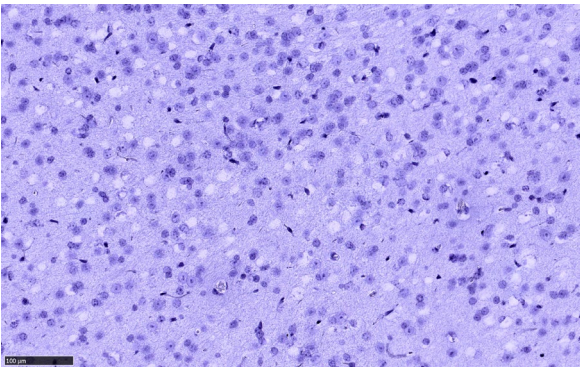
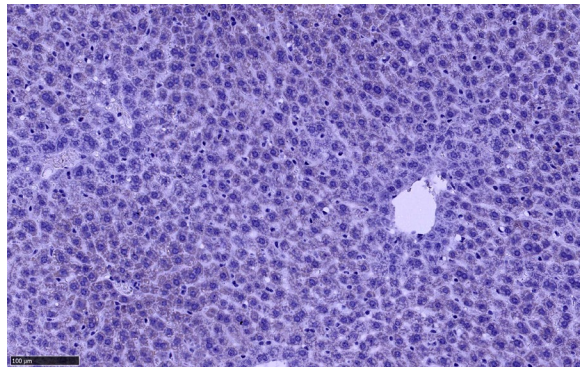


