Where indicated, membranes were physically cut according to molecular weight before antibody incubation.
The resulting membrane sections were incubated separately with the indicated antibodies and placed together for simultaneous imaging.
Red arrows indicate the positions at which the membranes were cut.

Primary Antibody	Host species	Supplier	Catalog number	Dilution	Observed MW	Specificity validation
anti-V5	Mouse	Invitogen	R960-25	1:1000	~230 kDa	EV vs V5-tagged OE, loss of V5 signal after KO, IF localization
anti-PHD3	Rabbit	Novus Biology	NB100-303	1:1000	~27 kDa	KD, OE, hypoxia-treatment
anti-P65	Rabbit	Abcam	ab32536	1:1000	~70 kDa	well-characterized antibody, KD, TNFα-induced nuclear translocation
anti-P65	Mouse	Santa Cruz	sc-109	1:500	~70 kDa	well-characterized antibody, KD, TNFα-induced nuclear translocation
anti-P65(S536)	Rabbit	Cell Signaling	3033	1:1000	~70 kDa	well-characterized antibody, TNFα-induced phosphorylation
anti-pIKKα/β(S176/180)	Rabbit	Cell Signaling	2697	1:1000	~105 kDa / ~95 kDa	well-characterized antibody, TNFα-induced phosphorylation
anti-IKKα	Rabbit	Cell Signaling	2682	1:1000	~95 kDa	Single specific band at the expected MW, well characterized
anti-IKKβ	Rabbit	Cell Signaling	8943	1:1000	~105 kDa	Single specific band at the expected MW, well characterized
anti-pIKBα(S32)	Rabbit	Cell Signaling	2859	1:1000	~40 kDa	well-characterized antibody, TNFα-induced phosphorylation
anti-IKBα	Mouse	Santa Cruz	sc-1643	1:500	~40 kDa	well-characterized antibody, TNFα-induced degradation
anti-P105/P50	Rabbit	Abcam	ab32360	1:1000	~120 kDa / ~50 kDa	TNFα-induced nuclear translocation of p50, cytoplasmic localization of p105 confirmed by subcellular fractionation
anti-P62	Rabbit	Abcam	ab109012	1:5000	~62 kDa	well characterized, KO validation
anti-pP62(S349)	Rabbit	Cell Signaling	16177	1:1000	~62 kDa	KO validation
anti-MDM4	Mouse	Sigma-Aldrich	04-1556	1:1000	~100 kDa	Doxorubicin treatment
anti-Halo	Mouse	Promega	G9211	1:1000	~	Halo-tagged OE validation
anti-VDAC1/3	Mouse	Abcam	ab14734	1:1000	~35 kDa	detection by subcellular fractionation, expected MW
anti-Calnexin	Rabbit	Abcam	ab22595	1:1000	~110 kDa	detection by subcellular fractionation, expected MW
anti-LC3 A/B	Rabbit	Cell Signaling	12741	1:1000	~17 kDa / ~13 kDa	Expected LC3-I/II pattern, altered signal in p62-KO cells, expected MW
anti-Lamin A/C	Mouse	Cell Signaling	4777	1:1000	~70kDa / ~65 kDa	Predominantly detected in the nuclear fraction, expected MW
anti-Lamin B1	Rabbit	Abcam	ab16048	1:2000	~65 kDa	Weak signal at the expected ~65 kDa, with a prominent additional band at ~110 kDa.
anti-αTUBULIN	Mouse	Sigma-Aldrich	T5168	1:5000	~57 kDa	Widely used loading controls, specific bands at the expected MW, well characterized
anti-GAPDH	Mouse	Invitogen	MA5-15738	1:2500	~35 kDa	
anti-βACTIN	Mouse	Sigma-Aldrich	A1978	1:10000	~48 kDa	

