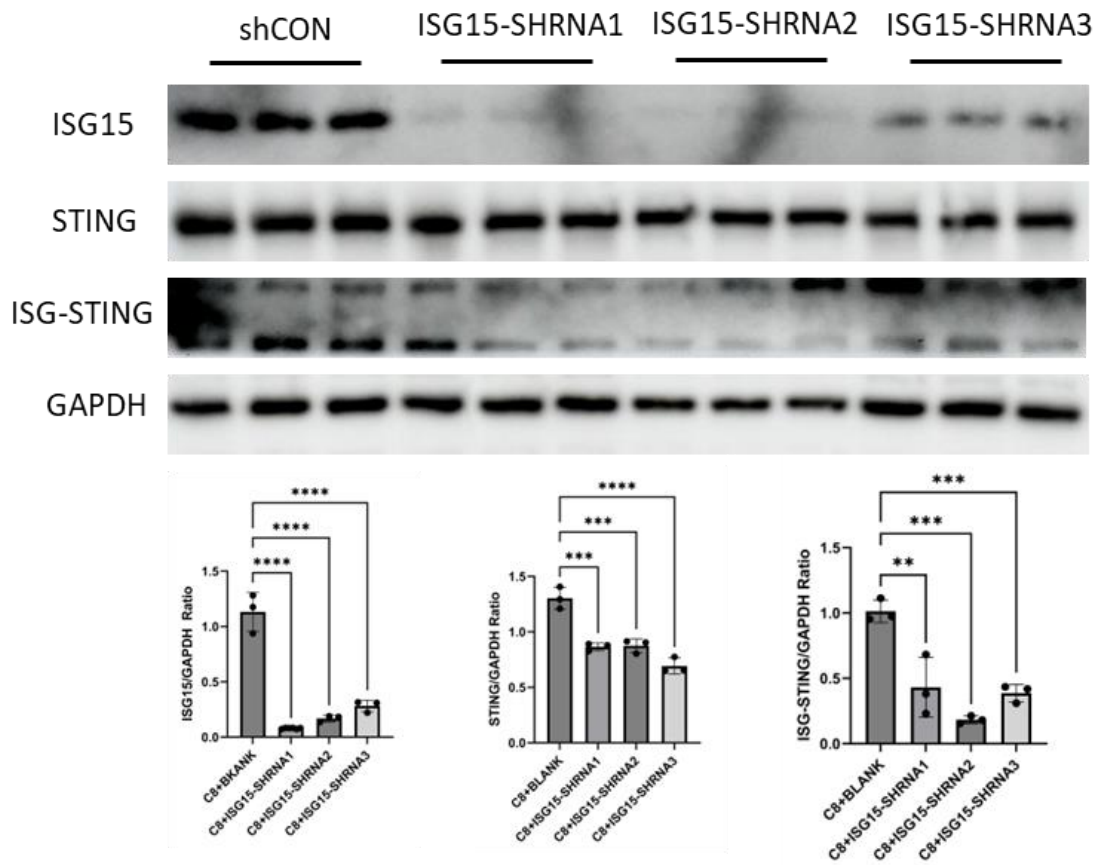
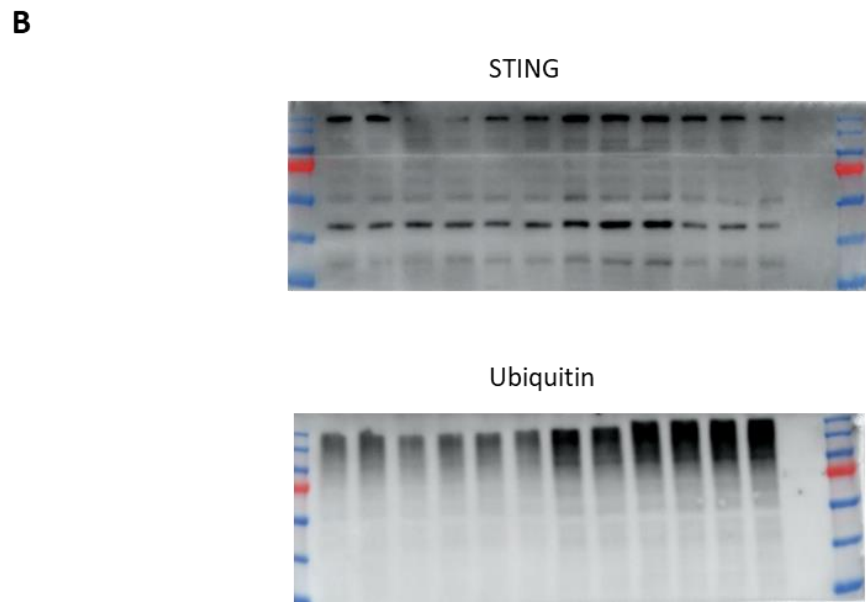
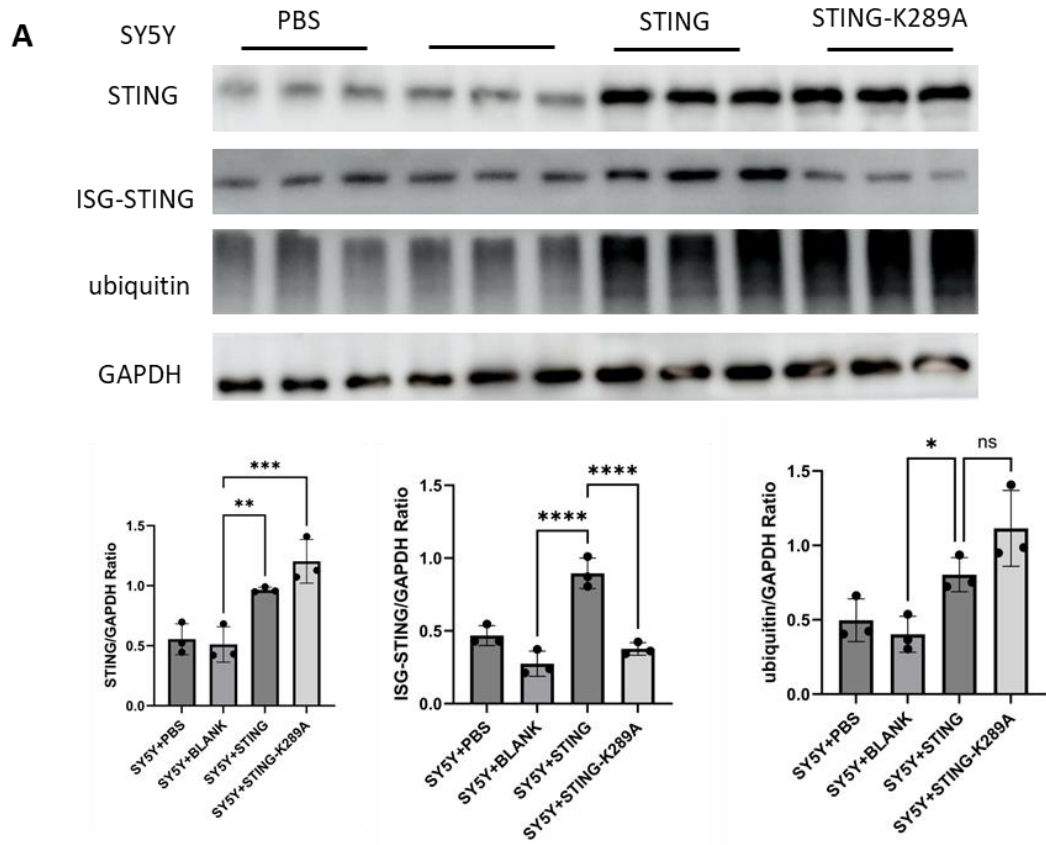


