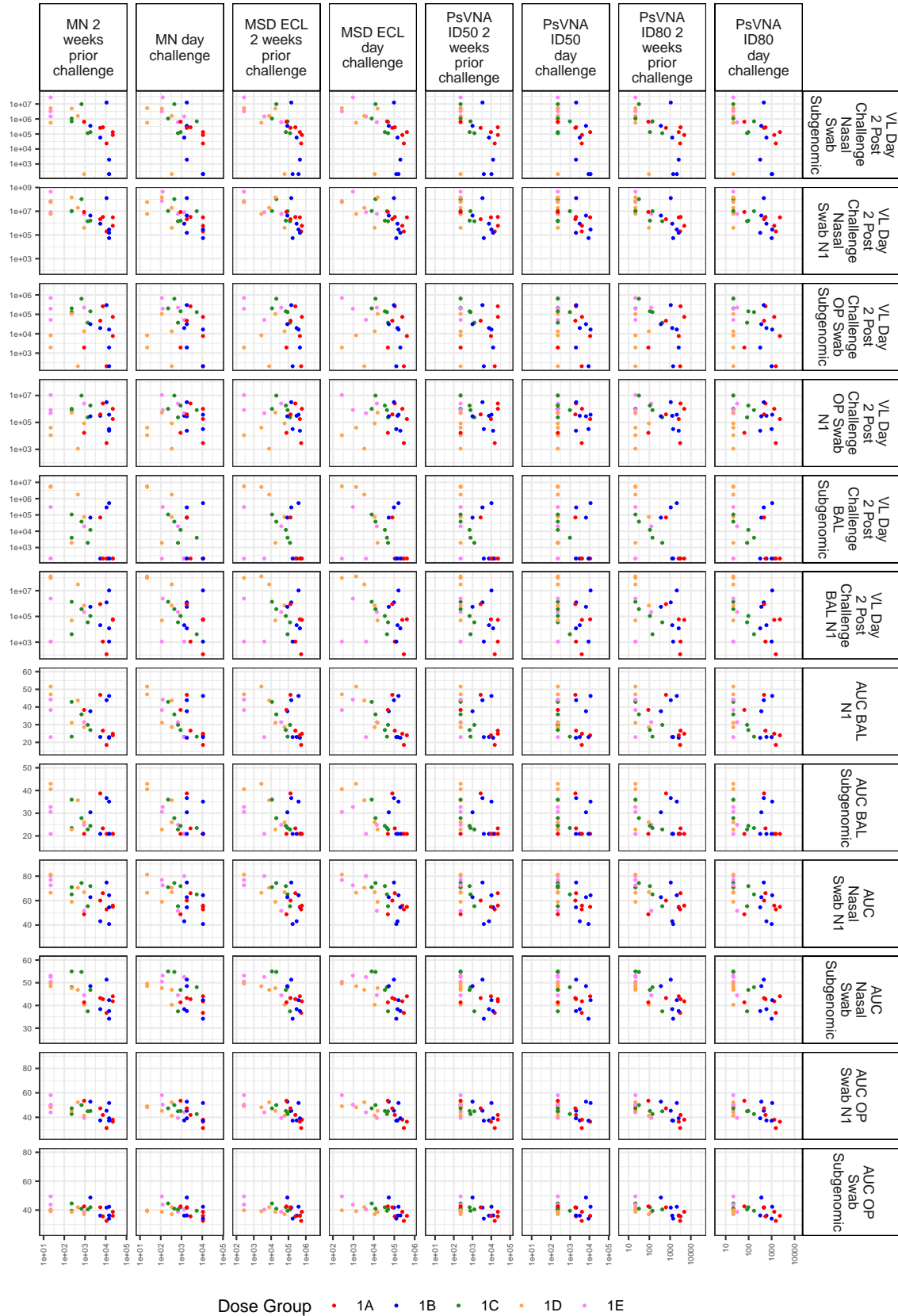