Figure 2A

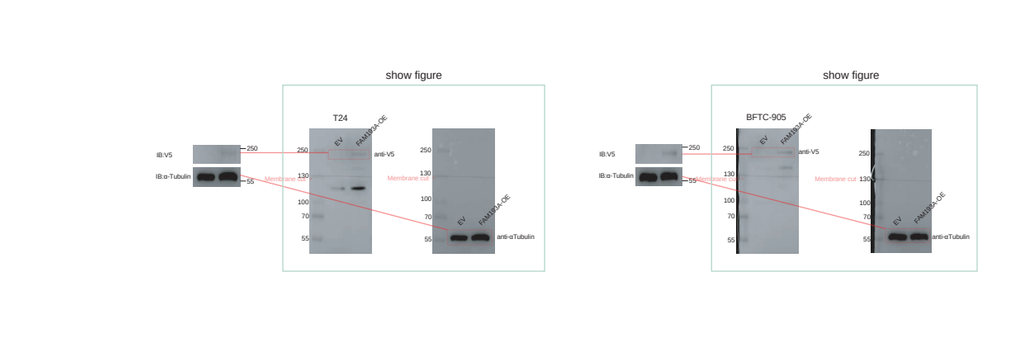


Figure 3A

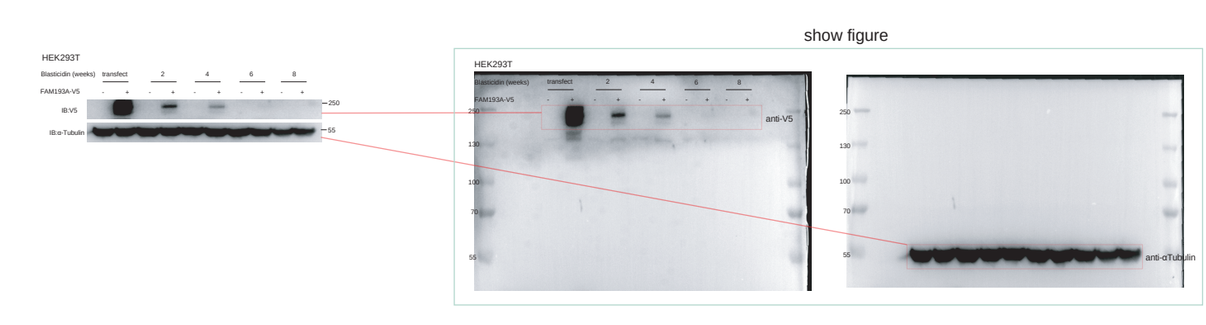


Figure 3B

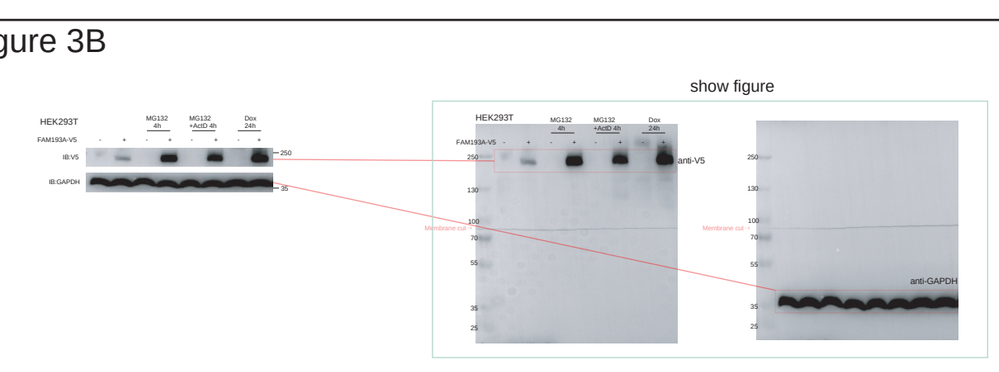


Figure 3C

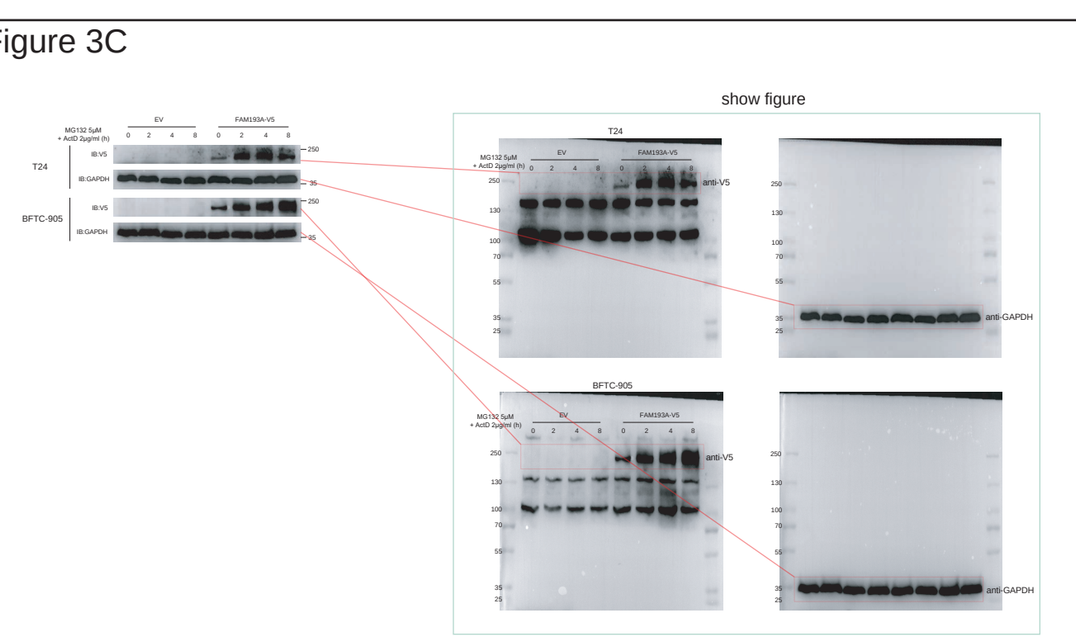


Figure 3D

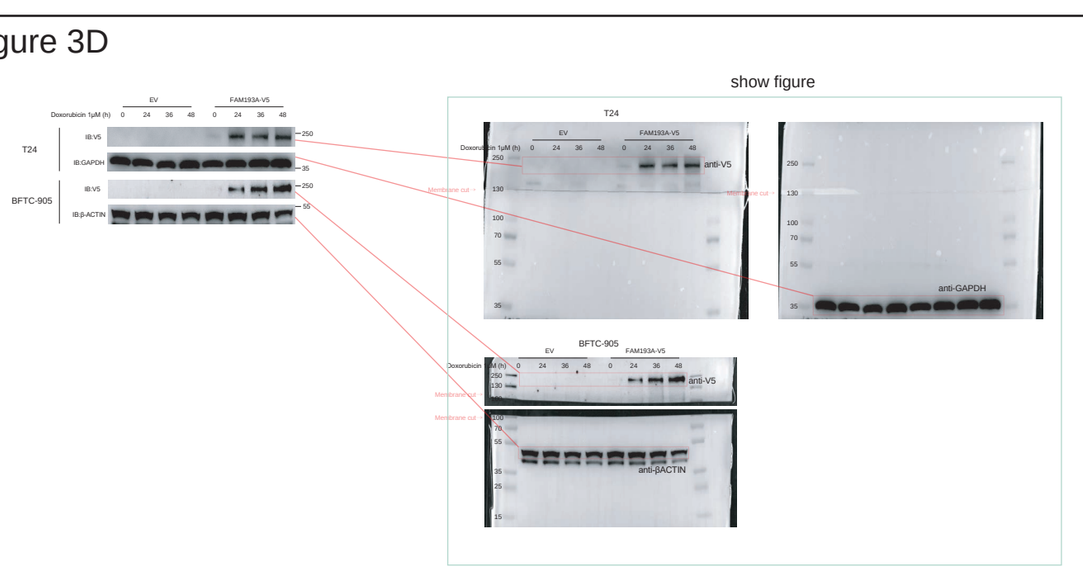


Figure 3E

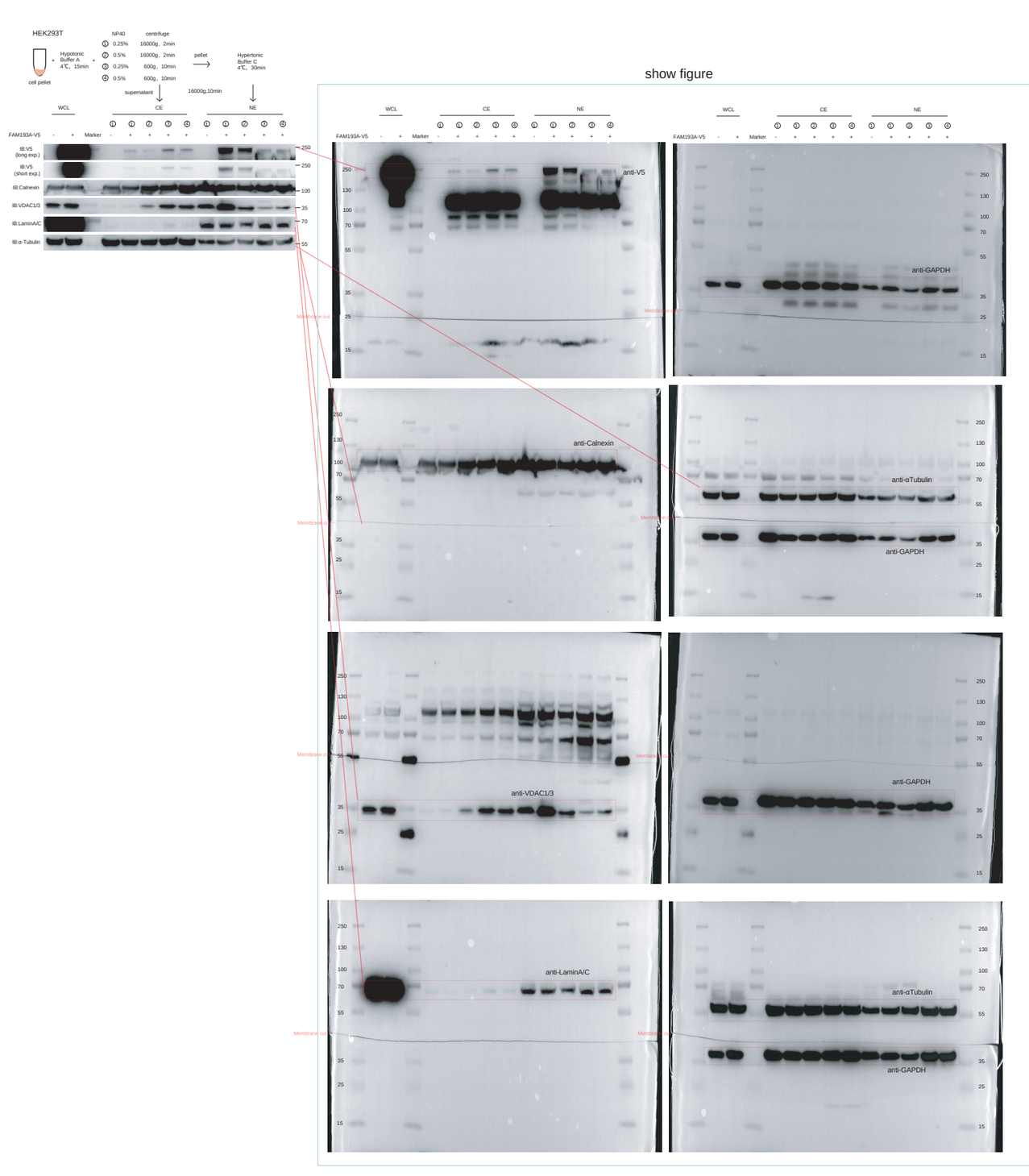