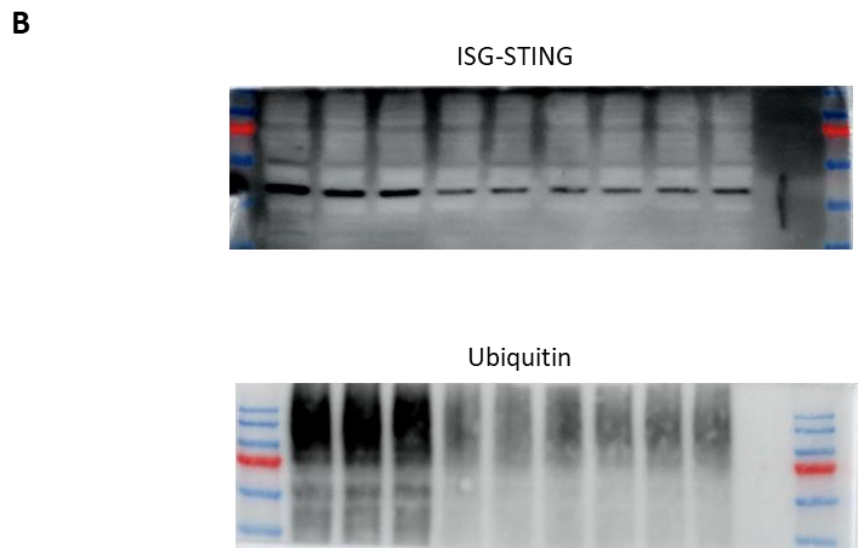
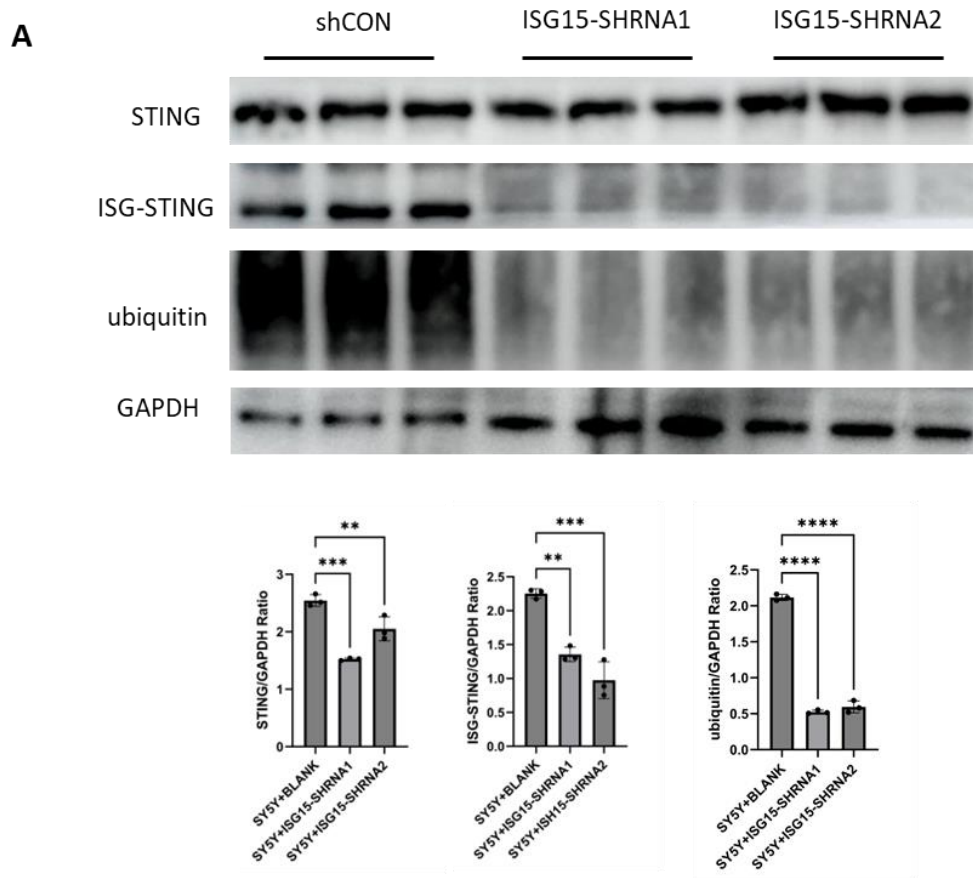
## Supplementary Figure and Figure legend



**Supplementary Fig. 1** shISG15 knockdown ISG and ISGylation of STING in C8-CIA. C8-CIA were infected with PLV-ShCon and three sets of shISG15 a-c for 3 days and then processed to WB with indicated antibodies and quantified with ImageJ. n=4.



**Supplementary Fig. 2** STING-K289A blocked ISGylation of STING but was not associated with ubiquitination. (A) SH-SY5Y cells were infected with PLV-CON, PLV-STING-WT, and PLV-STING-K289A for 2 days and processed for WB with the indicated antibodies, and quantified with ImageJ. n=4. (B) Full blot of WB for STING and ubiquitination.

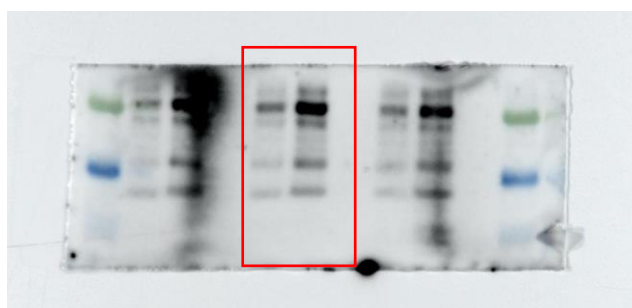


**Supplementary Fig. 3** shISG15 blocked ISGylation of STING but was not associated with ubiquitination. (A) SH-SY5Y cells were infected with PLV-shCon and PLV-shISG15 for 3 days and processed for WB with the indicated antibodies, and quantified with ImageJ. n=4. (B) Full blot of WB for STING and ubiquitination.