Figure 6.2.8

Janssen

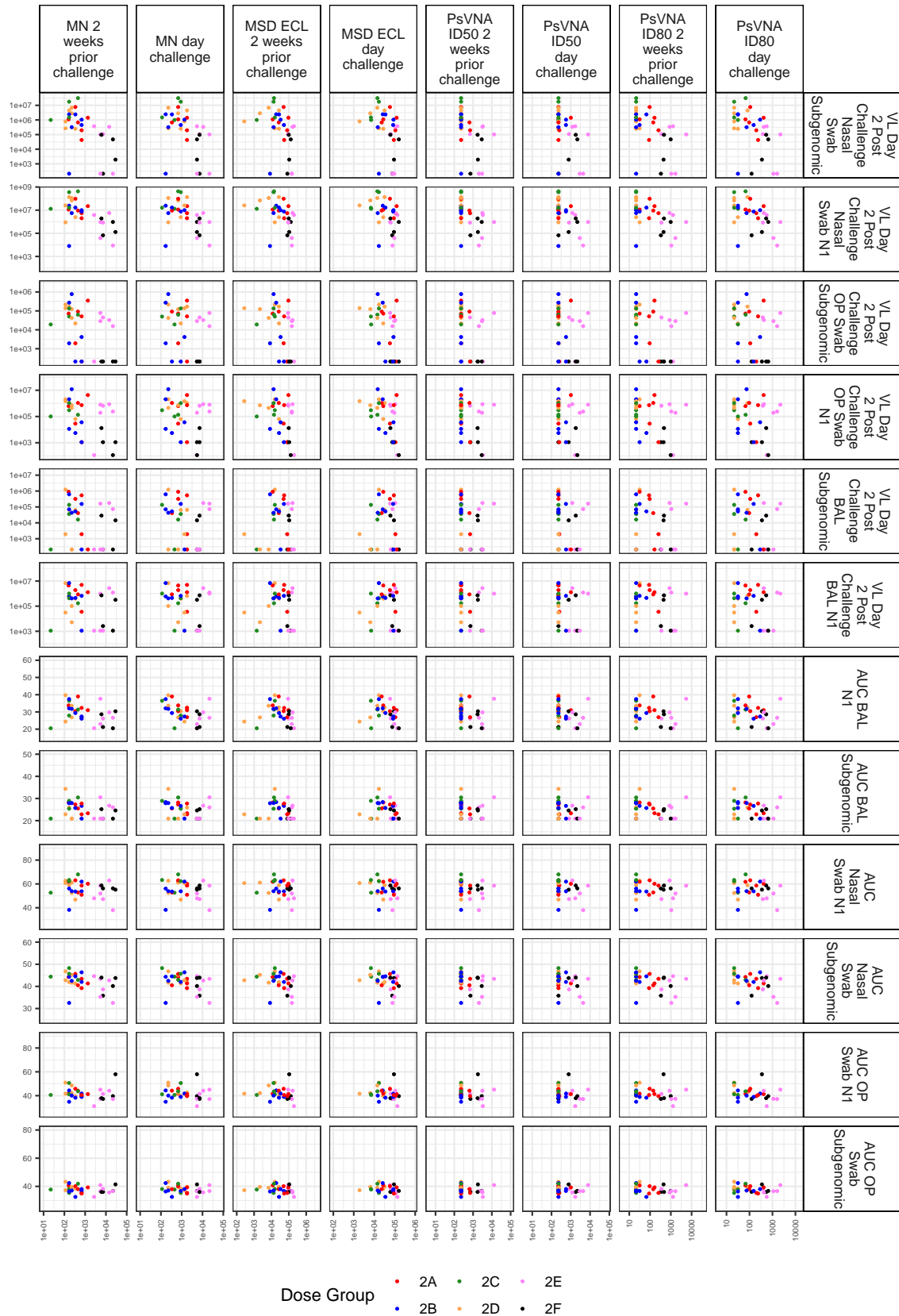