Figure 3I

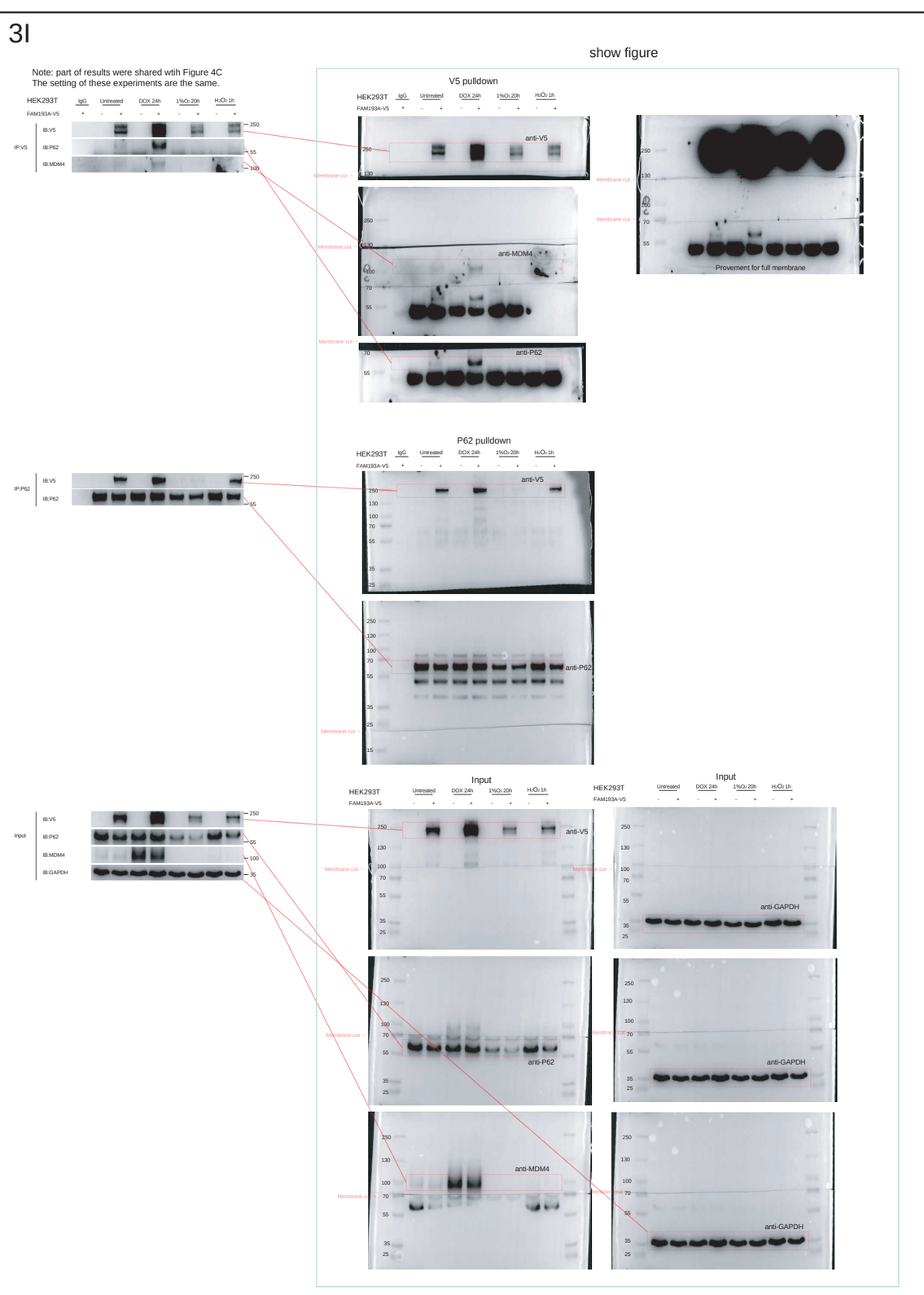


Figure 3J

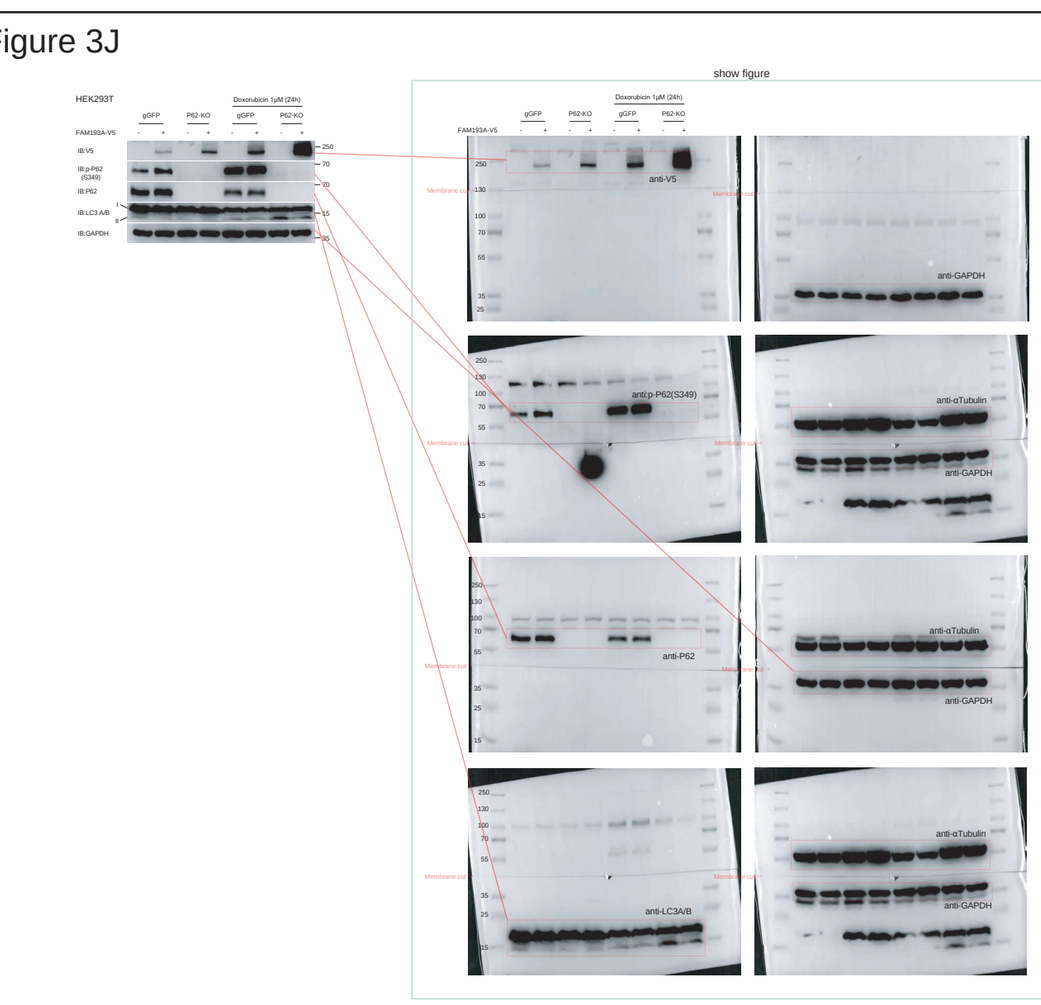


Figure 4A

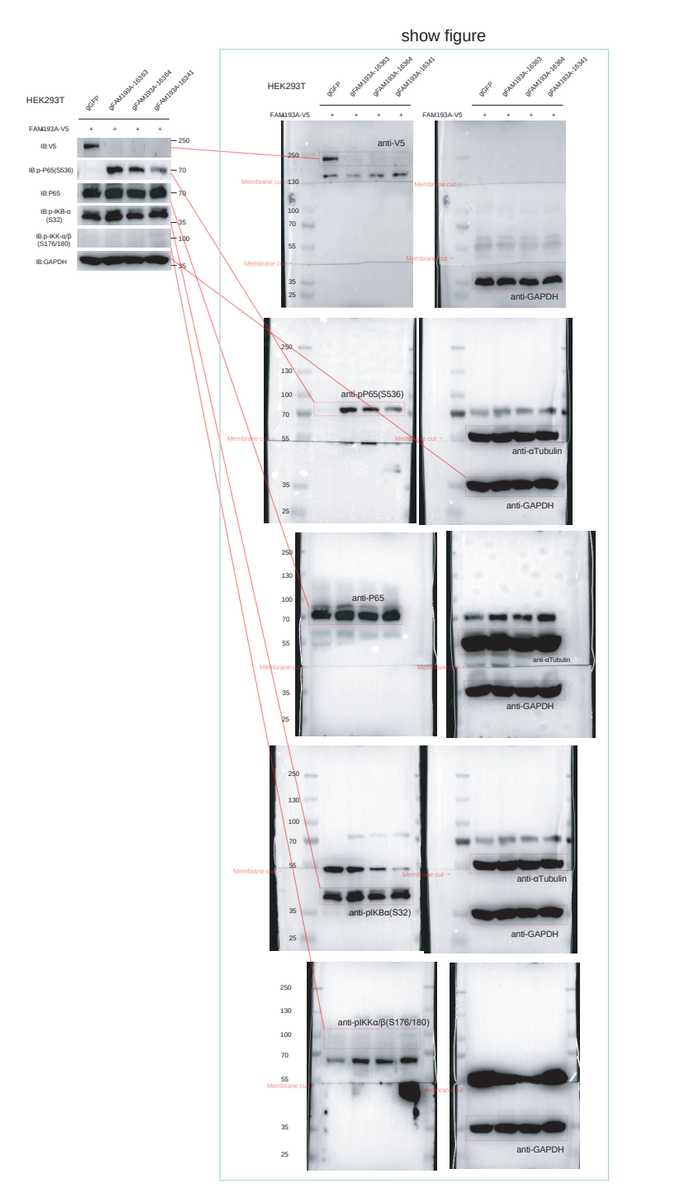


Figure 4D

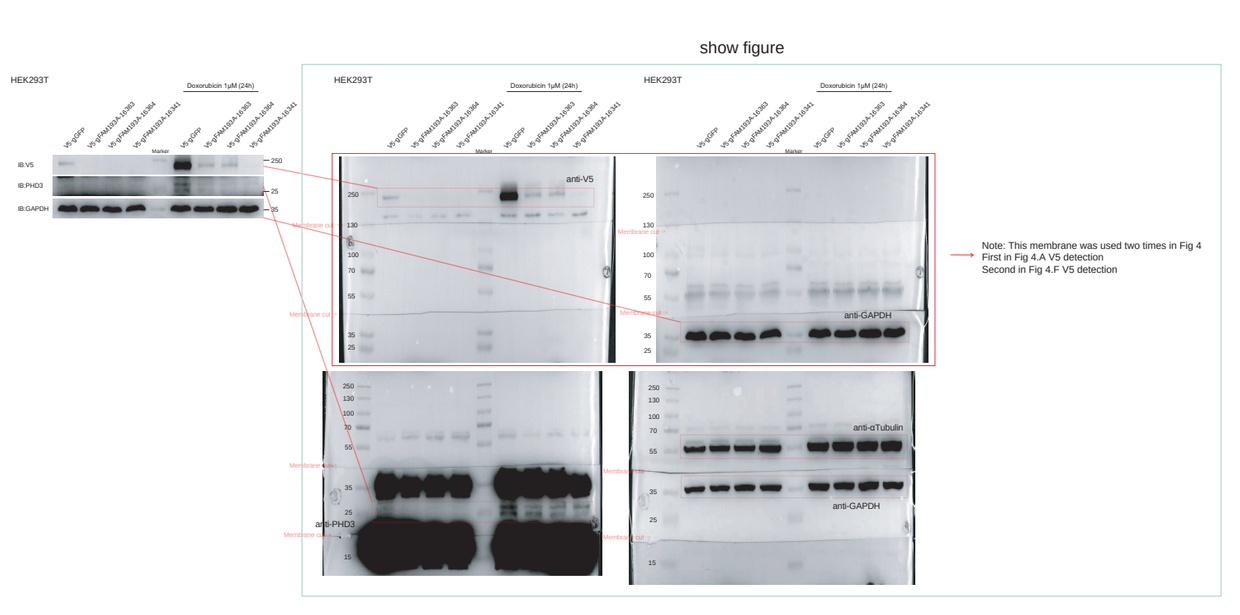


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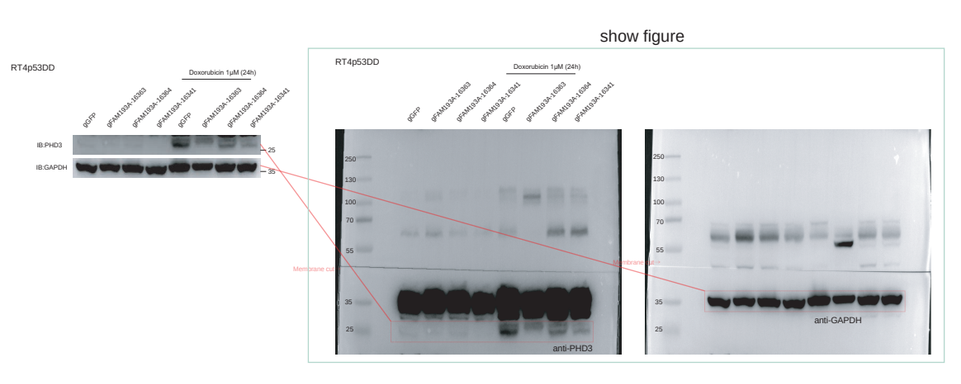