# Supplemental Figure 4 Uncropped Western blot

**Fig. 1A**

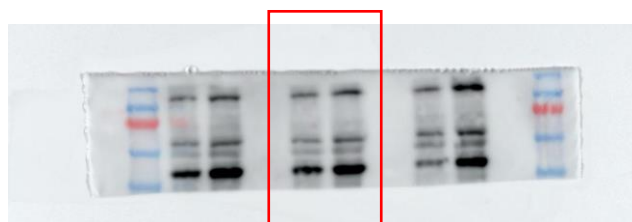
ISG15



STING



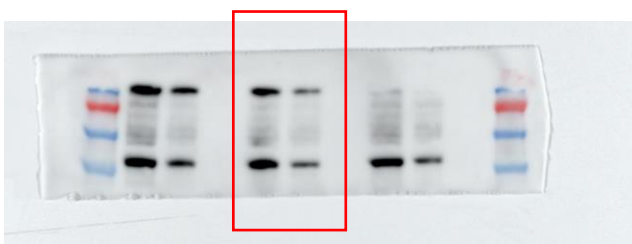
ISG15-ISG-STING



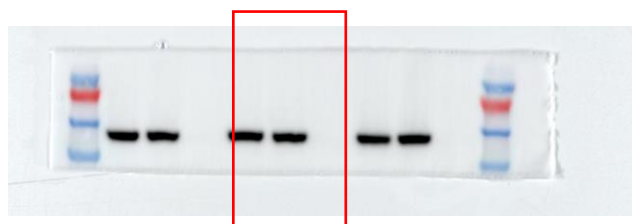
STING-ISG-STING



TH

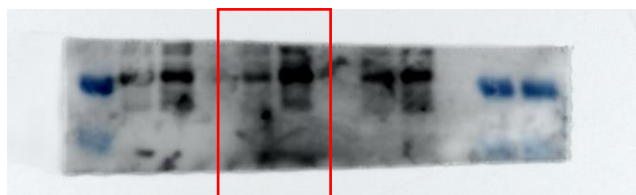


$\alpha$ -tublin

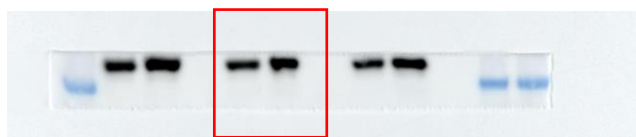


**Fig. 1B**

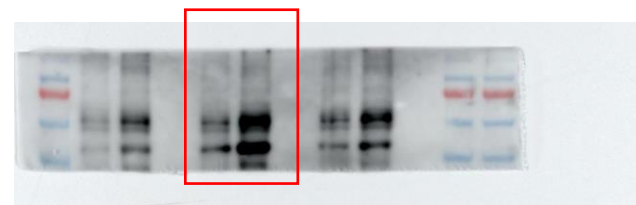
ISG15



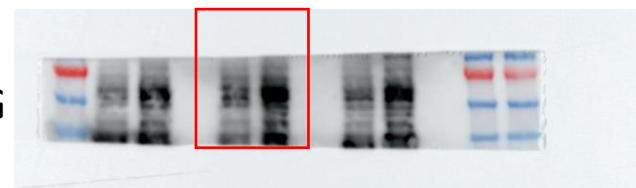
STING



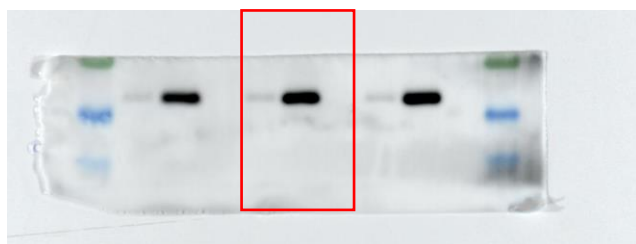
ISG15-ISG-STING



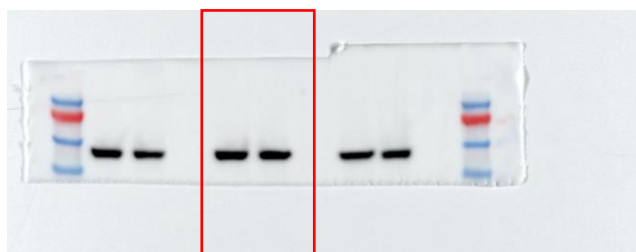
STING-ISG-STING



$\alpha$ -syn

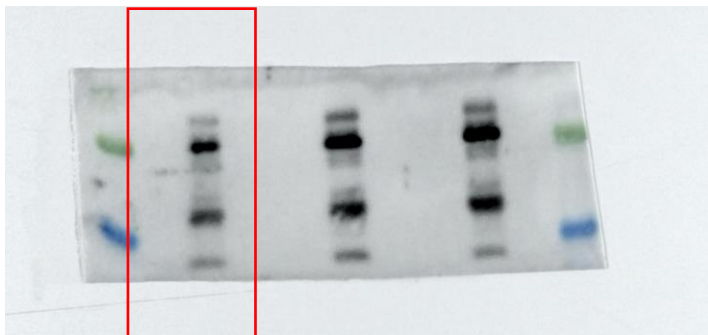


$\alpha$ -tubulin

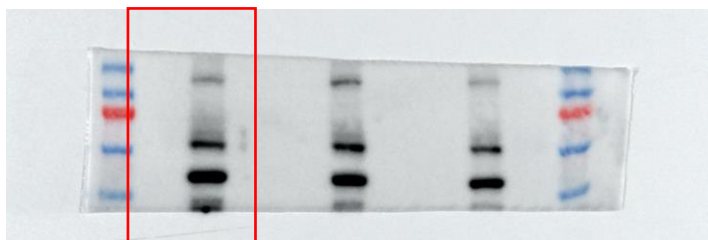


**Fig. 1C**

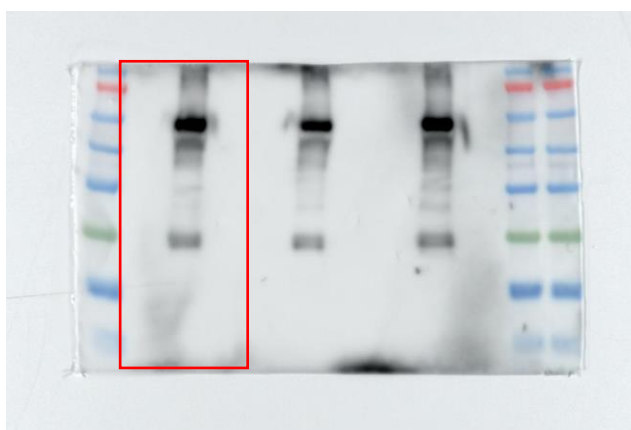
ISG15



ISG-STING



ISG15

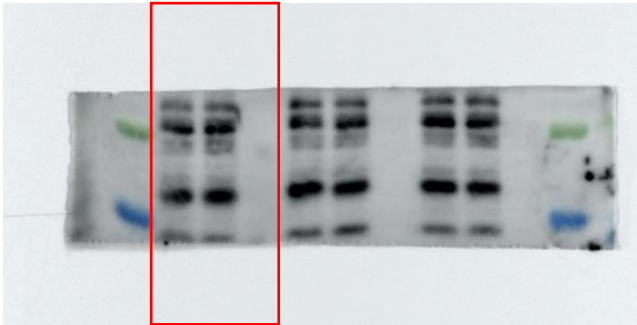


STING

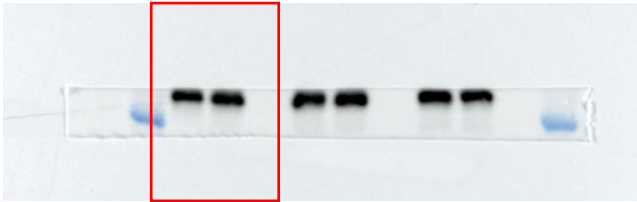


**Fig. 1C**

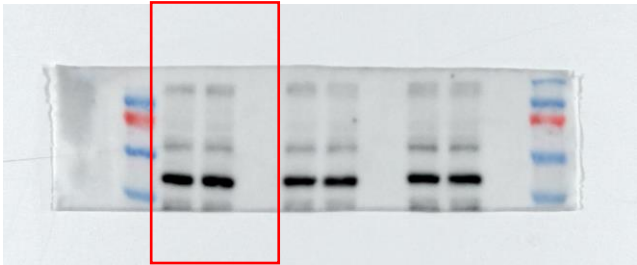
ISG15



STING

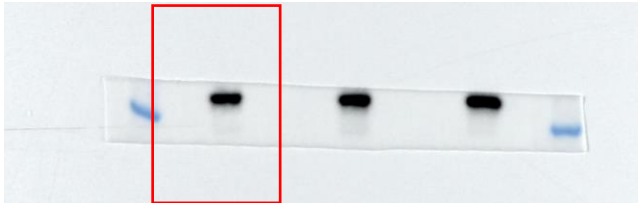


ISG-STING



**Fig. 1D**

STING



