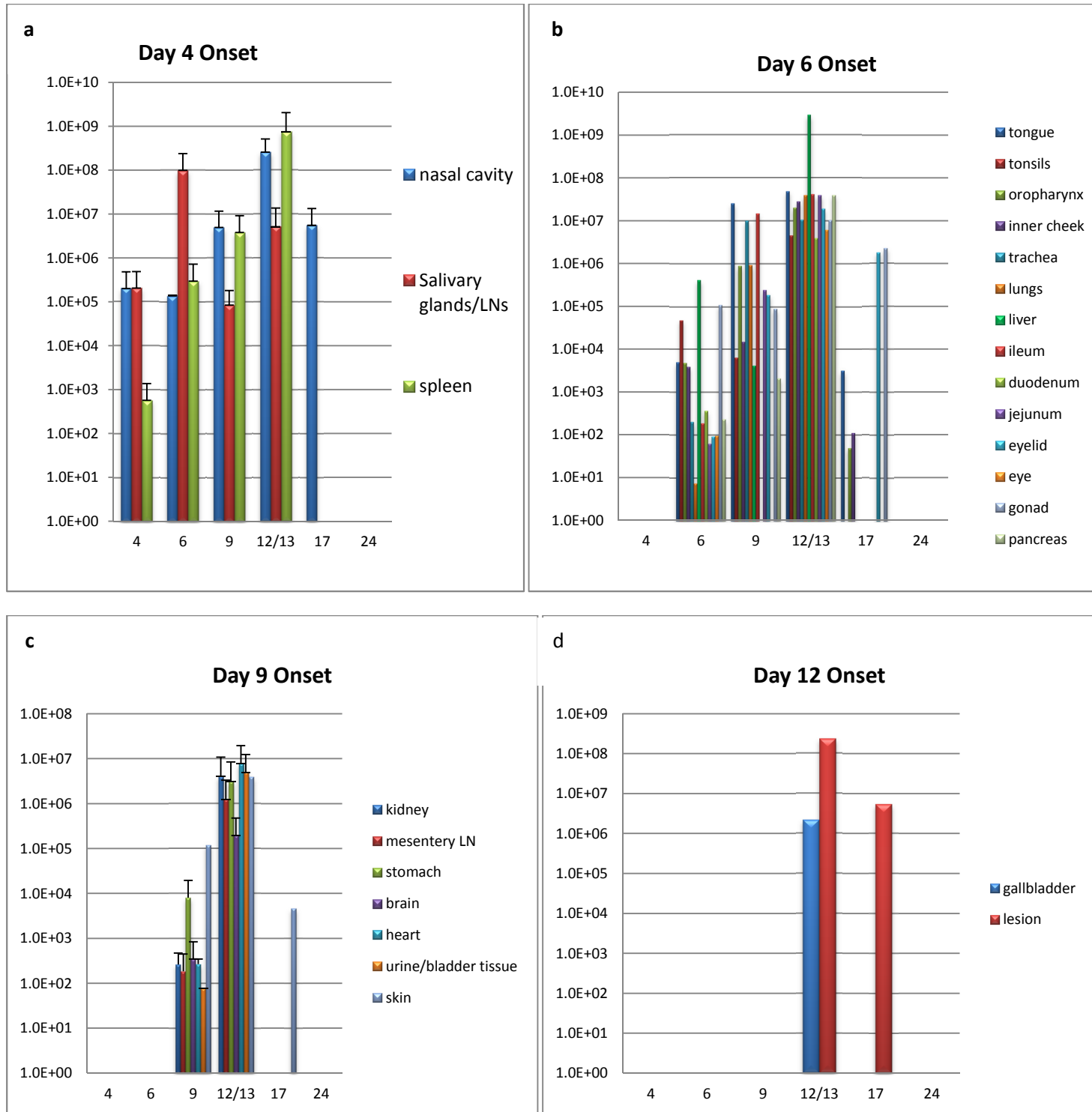Supplementary Figure 1: Mean viral loads in tissues from prairie dogs intranasally challenged (8x10^3pfu) with West African (WA) MPXV. Groups of prairie dogs were serially sacrificed (days 2, 4, 6, 9, 12, 17 and 24) following challenge. Samples were evaluated for the presence of virus and were grouped by initial detection of viable virus (day 6 (a), 9 (b), or 12 (c) p.i.). pfu/gram of tissue are shown on a log scale.