Figure 4F

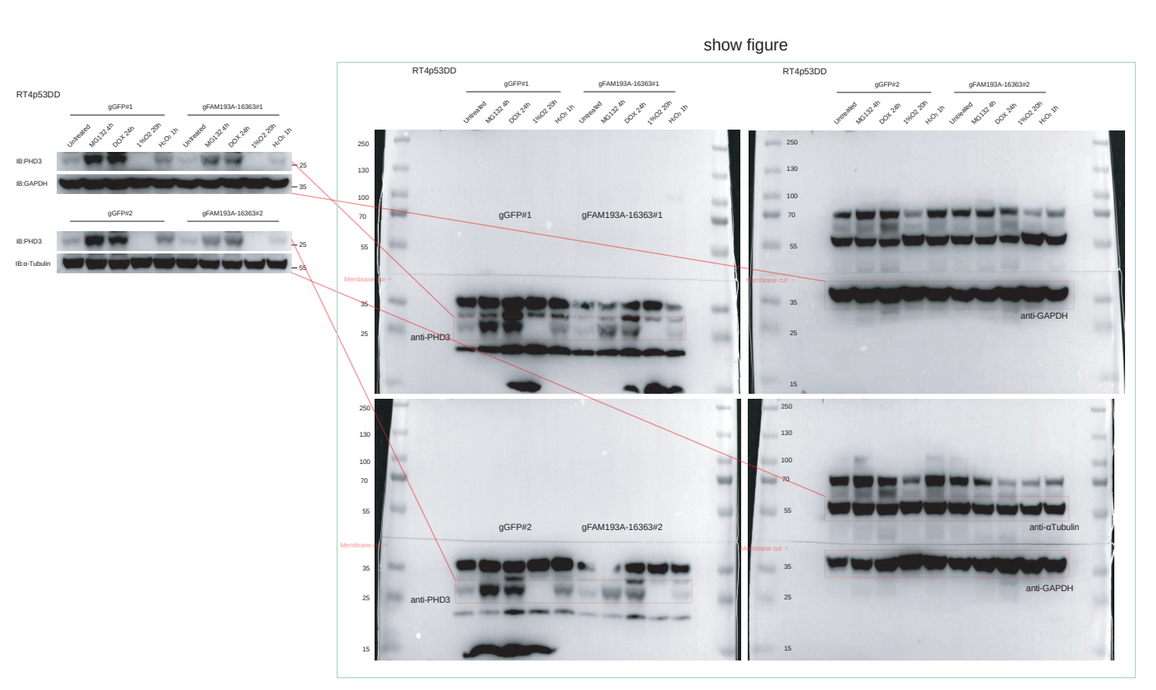


Figure 4G

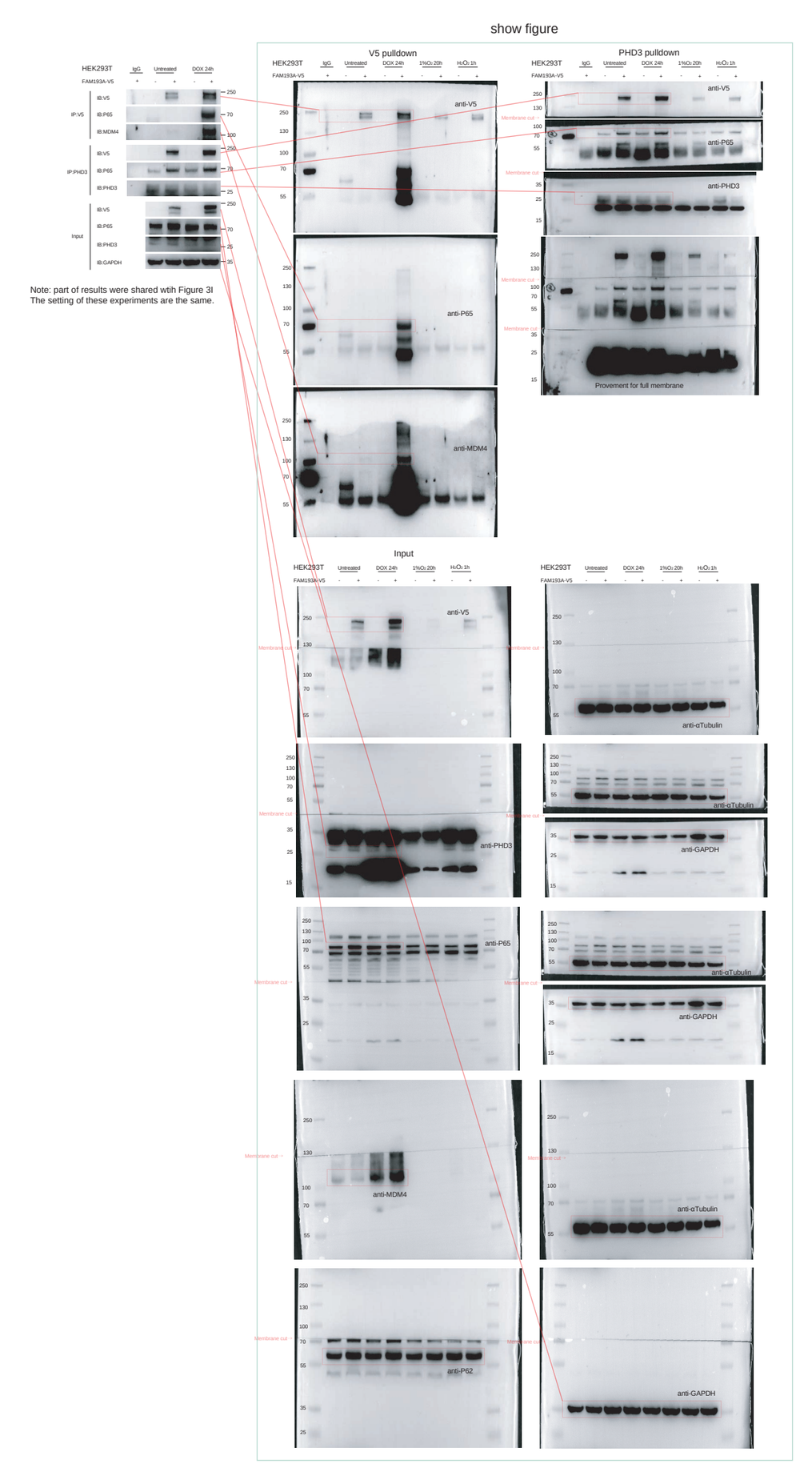


Figure 4H

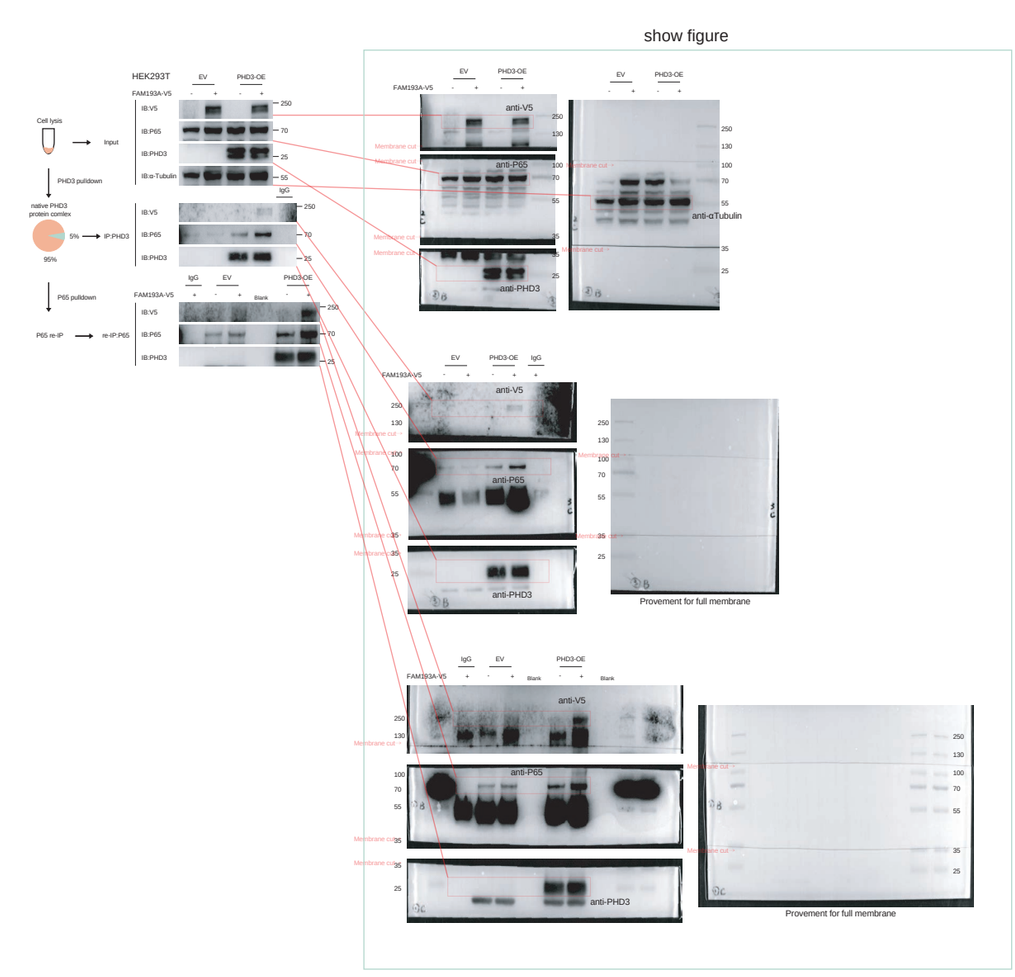