ISG-STING



ISG15

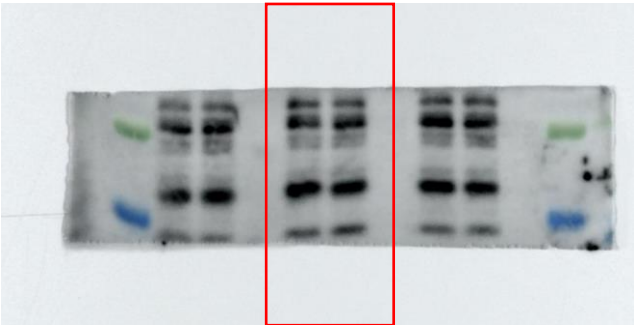


STING

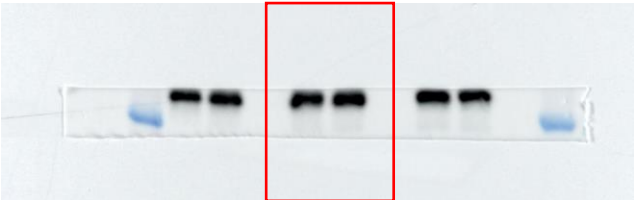


**Fig. 1D**

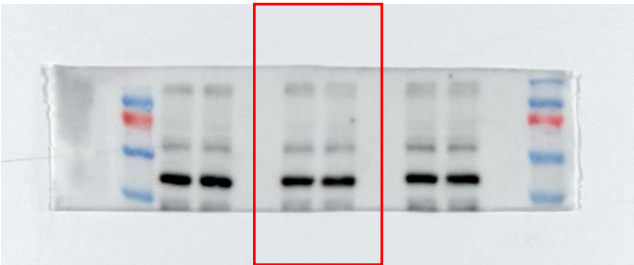
ISG15



STING

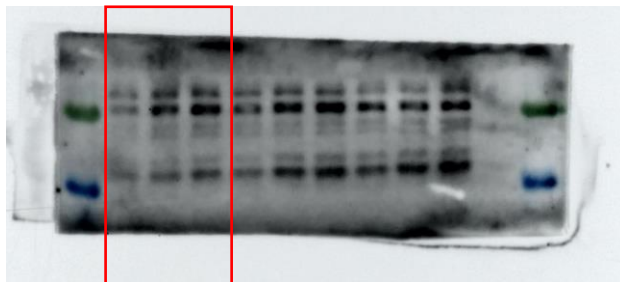


ISG-STING



**Fig. 2C**

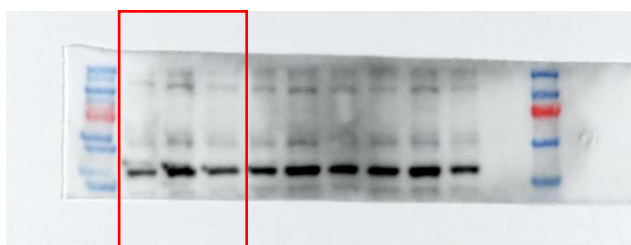
ISG15



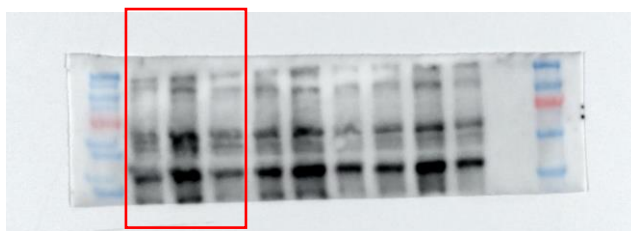
STING



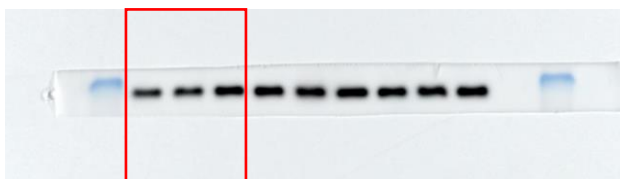
ISG-STING



C-FOS

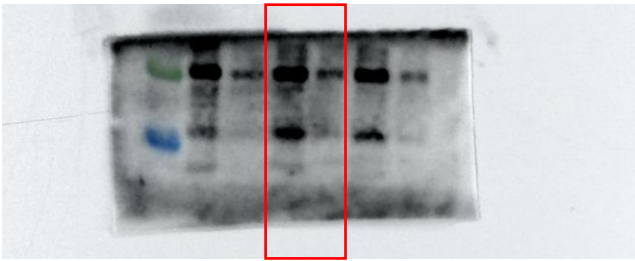


GAPDH

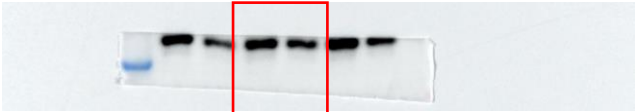


**Fig. 2D**

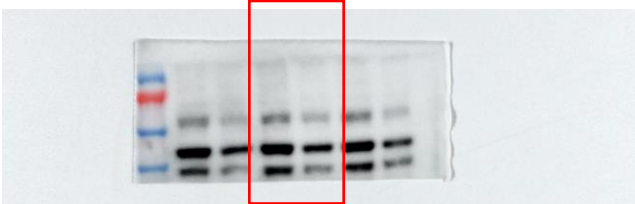
ISG15



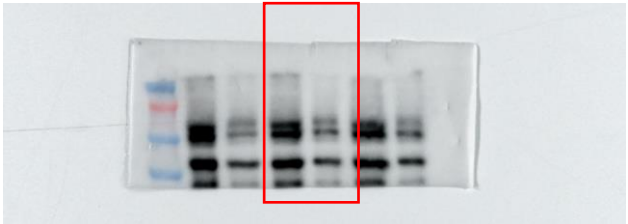
STING



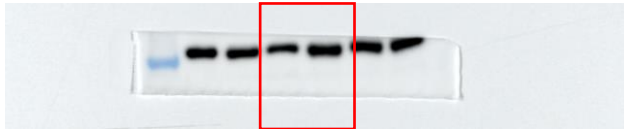
ISG-STING



C-FOS

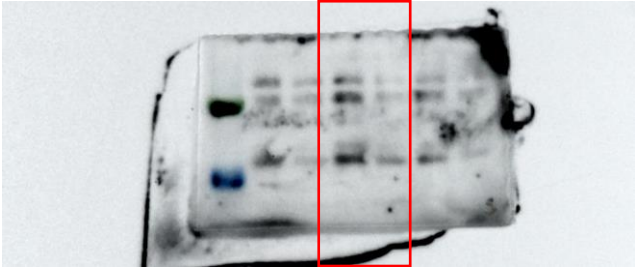


GAPDH

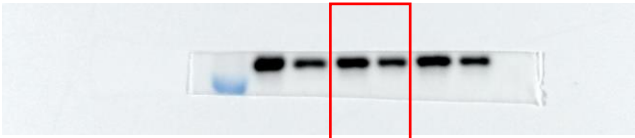


**Fig. 2E**

ISG15



STING



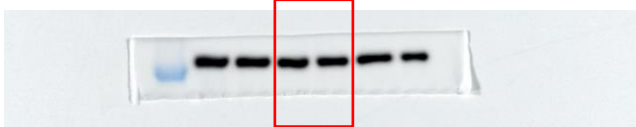
ISG-STING



C-FOS



GAPDH



**Fig. 3A**

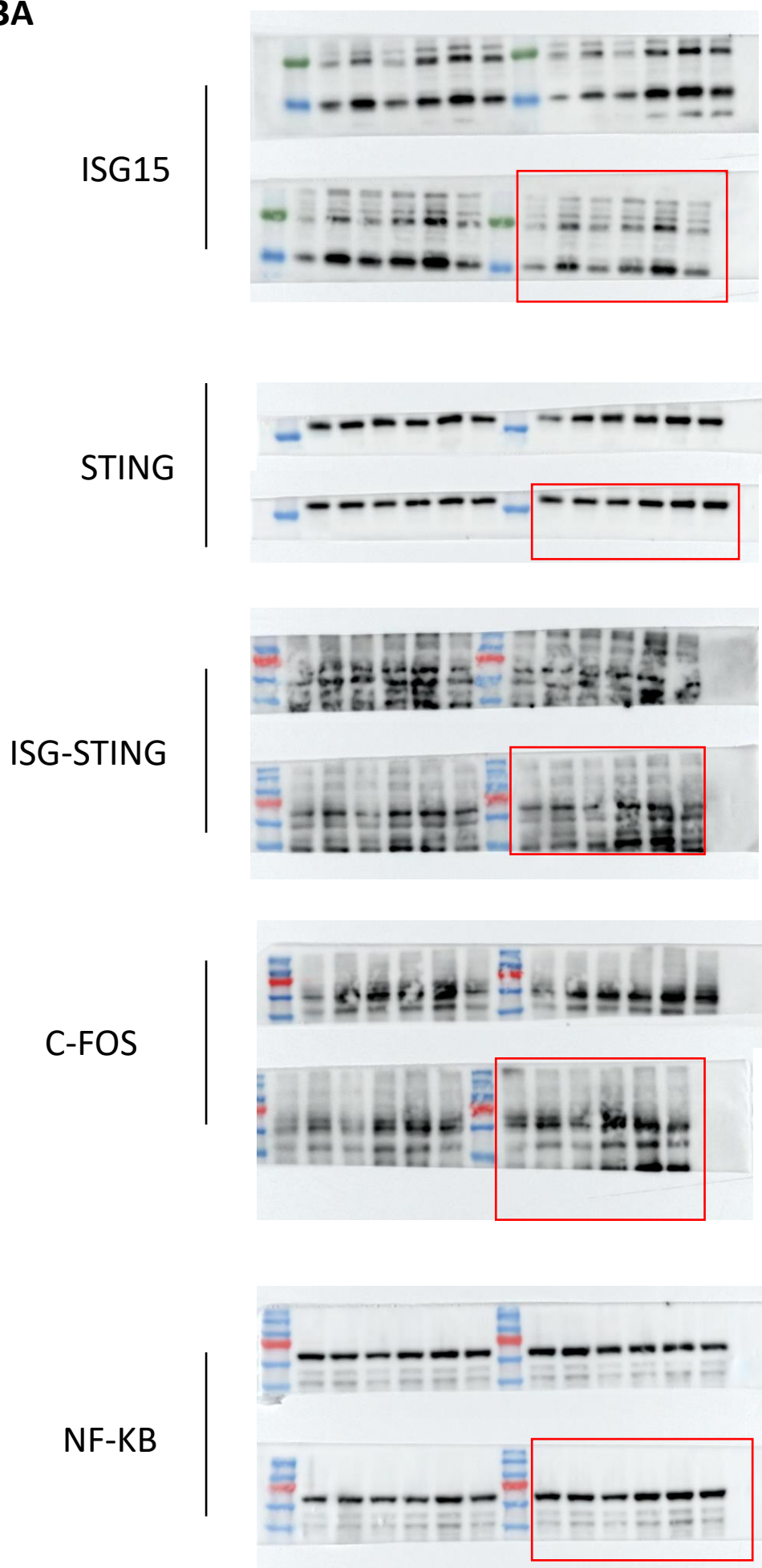
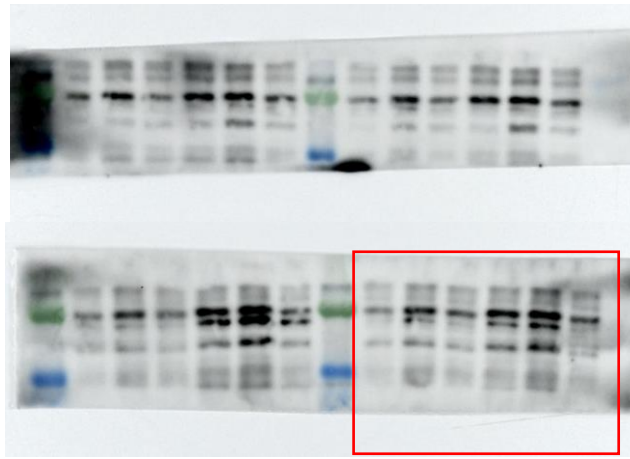
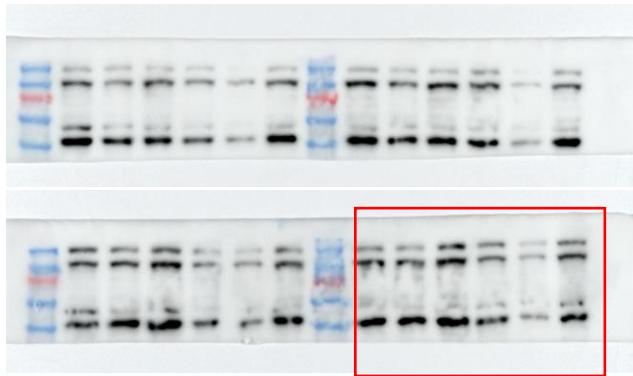