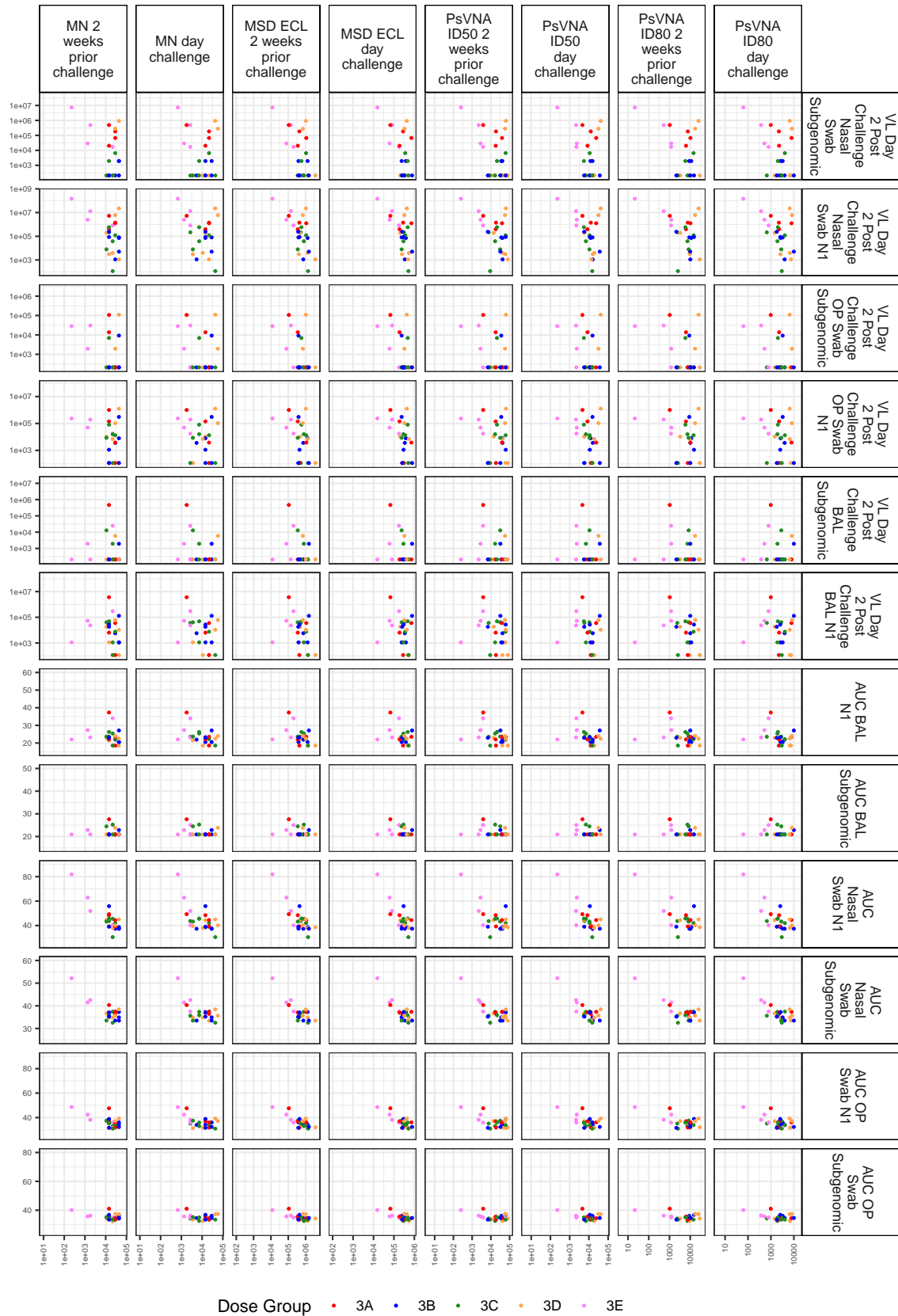