Figure 5A

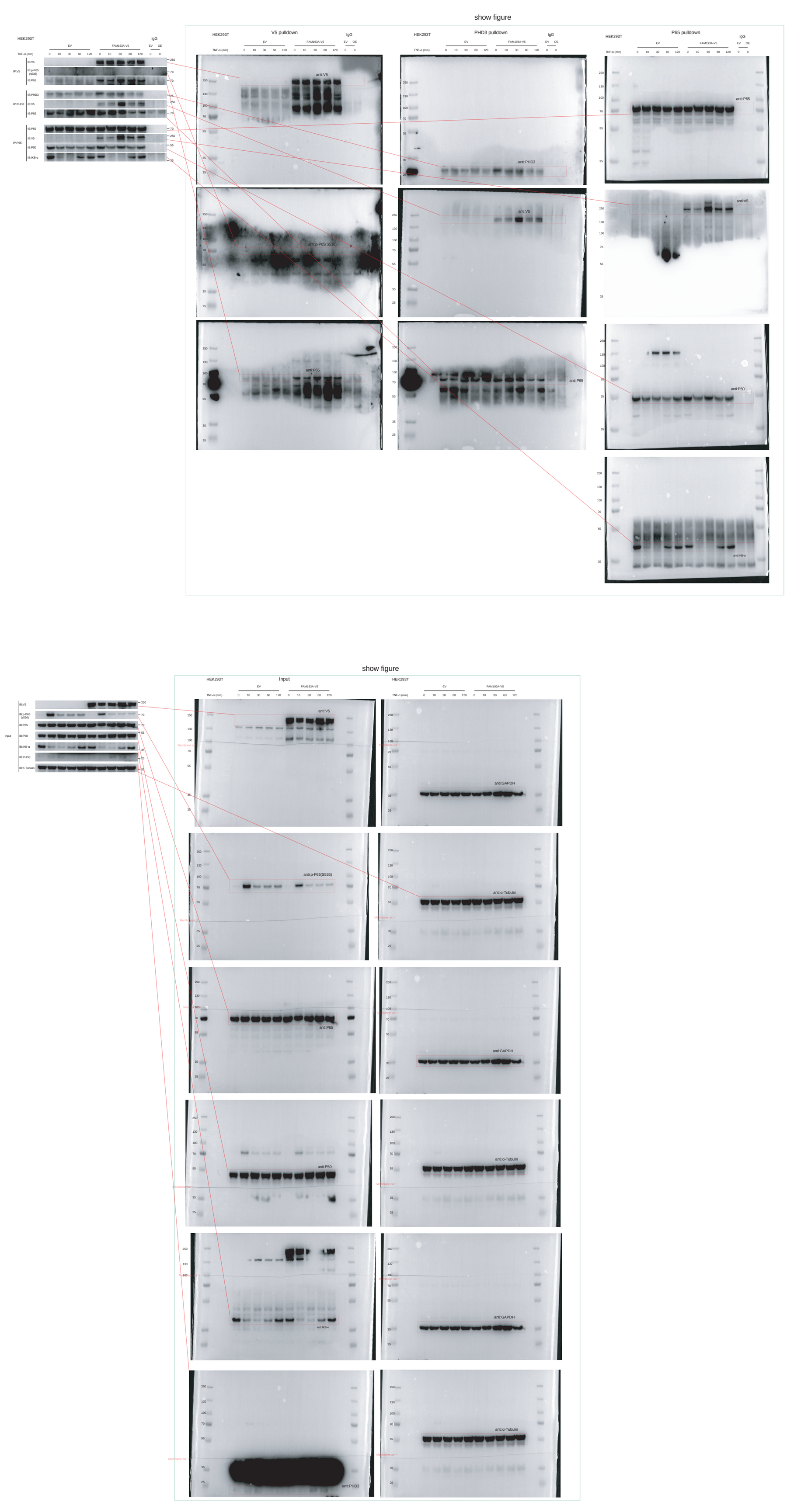


Figure 5B

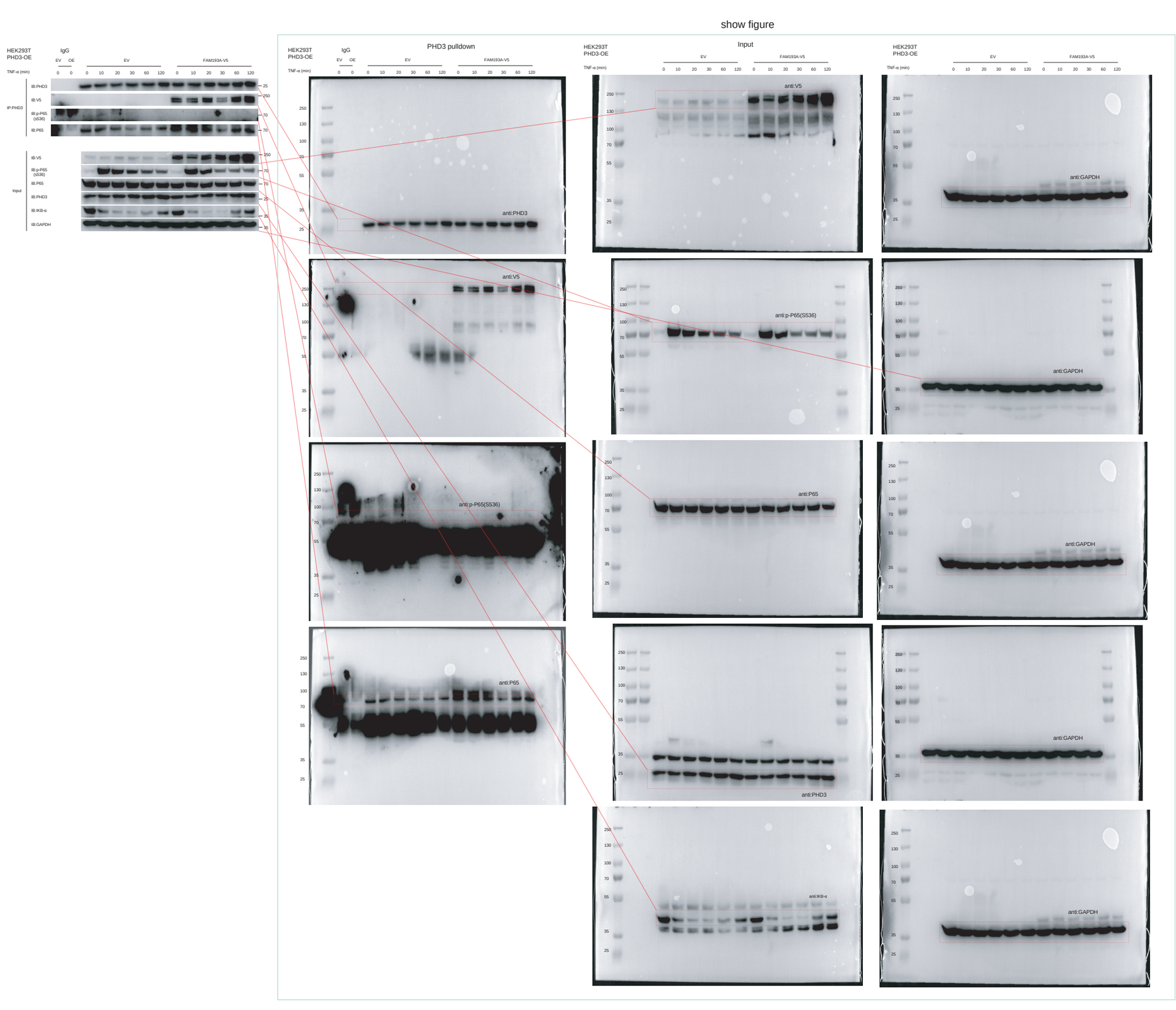


Figure 5F

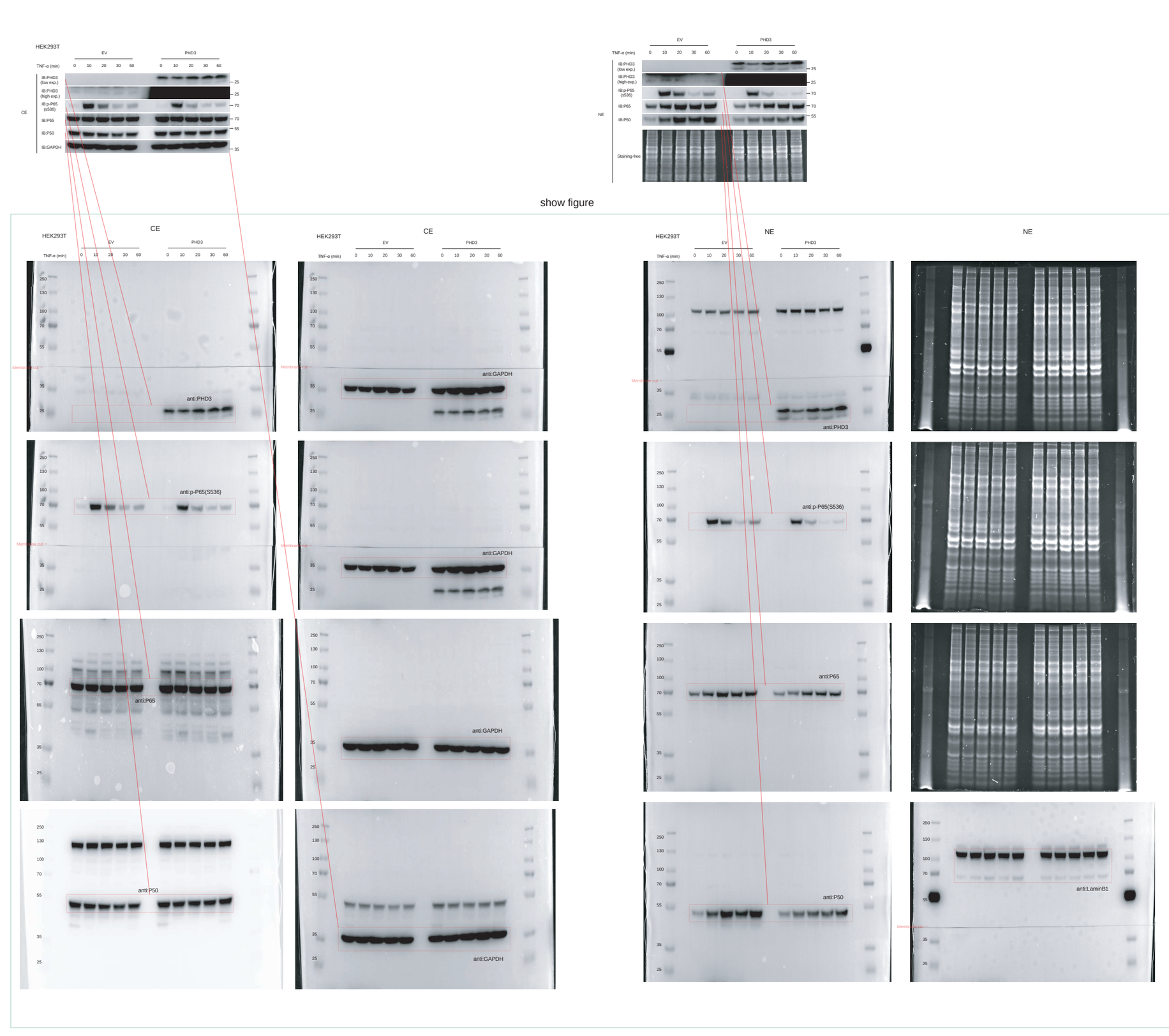