Fig. 3A

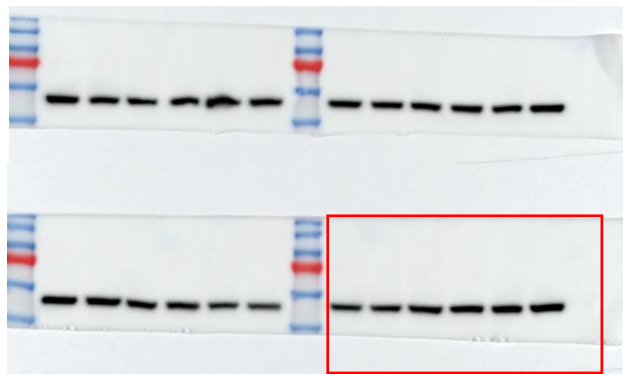
TNF- $\alpha$



TH



$\alpha$ -tubulin

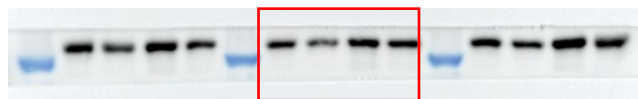


**Fig. 3C**

ISG15



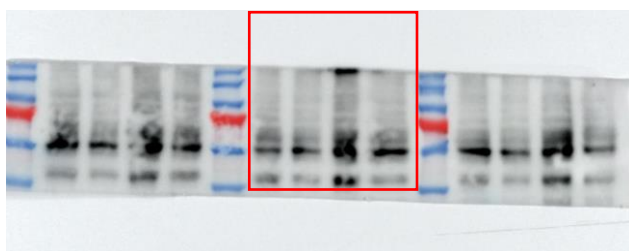
STING



ISG-STING



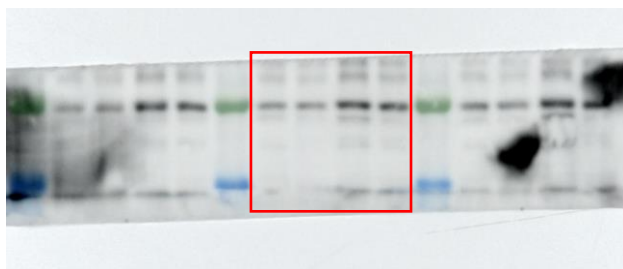
C-FOS



NF-KB



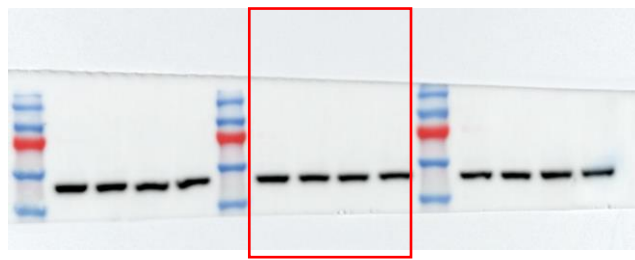
TNF- $\alpha$



TH



$\alpha$ -tubulin



**Fig. 3E**

ISG15



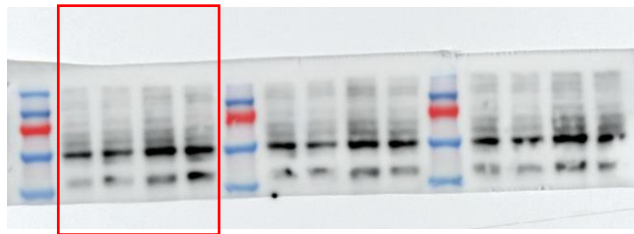
STING



ISG-STING



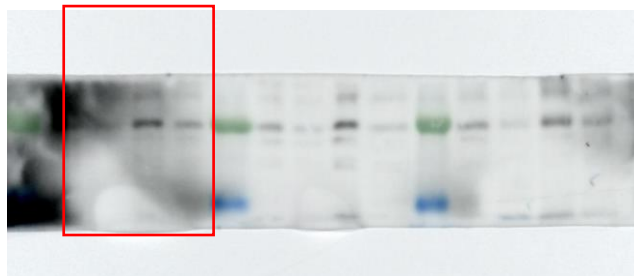
C-FOS



NF-KB



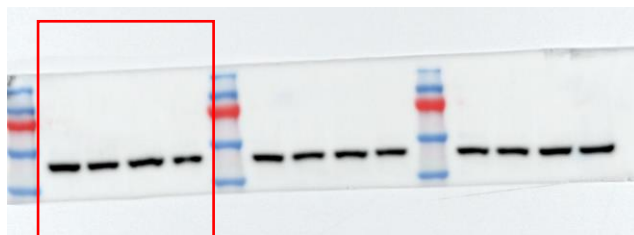
TNF- $\alpha$



TH

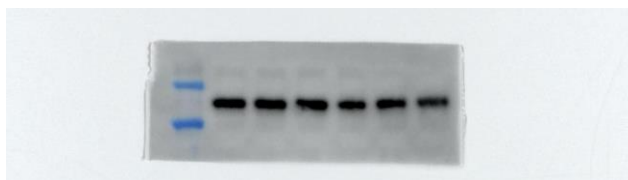


$\alpha$ -tublin

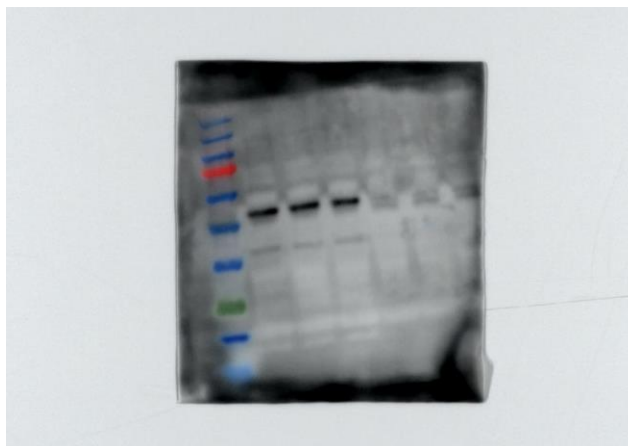


**Fig. 3F**

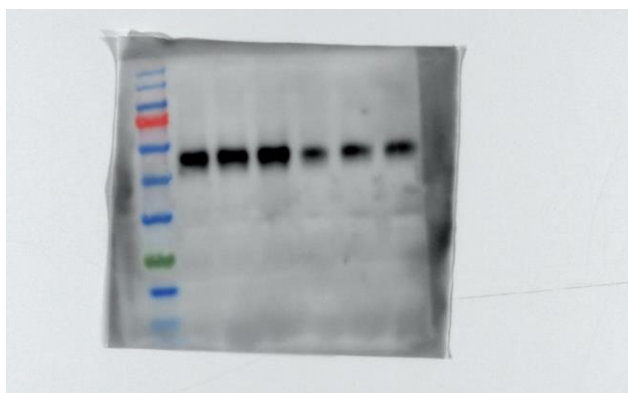
STING



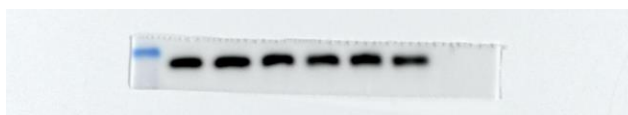