Supplementary Figure 2: Mean viral loads in tissues from prairie dogs intranasally challenged (8x10^3pfu) with Congo Basin (CB) MPXV. Groups of prairie dogs were serially sacrificed (days 2, 4, 6, 9, 12, 17 and 24) following challenge. Samples were evaluated for the presence of virus and were grouped by initial detection of viable virus (day 4 (a), 6 (b), 9 (c) or 12 (d) p.i.). pfu/gram of tissue are shown on a log scale.

	(A) West African MPXV							(B) Congo Basin MPXV							(C) PBS						
	Necropsy day							Necropsy day							Necropsy day						
	2	4	6	9	12	17	24	2	4	6	9	12	17	24	2	4	6	9	12	17	24
NA	4.9%	3.7%	2.1%	-1.4%	1.4%	-2.16%	n/a	7.23%	2.98%	-8.66%	0%	-0.72%	-2.57%	-13.89%	n/a	n/a	6.62%	2.21%	n/a	0%	n/a
K	63.9%	-1.7%	8.7%	-28.2%	3.66%	1.71%	n/a	15.8%	30.87%	-42.86%	42.7%	1.85%	2.17%	-10.7%	n/a	n/a	14.89%	35.42%	n/a	8.70%	n/a
tCO2	1.79%	-9.2%	n/a	6.06%	n/a	-1.2%	n/a	36.3%	8.14%	29.63%	0.21%	-18.75%	-6.16%	0%	n/a	n/a	-5.88%	12.9%	n/a	n/a	n/a
CL	-3.56%	8.77%	n/a	3.75%	n/a	2.5%	n/a	0%	8.77%	n/a	6.17%	n/a	8.77%	n/a	n/a	n/a	7.59%	3.66%	n/a	n/a	n/a
GLU	-76%	36%	49.6%	16.35%	5.9%	69.58%	n/a	-50.93%	65.63%	14.63%	12.09%	20.15%	24.48%	37.2%	n/a	n/a	49.15%	-22.64%	n/a	-3.74%	n/a
CA	10.05%	-5.23%	-0.94%	30.67%	-24.52%	-3.8%	n/a	30.42%	28.9%	45.92%	-3.73%	-5.94%	-12.9%	-13.4%	n/a	n/a	0%	-3.13%	n/a	-15.84%	n/a
BUN	11.16%	-2.5%	-36.8%	22.22%	10.55%	-17.7%	n/a	3.11%	10%	-25%	-4.55%	5.56%	-4%	50%	n/a	n/a	15%	-11.11%	n/a	8.70%	n/a
CRE	12.5%	6.1%	-25%	-22%	-21.4%	-23.6%	n/a	-4.44%	18.1%	-37.5%	22.22%	12.5%	0%	-55.56%	n/a	n/a	28.57%	28.57%	n/a	-22.22%	n/a
ALP	26.6%	8.84%	11.19%	-29.11%	3.03%	-36.9%	n/a	17.82%	13.76%	7.69%	-6.52%	-7.69%	-39.22%	-49.06%	n/a	n/a	77.78%	22.73%	n/a	-1.89%	n/a
ALT	-29.4%	-25.8%	125%	-30%	30%	-20%	n/a	-20.78%	15.18%	12.78%	35.71%	n/a	-29.76%	n/a	n/a	n/a	-8.33%	75%	n/a	-22.22%	n/a
AST	52.49%	-75.97%	n/a	-79.7%	n/a	-24.2%	n/a	26.99%	35.36%	-21.43%	35.36%	-62.75%	-5.78%	-8.70%	n/a	n/a	0%	-25%	n/a	n/a	n/a
TBIL	8.3%	25%	-33.3%	0	0	0	n/a	35.36%	8.33%	-16.67%	-16.67%	50	70.71%	0%	n/a	n/a	0%	0%	n/a	0%	n/a
ALB	-4.7%	-12.88%	68.4%	-9.09%	38.7%	-29.5%	n/a	-11.52%	-2.5%	18.32%	-10.44%	-22.27%	-61.22%	-30	n/a	n/a	-17.39%	-4.76%	n/a	52.4%	n/a
TP	-3.14%	-8.23%	-4.84%	-1.64%	-5.54%	8.02%	n/a	-8.93%	-2.4%	-12.48%	3.38%	-8.62%	-21.46%	-11.67%	n/a	n/a	-15.15%	-10.34%	n/a	-3.51%	n/a