Figure 6A

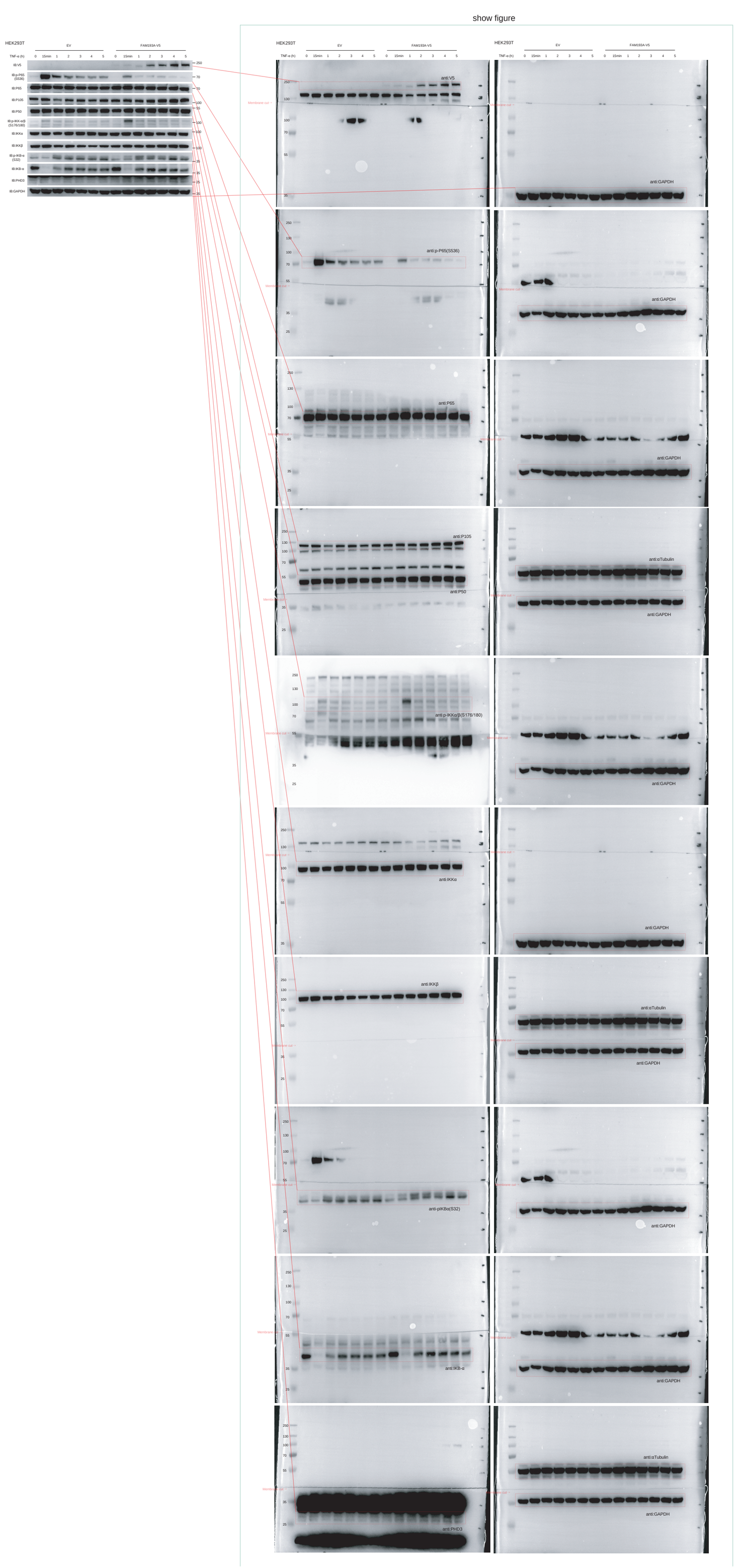


Figure 6B

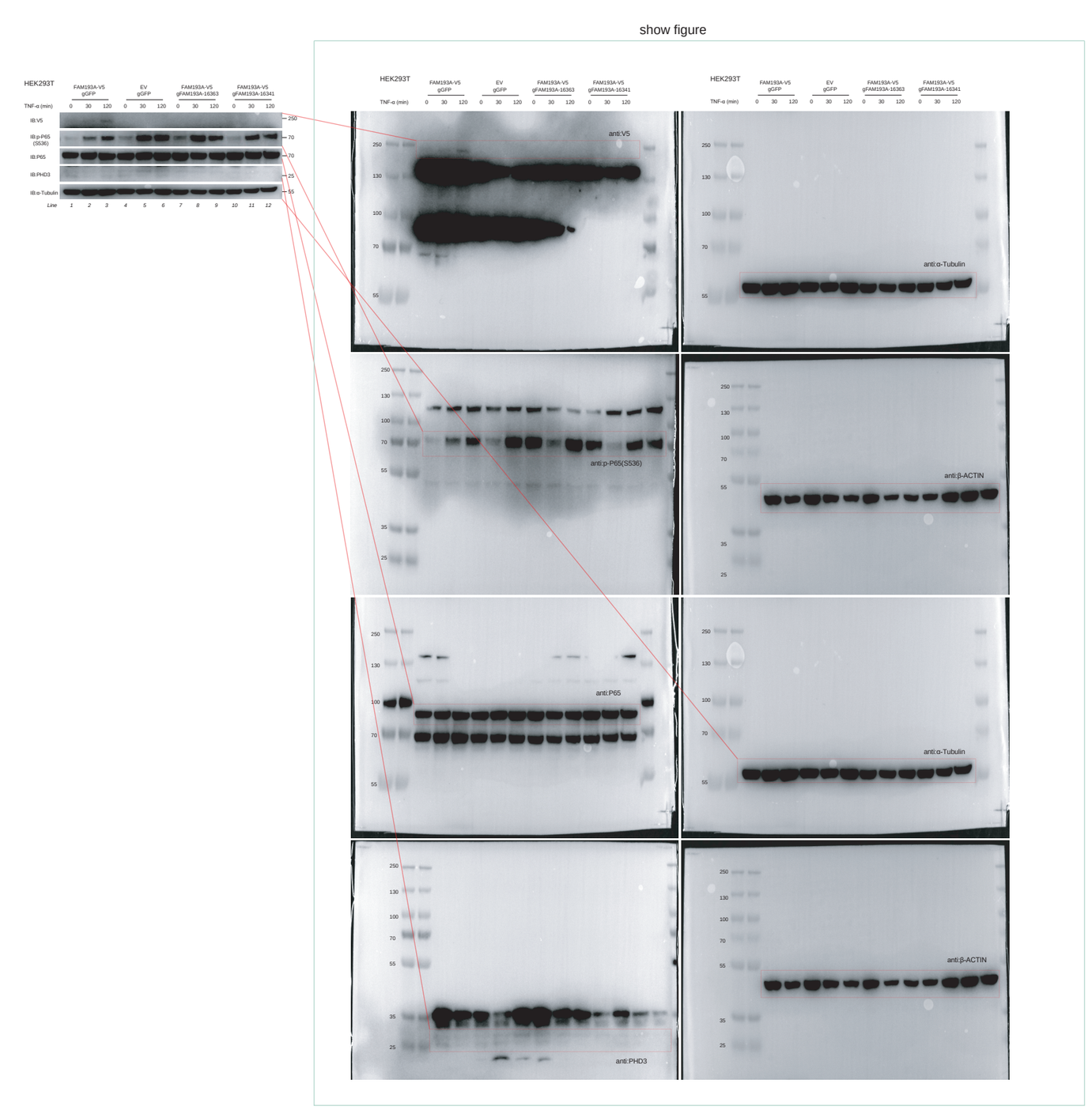


Figure 6C

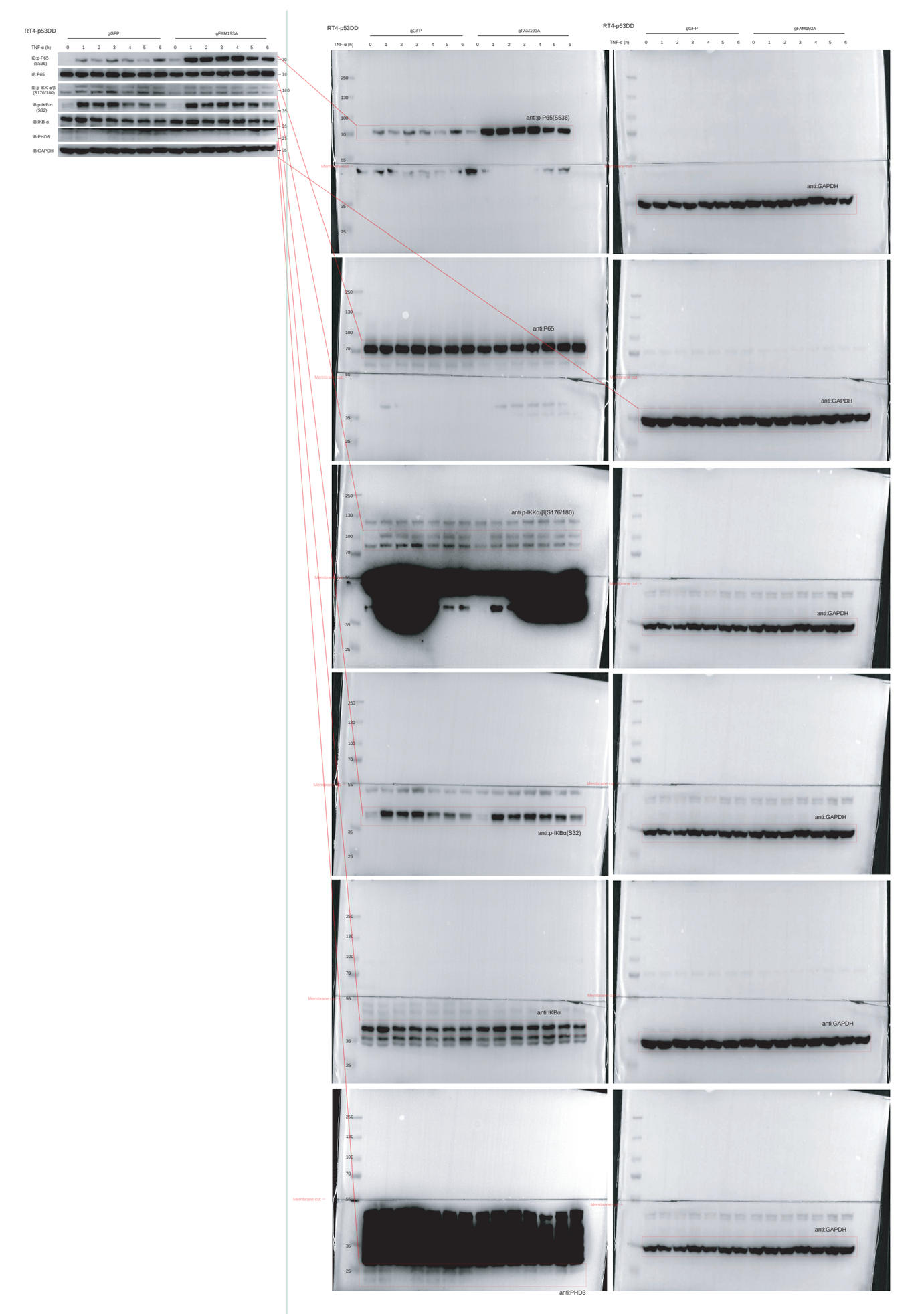