ISG-STING



ubiquitin

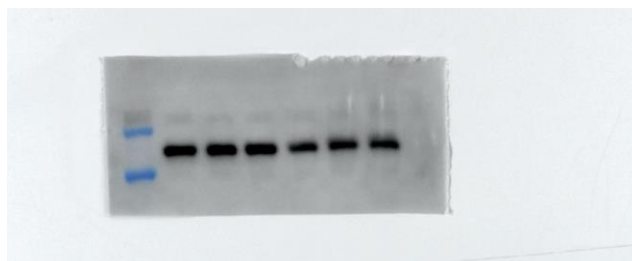


GAPDH

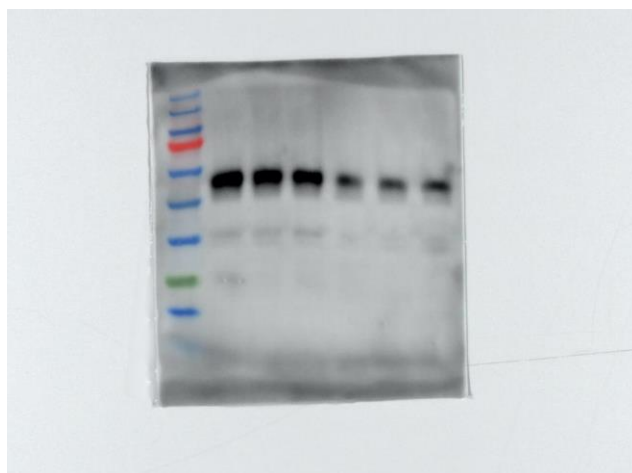


**Fig. 3F**

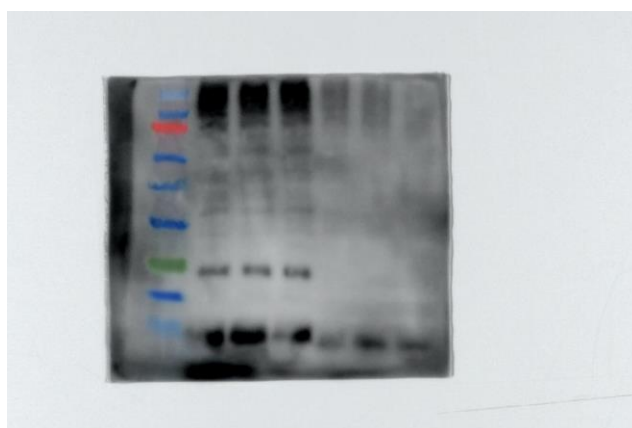
STING



ISG-STING



ubiquitin

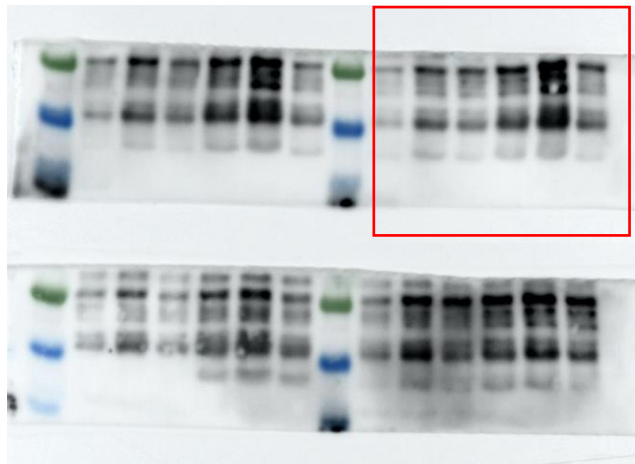


GAPDH



**Fig. 4A**

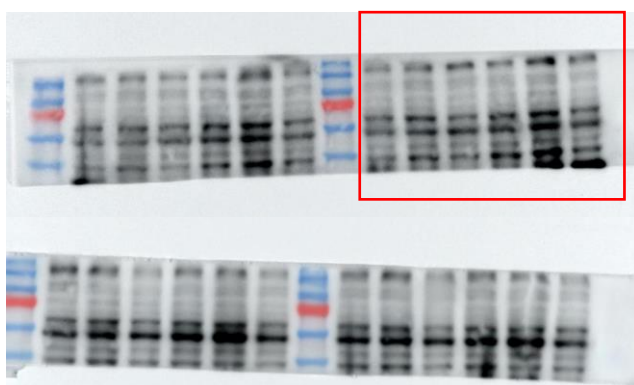
ISG15



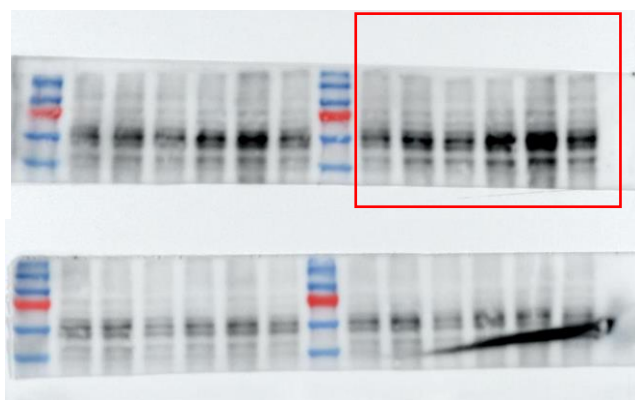
STING



ISG-STING



C-FOS

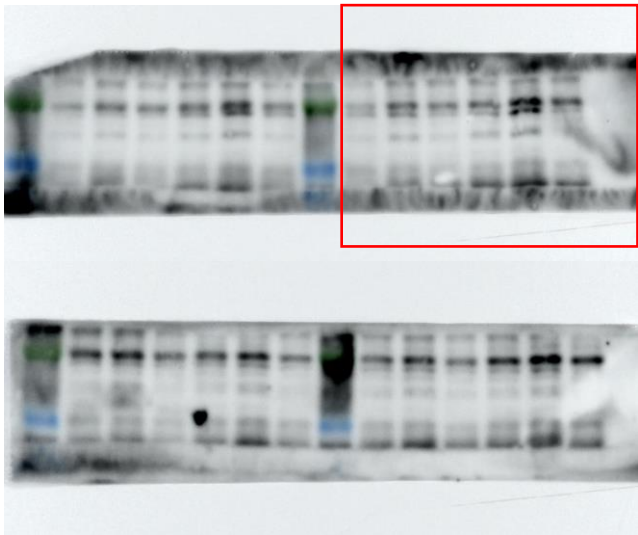


NF-KB

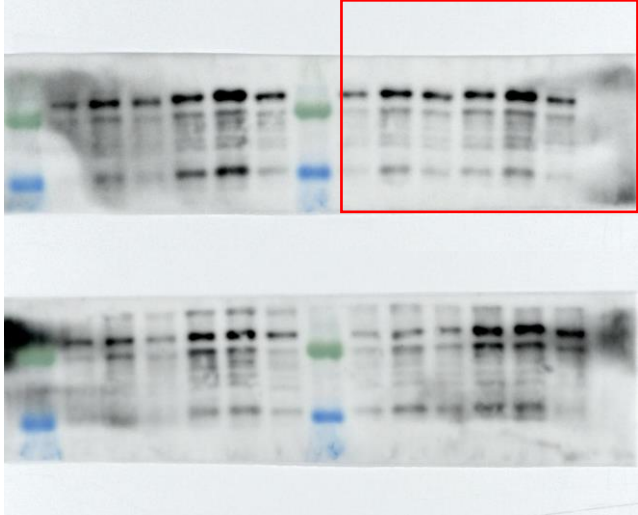


Fig. 4A

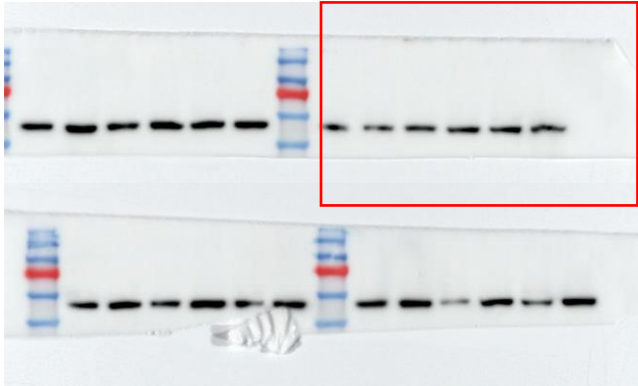
TNF- $\alpha$



TH

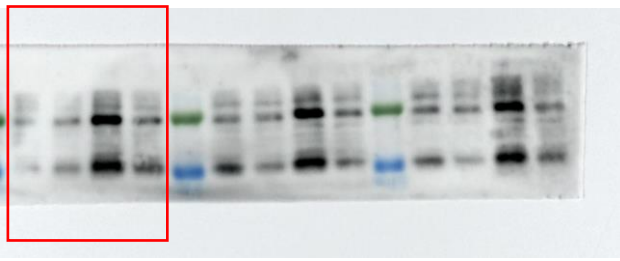


$\alpha$ -tubulin



**Fig. 4C**

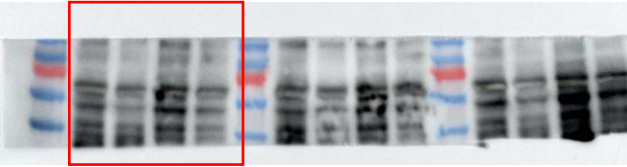
ISG15



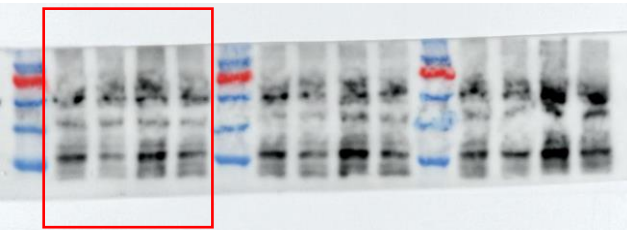
STING



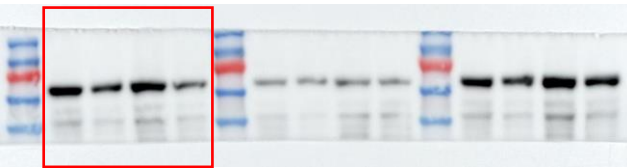
ISG-STING