Figure 6.2.9

Novavax



Dose Group • 3A • 3B • 3C • 3D • 3E

Figure 6.2.10

Correlations - Numeric Viral Load

Spearman's correlations of all numeric viral load measurements with each other will be calculated.

Table 6.2.2: Spearman Correlations of Viral Load Outcomes

	AUC BAL N1	AUC BAL Subge- nomic	AUC Nasal Swab N1	AUC Nasal Swab Subge- nomic	AUC OP Swab N1	AUC OP Swab Subge- nomic	log VL Day2 Post Chal- lenge BAL N1	log VL Day2 Post Chal- lenge BAL Subge- nomic	log VL Day2 Post Chal- lenge OP- swab N1	log VL Day2 Post Chal- lenge OP- swab Subge- nomic	log VL Day2 Post Chal- lenge Nasal- Swab N1	log VL Day2 Post Chal- lenge Nasal- Swab Subge- nomic
AUC BAL N1	-	-	-	-	-	-	-	-	-	-	-	-
AUC BAL Subgenomic	0.88 (0.83, 0.91)	-	-	-	-	-	-	-	-	-	-	-
AUC Nasal Swab N1	0.61 (0.49, 0.71)	0.59 (0.46, 0.69)	-	-	-	-	-	-	-	-	-	-
AUC Nasal Swab Subgenomic	0.62 (0.5, 0.72)	0.55 (0.42, 0.66)	0.87 (0.82, 0.91)	-	-	-	-	-	-	-	-	-
AUC OP Swab N1	0.73 (0.64, 0.81)	0.61 (0.49, 0.71)	0.78 (0.7, 0.84)	0.76 (0.67, 0.82)	-	-	-	-	-	-	-	-
AUC OP Swab Subgenomic	0.7 (0.6, 0.78)	0.59 (0.46, 0.69)	0.69 (0.59, 0.78)	0.69 (0.59, 0.77)	0.89 (0.85, 0.92)	-	-	-	-	-	-	-
log VL Day2 PostChal- lenge BAL N1	0.86 (0.81, 0.9)	0.88 (0.83, 0.91)	0.48 (0.33, 0.61)	0.47 (0.32, 0.6)	0.57 (0.44, 0.68)	0.55 (0.41, 0.66)	-	-	-	-	-	-
log VL Day2 PostChal- lenge BAL Subgenomic	0.82 (0.75, 0.87)	0.93 (0.9, 0.95)	0.48 (0.33, 0.6)	0.47 (0.32, 0.6)	0.55 (0.42, 0.66)	0.52 (0.37, 0.63)	0.93 (0.9, 0.95)	-	-	-	-	-
log VL Day2 PostChal- lenge OPswab N1	0.43 (0.27, 0.56)	0.35 (0.19, 0.5)	0.45 (0.3, 0.58)	0.47 (0.32, 0.59)	0.52 (0.38, 0.64)	0.57 (0.44, 0.68)	0.31 (0.14, 0.46)	0.27 (0.1, 0.42)	-	-	-	-
log VL Day2 PostChal- lenge OPswab Subgenomic	0.45 (0.3, 0.58)	0.39 (0.23, 0.52)	0.5 (0.35, 0.62)	0.51 (0.37, 0.63)	0.55 (0.42, 0.66)	0.63 (0.51, 0.73)	0.33 (0.16, 0.48)	0.3 (0.13, 0.45)	0.97 (0.95, 0.98)	-	-	-
log VL Day2 PostChal- lenge NasalSwab N1	0.55 (0.41, 0.66)	0.47 (0.32, 0.6)	0.71 (0.61, 0.79)	0.75 (0.67, 0.82)	0.66 (0.55, 0.75)	0.59 (0.46, 0.69)	0.45 (0.3, 0.58)	0.41 (0.25, 0.55)	0.48 (0.33, 0.6)	0.54 (0.4, 0.65)	-	-
log VL Day2 PostChal- lenge NasalSwab Subgenomic	0.55 (0.42, 0.66)	0.48 (0.34, 0.61)	0.71 (0.61, 0.79)	0.79 (0.71, 0.85)	0.67 (0.56, 0.75)	0.61 (0.49, 0.71)	0.45 (0.3, 0.58)	0.43 (0.27, 0.56)	0.48 (0.33, 0.6)	0.54 (0.4, 0.65)	0.97 (0.96, 0.98)	-

For numeric viral load, Spearman correlations with each virus-specific Ab will be calculated.