Figure 6D
Figure 6E

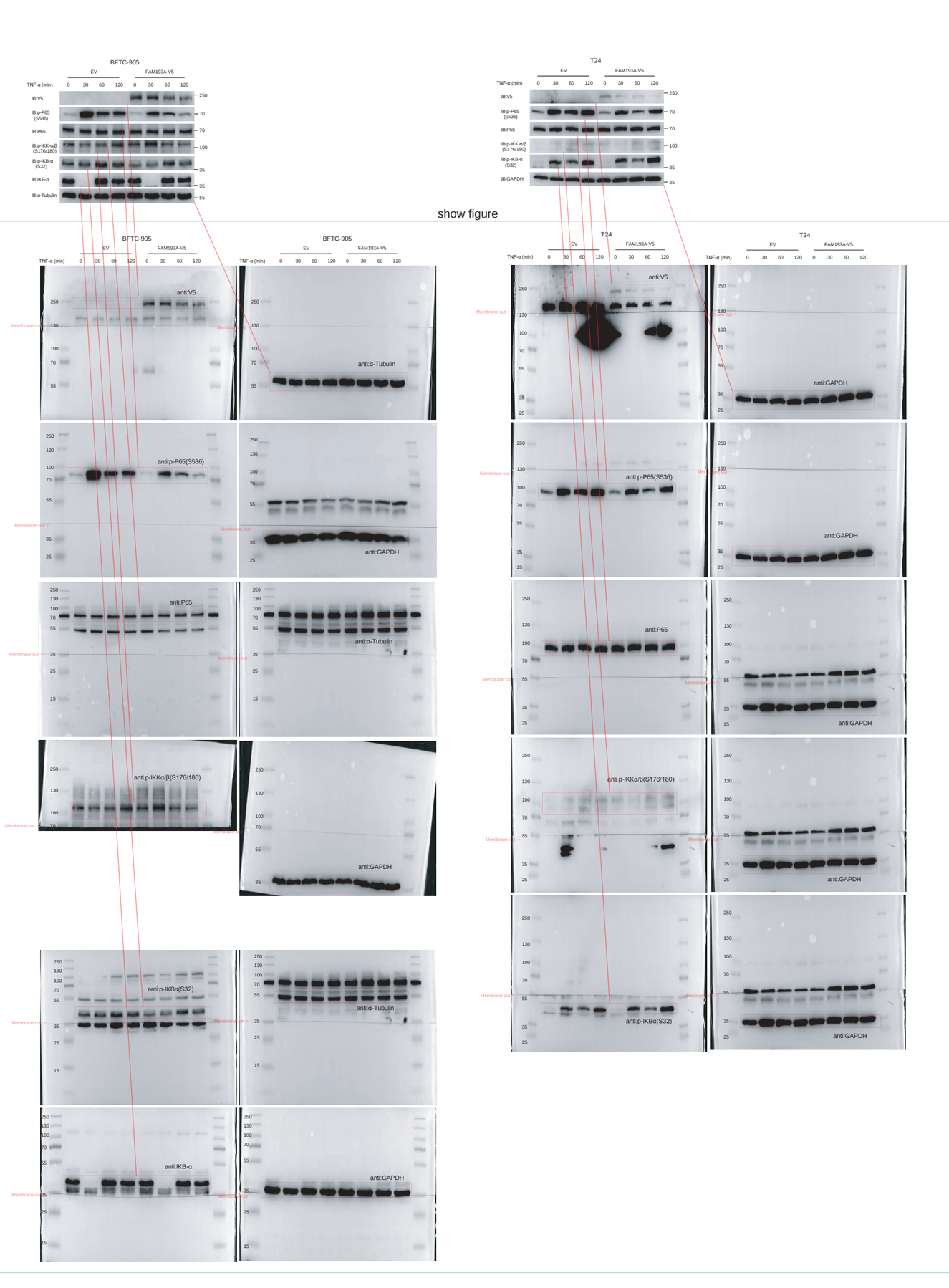


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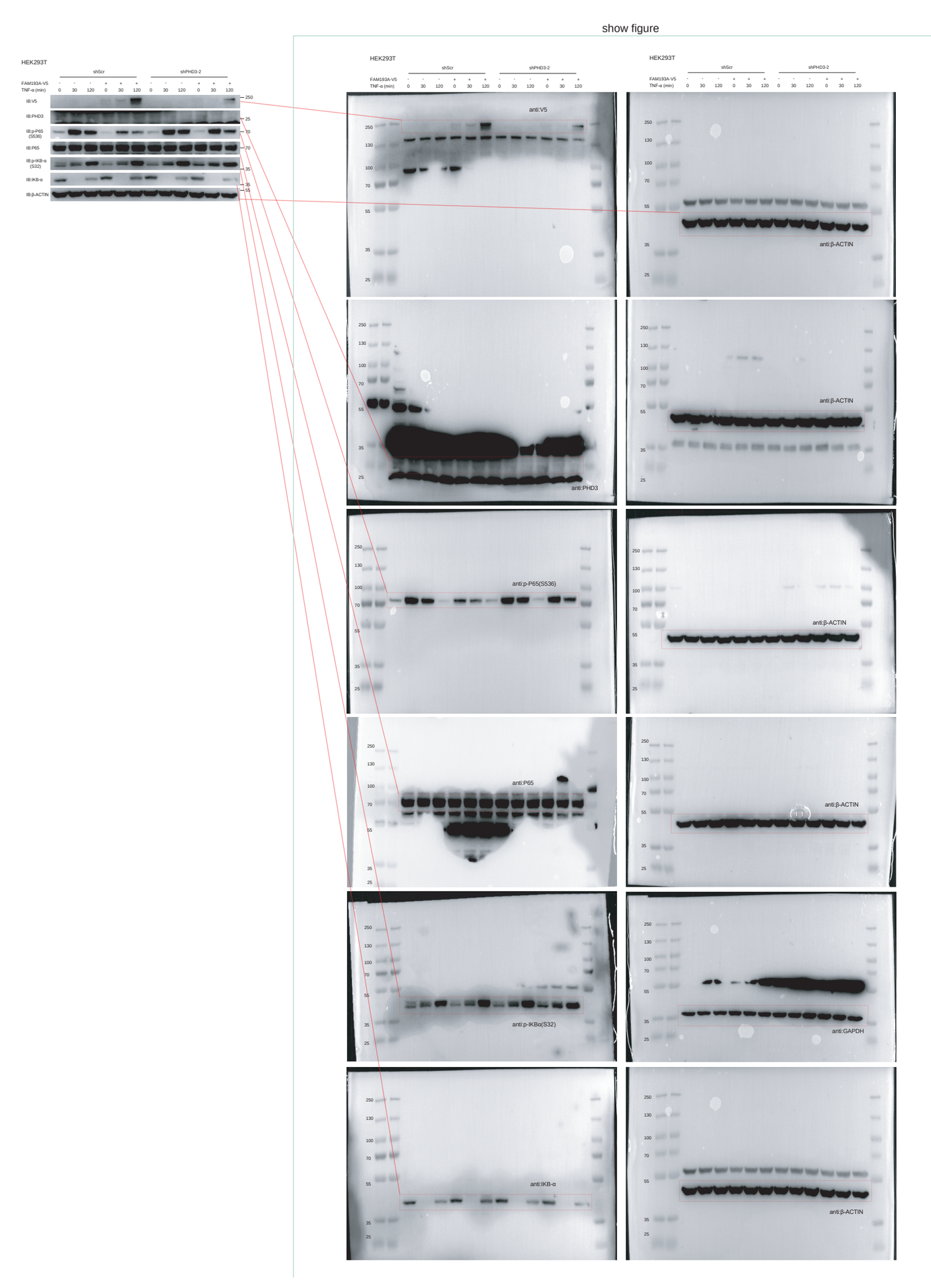