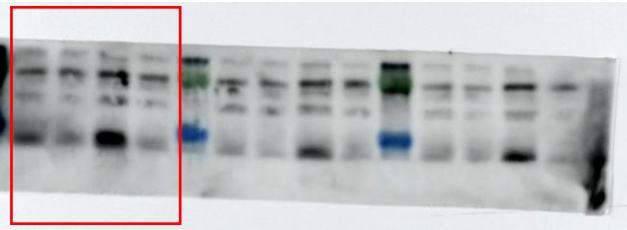
C-FOS



NF- $\kappa$ B



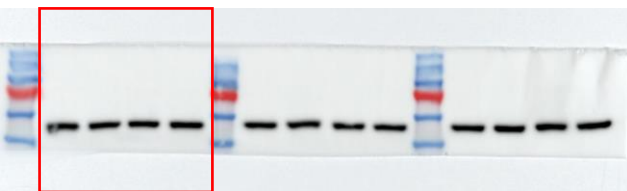
TNF- $\alpha$



$\alpha$ -syn

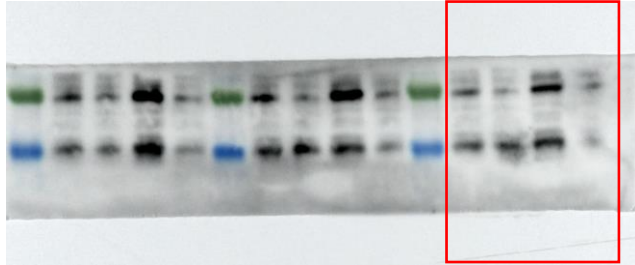


$\alpha$ -tublin

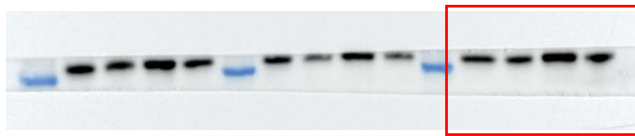


**Fig. 4E**

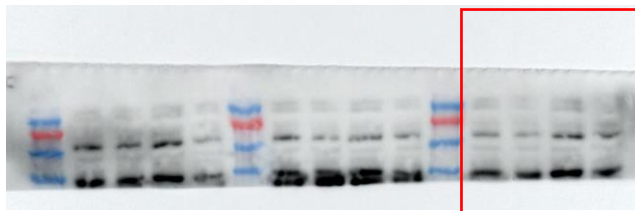
ISG15



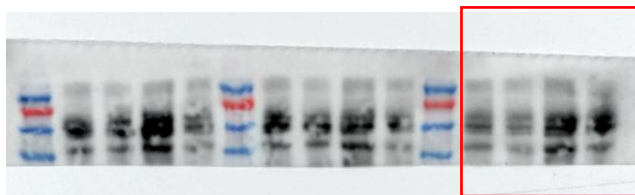
STING



ISG-STING



C-FOS



NF-KB



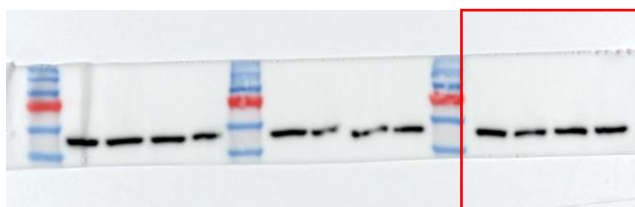
TNF- $\alpha$



$\alpha$ -syn

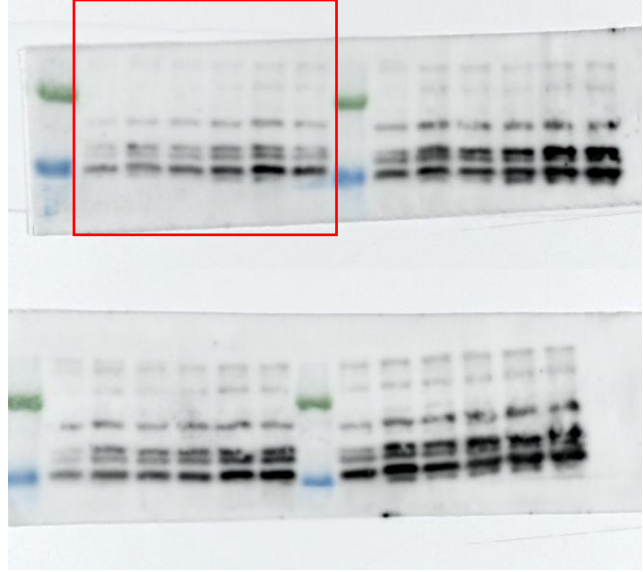


$\alpha$ -tublin



**Fig. 5G**

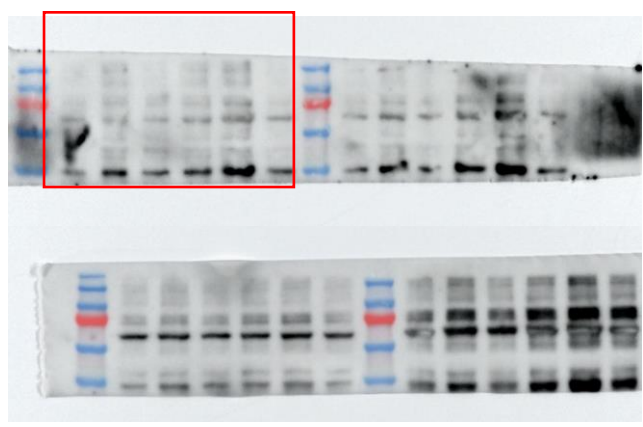
ISG15



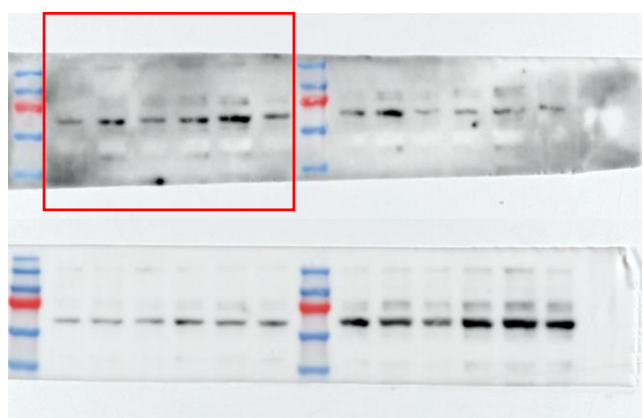
STING



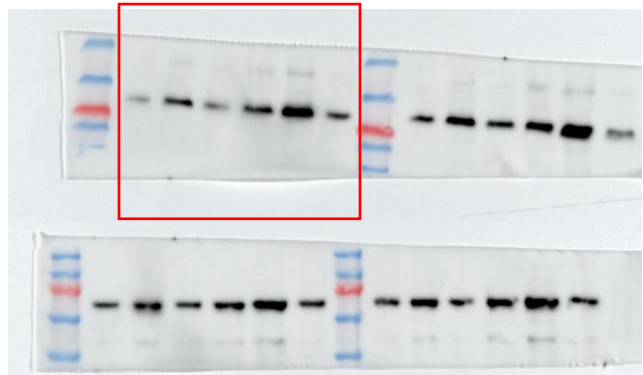
ISG-STING



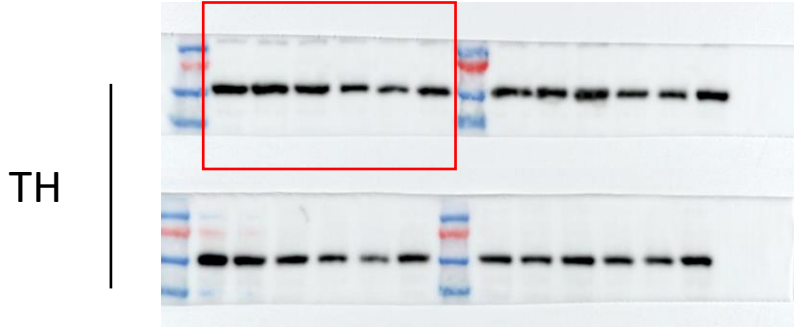
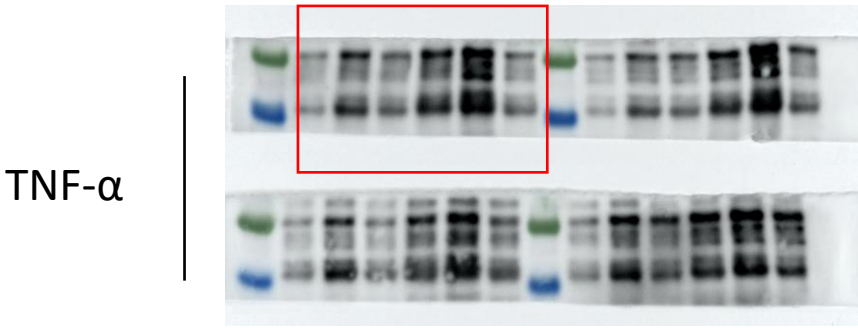
C-FOS