Table 6.2.3: Spearman Correlations of Virus-Specific Antibodies with Viral Load Measurements

	log MN 2 weeks prior chal- lenge	log MN day chal- lenge	log MSD ECL 2 weeks prior chal- lenge	log MSD ECL day chal- lenge	log PsVNA ID50 2 weeks prior chal- lenge	log PsVNA ID50 day chal- lenge	log PsVNA ID80 2 weeks prior chal- lenge	log PsVNA ID80 day chal- lenge
AUC BAL N1	-0.63 (-0.72, -0.51)	-0.71 (-0.79, -0.61)	-0.65 (-0.74, -0.54)	-0.67 (-0.75, -0.56)	-0.62 (-0.72, -0.5)	-0.59 (-0.69, -0.46)	-0.63 (-0.72, -0.51)	-0.65 (-0.74, -0.54)
AUC BAL Subgenomic	-0.57 (-0.68, -0.44)	-0.62 (-0.72, -0.5)	-0.59 (-0.69, -0.47)	-0.61 (-0.71, -0.48)	-0.54 (-0.66, -0.41)	-0.5 (-0.62, -0.35)	-0.55 (-0.66, -0.42)	-0.57 (-0.67, -0.43)
AUC Nasal Swab N1	-0.69 (-0.77, -0.59)	-0.69 (-0.77, -0.58)	-0.7 (-0.78, -0.6)	-0.73 (-0.8, -0.63)	-0.63 (-0.73, -0.52)	-0.65 (-0.74, -0.53)	-0.66 (-0.75, -0.55)	-0.73 (-0.8, -0.63)
AUC Nasal Swab Subgenomic	-0.72 (-0.8, -0.63)	-0.73 (-0.8, -0.63)	-0.72 (-0.79, -0.62)	-0.73 (-0.8, -0.63)	-0.67 (-0.76, -0.57)	-0.65 (-0.74, -0.54)	-0.7 (-0.78, -0.6)	-0.74 (-0.81, -0.66)
AUC OP Swab N1	-0.66 (-0.75, -0.54)	-0.68 (-0.77, -0.58)	-0.71 (-0.79, -0.61)	-0.72 (-0.8, -0.63)	-0.65 (-0.74, -0.53)	-0.63 (-0.72, -0.51)	-0.67 (-0.76, -0.56)	-0.72 (-0.79, -0.62)
AUC OP Swab Subgenomic	-0.59 (-0.7, -0.47)	-0.61 (-0.71, -0.48)	-0.62 (-0.72, -0.5)	-0.65 (-0.74, -0.54)	-0.58 (-0.69, -0.45)	-0.55 (-0.66, -0.41)	-0.61 (-0.71, -0.49)	-0.63 (-0.72, -0.51)
log VL Day2 PostChal- lenge BAL N1	-0.5 (-0.62, -0.35)	-0.57 (-0.67, -0.43)	-0.52 (-0.64, -0.38)	-0.53 (-0.64, -0.39)	-0.53 (-0.65, -0.4)	-0.47 (-0.6, -0.32)	-0.5 (-0.62, -0.36)	-0.52 (-0.64, -0.38)
log VL Day2 PostChal- lenge BAL Subgenomic	-0.52 (-0.64, -0.38)	-0.56 (-0.67, -0.43)	-0.54 (-0.65, -0.4)	-0.54 (-0.66, -0.41)	-0.53 (-0.64, -0.39)	-0.47 (-0.6, -0.33)	-0.51 (-0.63, -0.37)	-0.52 (-0.64, -0.38)
log VL Day2 PostChal- lenge OPswab N1	-0.42 (-0.56, -0.27)	-0.35 (-0.5, -0.19)	-0.38 (-0.52, -0.22)	-0.42 (-0.55, -0.26)	-0.37 (-0.51, -0.21)	-0.37 (-0.51, -0.21)	-0.39 (-0.53, -0.23)	-0.4 (-0.54, -0.25)
log VL Day2 PostChal- lenge OPswab Subgenomic	-0.49 (-0.61, -0.34)	-0.41 (-0.55, -0.26)	-0.45 (-0.58, -0.3)	-0.48 (-0.61, -0.33)	-0.44 (-0.57, -0.29)	-0.44 (-0.57, -0.29)	-0.46 (-0.59, -0.31)	-0.47 (-0.6, -0.32)
log VL Day2 PostChal- lenge NasalSwab N1	-0.7 (-0.78, -0.6)	-0.67 (-0.76, -0.56)	-0.7 (-0.78, -0.6)	-0.69 (-0.77, -0.58)	-0.69 (-0.77, -0.58)	-0.64 (-0.74, -0.53)	-0.71 (-0.79, -0.61)	-0.71 (-0.79, -0.61)
log VL Day2 PostChal- lenge NasalSwab Subgenomic	-0.72 (-0.79, -0.62)	-0.69 (-0.78, -0.59)	-0.71 (-0.79, -0.61)	-0.7 (-0.78, -0.6)	-0.7 (-0.78, -0.59)	-0.66 (-0.75, -0.55)	-0.72 (-0.79, -0.62)	-0.72 (-0.8, -0.63)