ISH, 200 ×

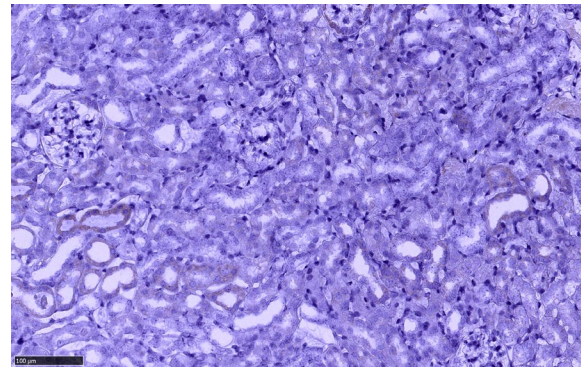
Brain



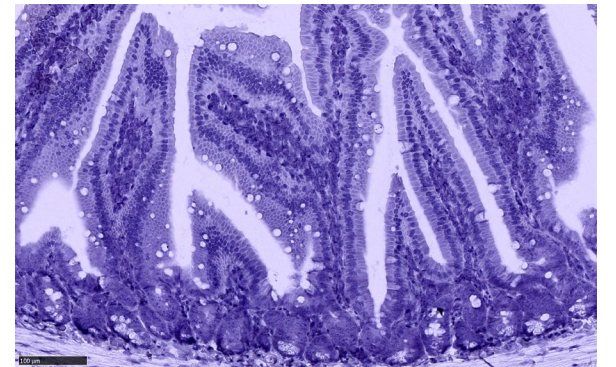
Liver



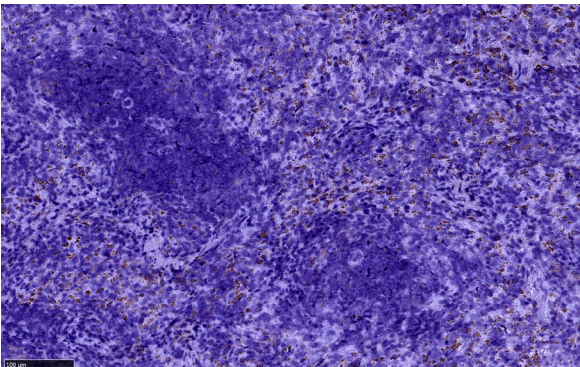
Kidney



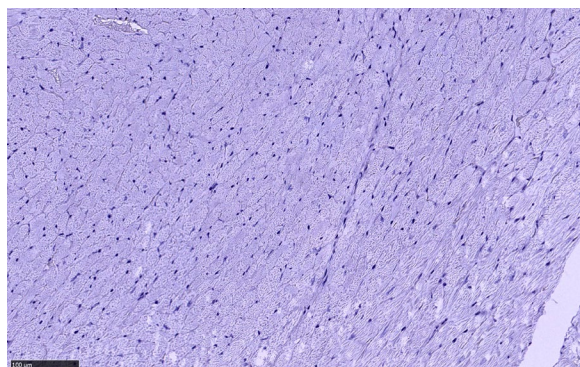
Duodenum



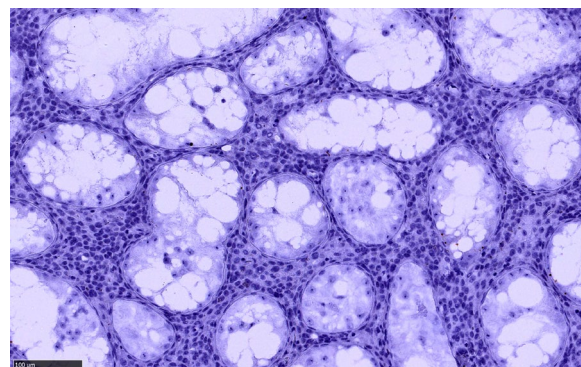
Spleen



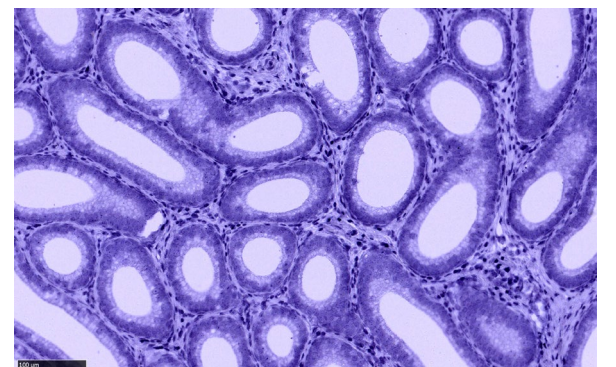
Heart



Testis

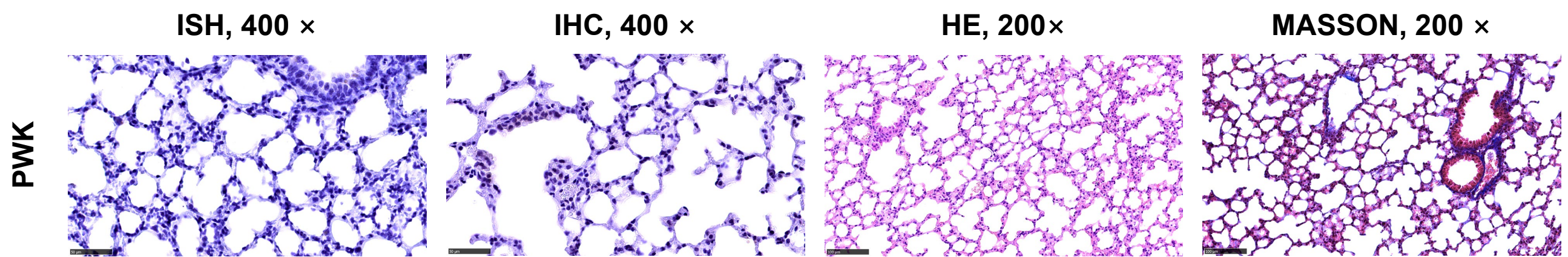


Epididymis



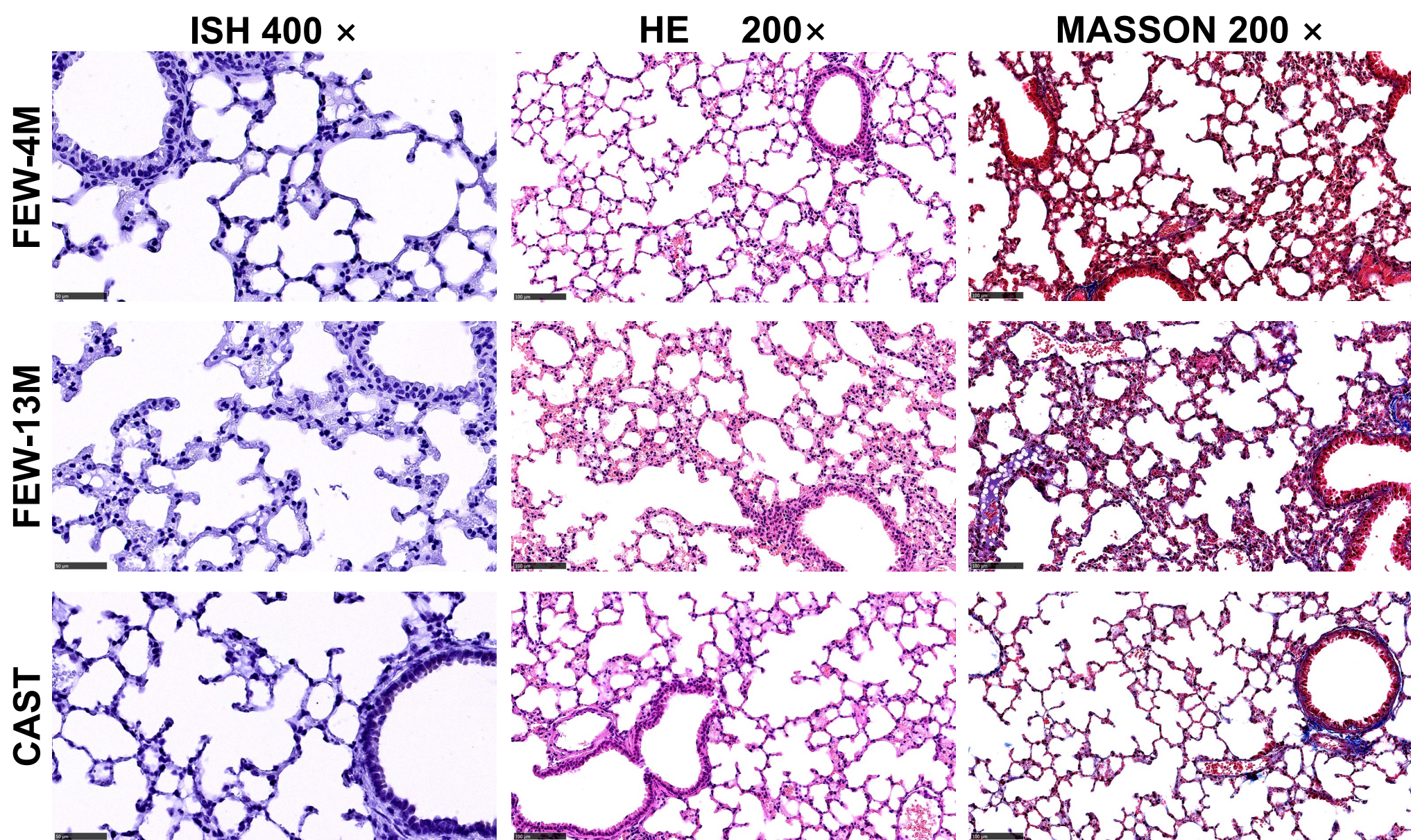
S1. Major organs of FEW after SARS-CoV-2 infection.

Viral RNA was detected by ISH in FEW, including the brain, liver, kidney, duodenum, spleen (the brown area indicated sinusoids, rather than the viral RNA), heart, testis, and epididymis. None of the tissues were affected by the SARS-CoV-2.