Supplementary Table 1: Mean Percent Change: (Day zero value - Necropsy day value)/Day zero value in blood chemistry values for prairie dogs experimentally infected with West African MPXV (A), Congo Basin MPXV (B) or PBS control animals (C). The value change from day zero to necropsy for each blood chemistry was compared between groups. Wilcoxon rank-sum test p-values range from 0.1-1.0.

LIVER APOPTOSIS

PD#	Day p.i	Avg # of apoptotic cells	PD#	Day p.i	Avg # of apoptotic cells
PD2	PBS	0.9±0.7	PD2	PBS	0.9±0.7

A. WAMPXV | **B.** CB MPXV

PD#	Day p.i	Avg # of apoptotic cells	PD#	Day p.i	Avg # of apoptotic cells
PD11	Day 4	1±0.6	PD25	Day 4	6.2±4.5
PD12	Day 4	0.7±0.6	PD26	Day 4	1.1±0.7
PD13	Day 6	4.4±2.0	PD27	Day 6	4.6±3.3
PD14	Day 6	5.3±2.9	PD28	Day 6	2.8±1.8
PD15	Day 9	10.1±11.0	PD29	Day 9	7.9±5.0
PD16	Day 9	0.8±1.0	PD30	Day 9	4.7±3.6
PD21	Day 12	6.9±4.0	PD32	Day 12	3.6±1.3

SPLEEN APOPTOSIS

PD#	Day p.i.	Avg # of apoptotic cells	PD#	Day p.i	Avg # of apoptotic cells
PD2	PBS	3.4±1.6	PD2	PBS	3.4±1.6

C. WA MPXV | **D.** CB MPXV

PD#	Day p.i.	Avg # of apoptotic cells	PD#	Day p.i	Avg # of apoptotic cells
PD11	Day 4	1.6±1.0	PD25	Day 4	1.5±1.5
PD12	Day 4	1.4±1.5	PD26	Day 4	2±1.9
PD13	Day 6	10.7±7.8	PD27	Day 6	17.2±10.0
PD14	Day 6	8.7±5.0	PD28	Day 6	12±7.2
PD15	Day 9	17.3±8.4	PD29	Day 9	22.1±8.7
PD16	Day 9	15±4.3	PD30	Day 9	34.9±13
PD21	127	Day 12	14.8±11.1	Day 12	TMTC (>100)

Supplementary Table 2 : Number of apoptotic cells in liver and spleen from MPXV infected prairie dogs. Prairie dogs intranasally
challenged (8x10^3pfu) with West African (WA; A, C) or Congo Basin (CB; B, D)MPXV were serially
sacrificed (days 2, 4, 6, 9, 12, 17 and 24)

following challenge. Paraffin-embedded prairie dog liver (A, B) and spleen (C, D) sections were stained with Millipore Apoptosis kit and

apoptotic cells were counted. Counting of positive cellswas performed by randomly moving each slide until 10 adjacent fields were counted;

average positive cells ± the standard deviation is shown. Apoptotic cells were identified by red-brown staining nucleus. (immunoperoxidase method,

Vector NovaRed chromogen, hematoxylin counterstain).