GMR - Binary Viral Load

For binary viral load, the geometric mean ratio (GMR) as the geometric mean of the virus-specific antibodies from those animals with a positive signal for the viral load measurement (e.g., viral sub-genomic RNA for nasal swab at day 2 post-challenge) over the geometric mean of the virus-specific antibodies from those animals without a positive signal will be calculated. The confidence interval and tests on the GMR will be calculated by t-test on the difference in means of the log₁₀ virus-specific antibody values, and back-transforming it to GMRs. NA is indicated when the binary responses are the same.

Table 6.2.4: Geometric Mean Ratios of Virus-Specific Antibodies with Binary Viral Load Measurements

	bin VL Day2 PostChal- lenge BAL N1	bin VL Day2 PostChal- lenge BAL Subge- nomic	bin VL Day2 PostChal- lenge OPswab N1	bin VL Day2 PostChal- lenge OPswab Subge- nomic	bin VL Day2 PostChal- lenge NasalSwab N1	bin VL Day2 PostChal- lenge NasalSwab Subge- nomic
log MN 2 weeks prior challenge	0.04 (0.02, 0.09)	0.11 (0.05, 0.25)	0.05 (0.02, 0.09)	0.13 (0.05, 0.34)	0.05 (NA)	0.07 (0.03, 0.14)
log MN day challenge	0.05 (0.03, 0.11)	0.13 (0.06, 0.25)	0.1 (0.04, 0.23)	0.27 (0.12, 0.63)	0.02 (NA)	0.12 (0.06, 0.24)
log MSD ECL 2 weeks prior challenge	0.03 (0.01, 0.1)	0.12 (0.05, 0.29)	0.06 (0.03, 0.14)	0.2 (0.07, 0.56)	0.03 (NA)	0.08 (0.04, 0.18)
log MSD ECL day challenge	0.07 (0.04, 0.12)	0.15 (0.07, 0.31)	0.09 (0.05, 0.16)	0.26 (0.1, 0.63)	0.06 (NA)	0.13 (0.07, 0.26)
log PsVNA ID50 2 weeks prior challenge	0.05 (0.02, 0.15)	0.15 (0.08, 0.29)	0.1 (0.04, 0.24)	0.19 (0.09, 0.41)	0.15 (NA)	0.11 (0.05, 0.27)
log PsVNA ID50 day challenge	0.09 (0.04, 0.19)	0.23 (0.13, 0.42)	0.12 (0.06, 0.25)	0.25 (0.13, 0.48)	0.07 (NA)	0.15 (0.07, 0.32)
log PsVNA ID80 2 weeks prior challenge	0.03 (0.01, 0.11)	0.12 (0.05, 0.26)	0.06 (0.02, 0.14)	0.14 (0.06, 0.33)	0.1 (NA)	0.08 (0.03, 0.19)
log PsVNA ID80 day challenge	0.05 (0.02, 0.12)	0.16 (0.09, 0.31)	0.09 (0.04, 0.19)	0.2 (0.1, 0.41)	0.07 (NA)	0.11 (0.05, 0.26)

Note:

NA is indicated when there is only 1 negative signal and so a 95% CI can not be calculated.