S2. Pathological study in the insusceptible line PWK after SARS-CoV-2 infection.

Viral RNA was not detected in YID by ISH, and viral S protein was not observed in YID by IHC. Histopathological changes in the lungs were observed by HE staining, and collagenous fibers were observed by Masson staining. And no obvious damages were observed in the lung of YID.

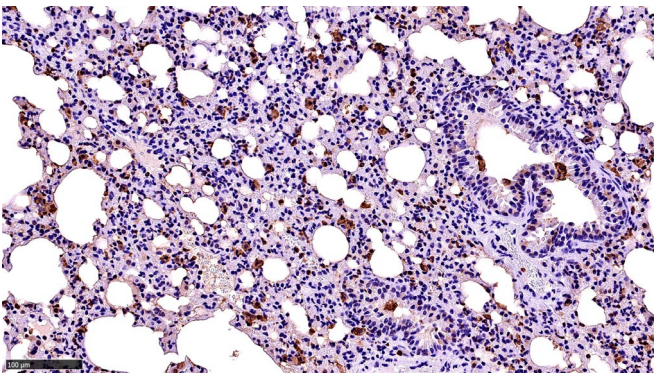


S3. Pathological study in the mock group of FEW and CAST.

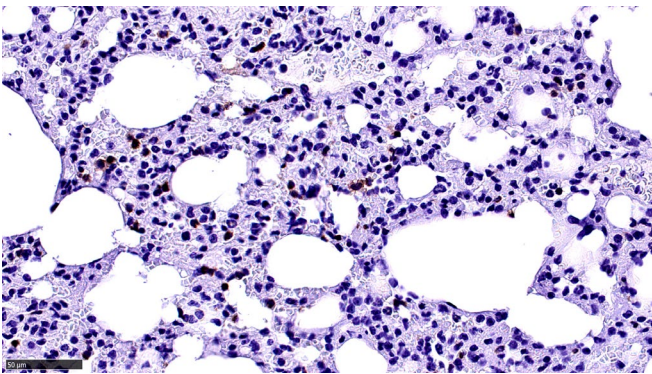
Viral RNA was not detected in the mock group of FEW and CAST by ISH. Histopathological changes in the lungs were observed by HE staining, and collagenous fibers were observed by Masson staining. No obvious damages were observed in the mock group.