Figure 6J

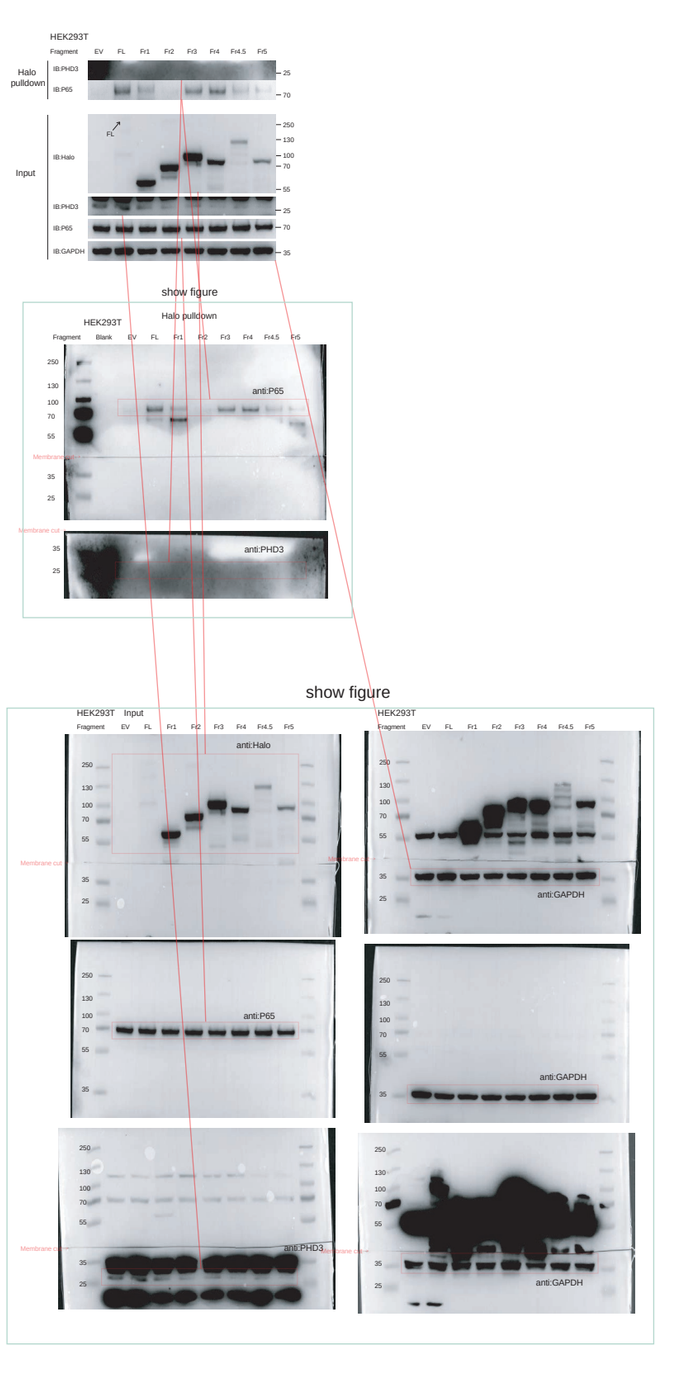


Figure 6K

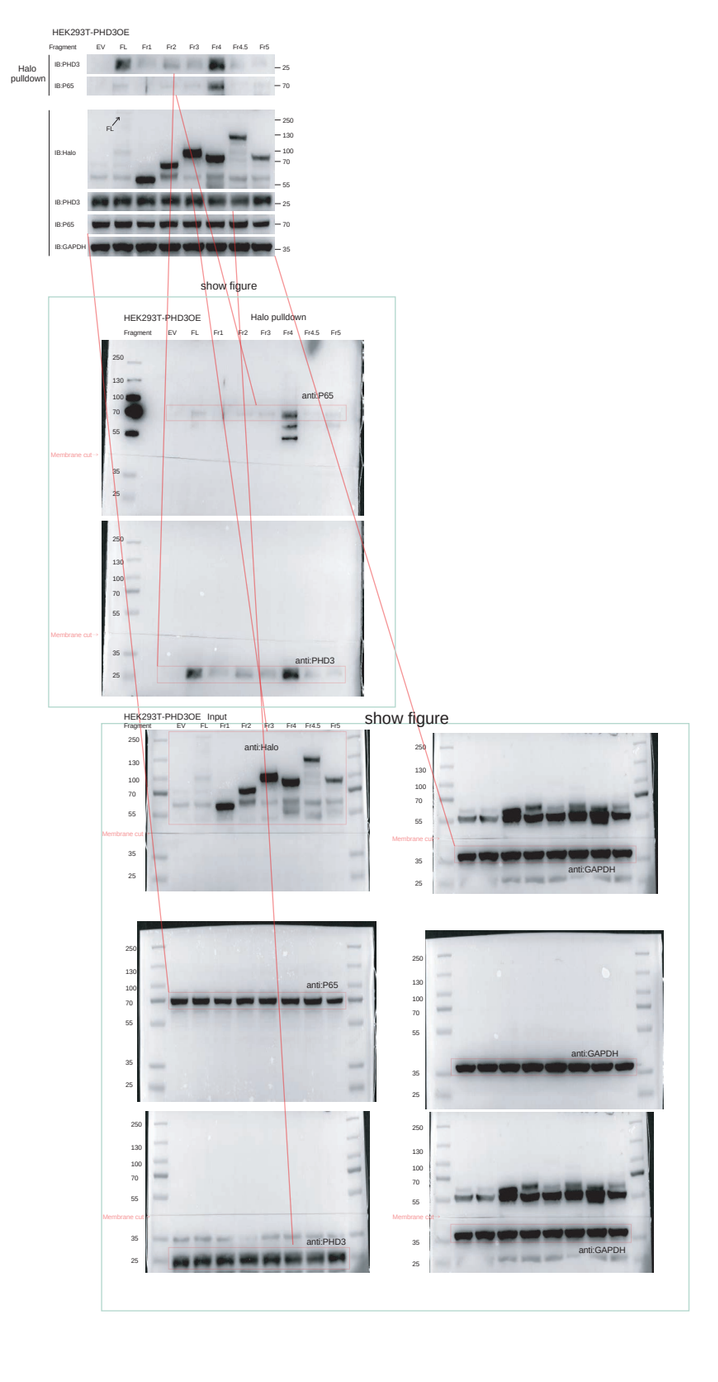
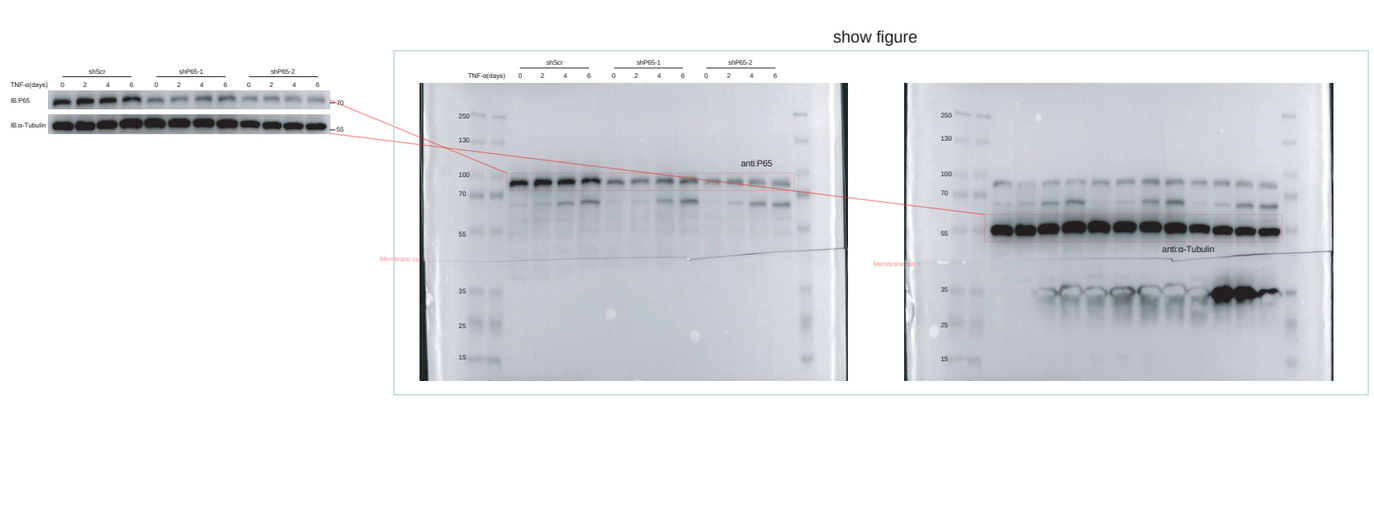


Figure 7F



Where indicated, membranes were physically cut according to molecular weight before antibody incubation.
The resulting membrane sections were incubated separately with the indicated antibodies and placed together for simultaneous imaging.
Red arrows indicate the positions at which the membranes were cut.

Figure S3A

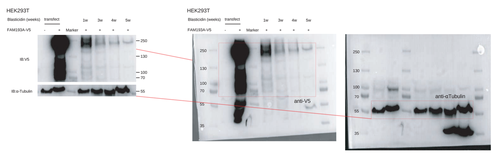


Figure S3B

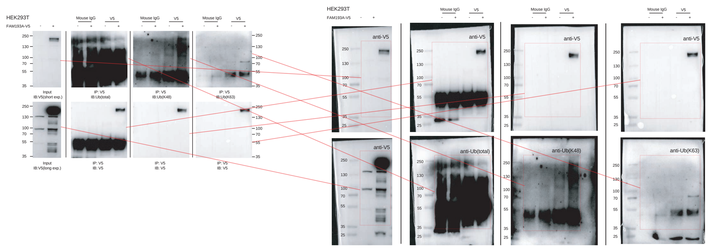


Figure S3C

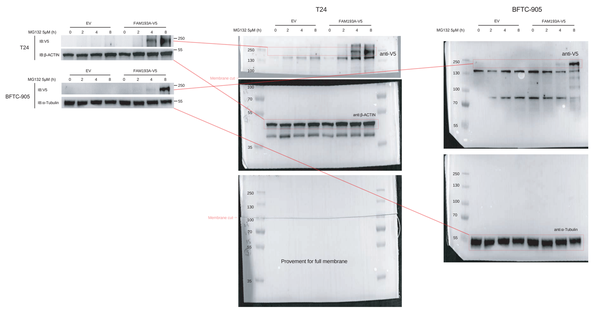


Figure S3D



Figure S4A

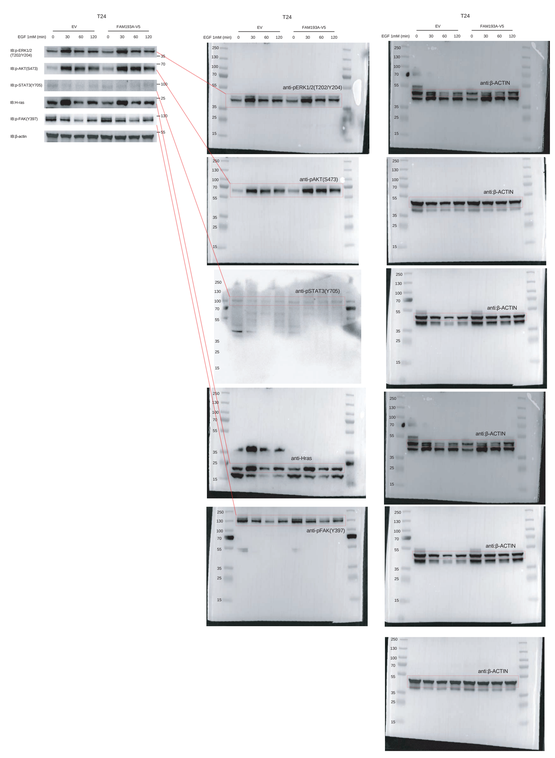


Figure S4B

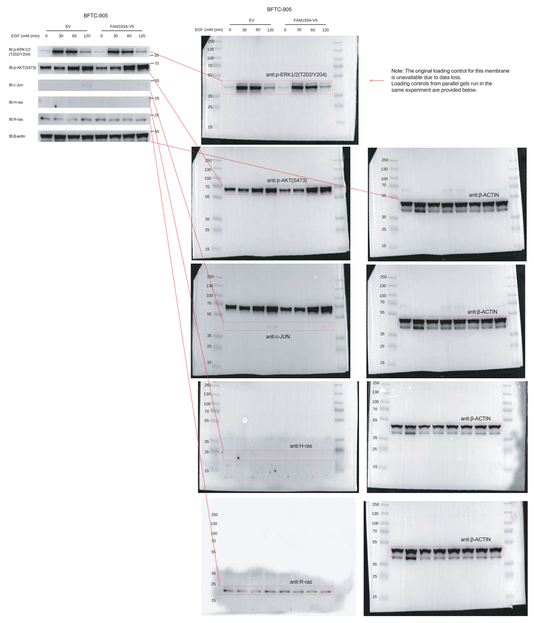


Figure S4C

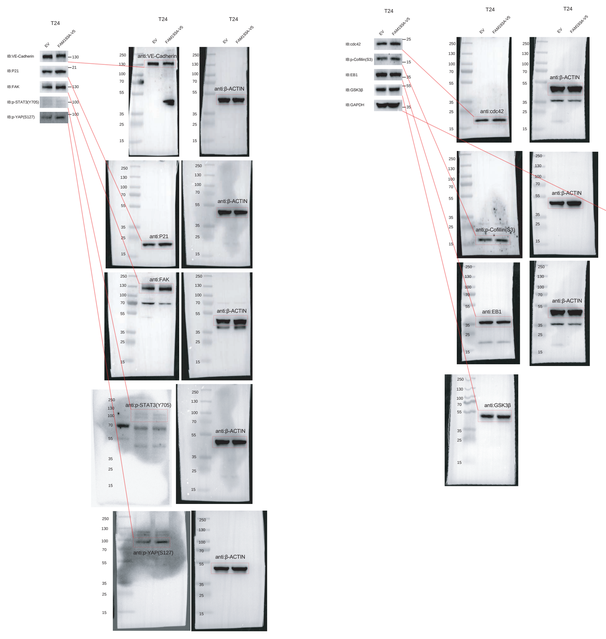


Figure S4D



Figure S4E

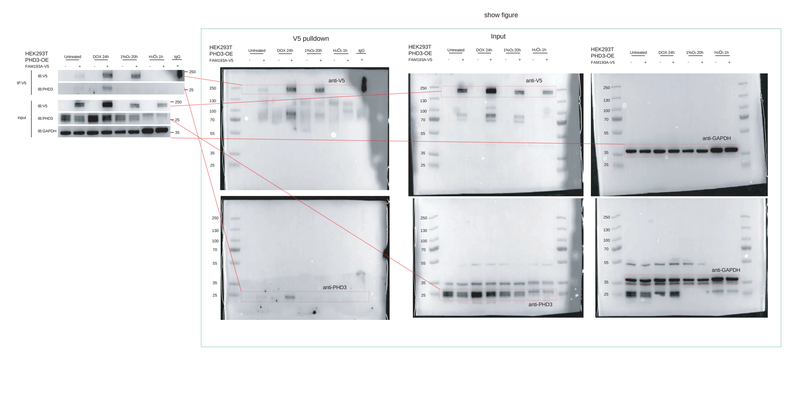


Figure S5B

Figure S5C

Figure S5D

Figure S6L

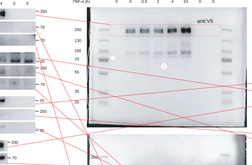


Figure S6M

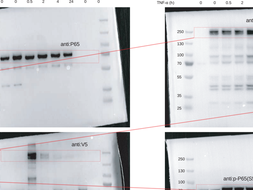


Figure S6N

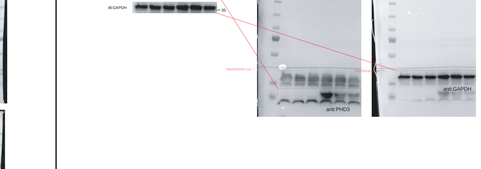


Figure S6O