Inflammation cells in FEW-13M after infection

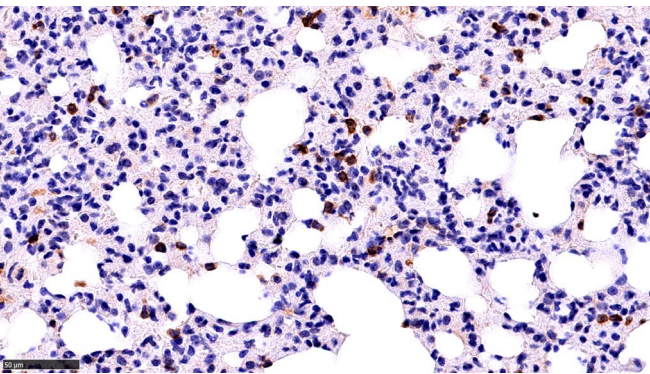
MAC-2, 200 ×



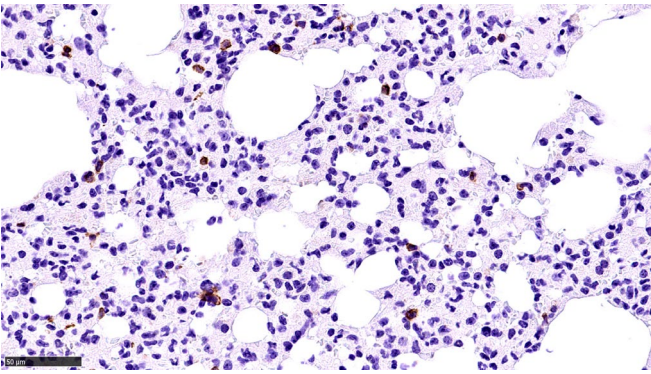
CD19, 400 ×



CD3, 400 ×



CD4, 400 ×



S4 Identification of infiltration of inflammatory cells in aged FEW after infection.

IHC was carried out to investigate the infiltration of inflammatory cells in SARS-CoV-2 infected FEW (13 M), including MAC2+ macrophages, CD19+ B lymphocytes, CD3+ and CD4+ T lymphocytes.

2nd Ab		SinoA5327-his Scale up/HRP	
Coating:		S3-SARS (WH2019)-RBD-mFc (Cat:40592-V05H; Lot:MM14MY0501)-2ug/mL	
Sampling		OD450	OD-B
Mouse ACE2 (m) with C-His tag (Cat:BD61-1; supernatant, ng/mL)	B	0.085	
	0.768	0.123	0.038
	3.84	0.135	0.050
	19.2	0.158	0.073
	96	0.154	0.069
	480	0.165	0.080
	2400	0.190	0.105
	12000	0.377	0.292
Mouse ACE2(mt) with C-His tag (Cat:BD61-1; Lot: MB15FE1007, ng/mL)	B	0.088	
	1.28	0.107	0.019
	6.4	0.124	0.036
	32	0.124	0.036
	160	0.123	0.035
	800	0.120	0.032
	4000	0.126	0.038
	20000	0.169	0.081

2nd Ab						
Coating:		Mouse ACE2 (mt) with C-His tag (Cat:BD61-1;Lot: supernatant)-2ug/mL	Mouse ACE2(mt) with C-His tag (Cat:BD61-1;Lot: MB15FE1007)-2ug/mL	0µg/mL		
Sampling		OD450	OD-B	OD450	OD-B	OD450
S3-SARS (WH2019) -RBD-mFc (Cat: 40592-V05H; Lot: MM14MY0501, ng/mL)	B	0.089		0.088		0.080
	1.28	0.084	-0.005	0.068	-0.020	0.064
	6.4	0.082	-0.007	0.070	-0.018	0.068
	32	0.097	0.008	0.061	-0.027	0.070
	160	0.090	0.001	0.063	-0.025	0.076
	800	0.087	-0.002	0.066	-0.022	0.073
	4000	0.107	0.018	0.073	-0.015	0.077
	20000	0.180	0.091	0.132	0.044	0.086

S5. The binding assay between mutated ACE2 and SARS-CoV-2-RBD

ELISA plates were coated with the mutated ACE2 or RBD respectively, his-tagged RBD or his-tagged mutated ACE2 were added for binding assay. Absorbance at 450 nm was measured, which suggesting the very low affinity between the mutated ACE2 and SARS-CoV-2-RBD.