NF-KB



**Fig. 5G**



**Fig. 7G**

ISG15



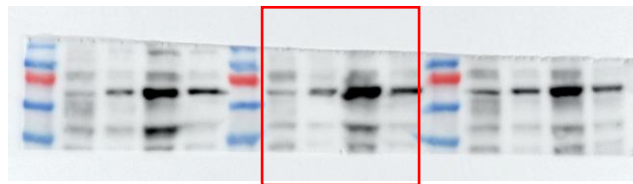
STING



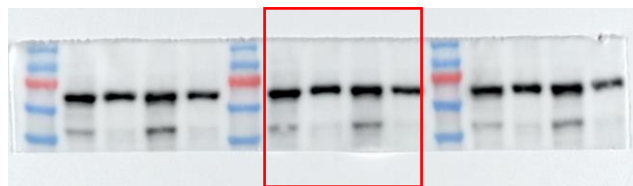
ISG-STING



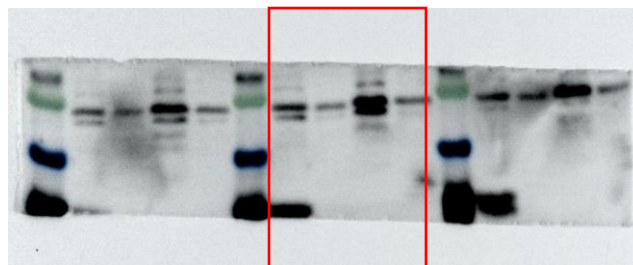
C-FOS



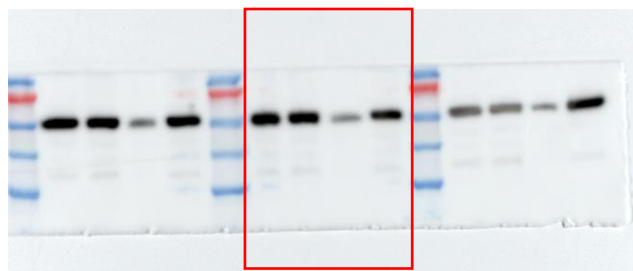
NF-KB



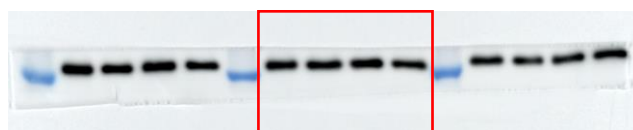
TNF- $\alpha$



TH



GAPDH



**Fig. 8G**

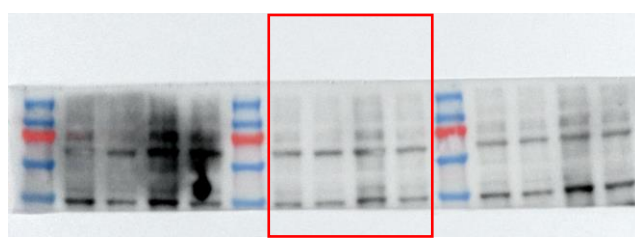
ISG15



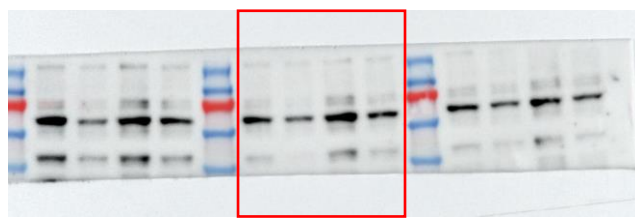
STING



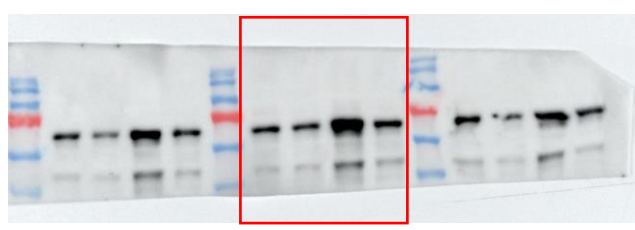
ISG-STING



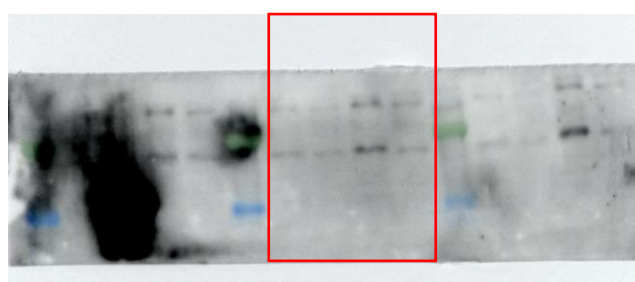
C-FOS



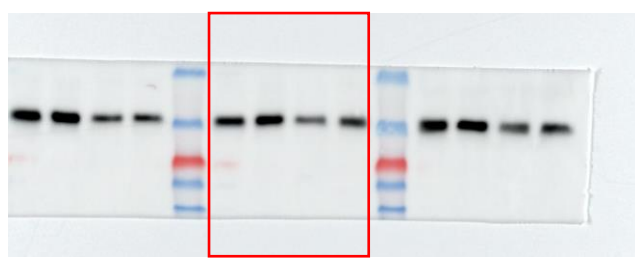
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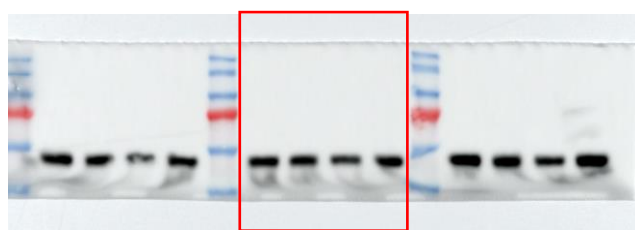
TNF- $\alpha$



TH

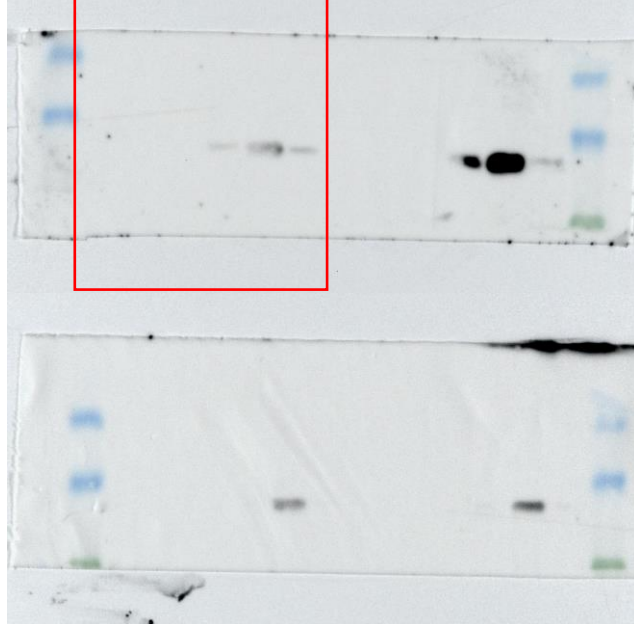


$\alpha$ -tublin



**Fig. 9G**

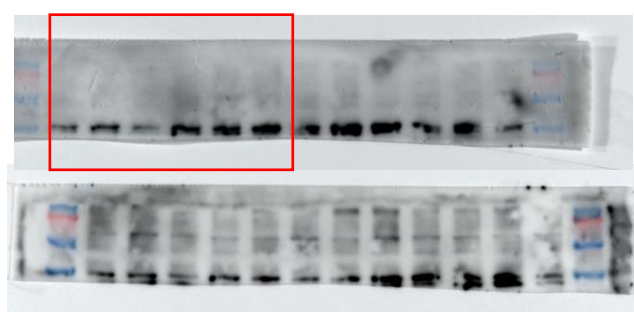
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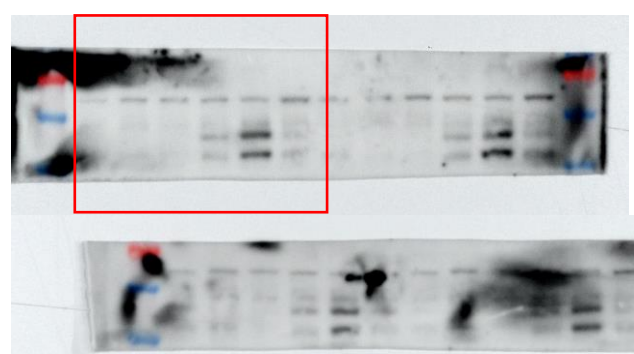
STING



ISG-STING



C-FOS



NF-KB

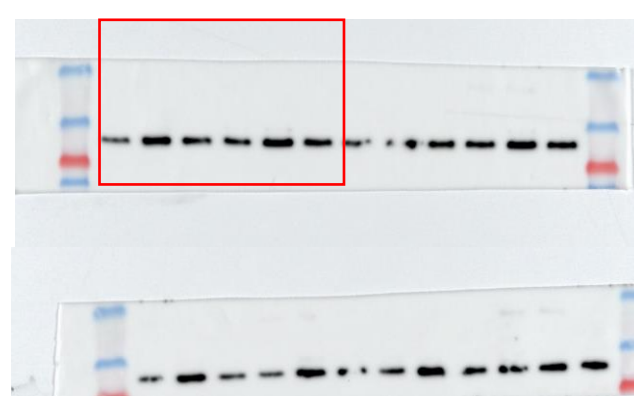
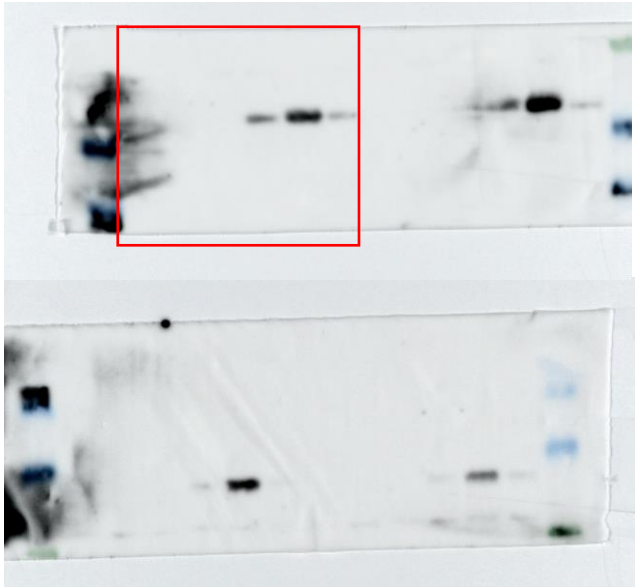
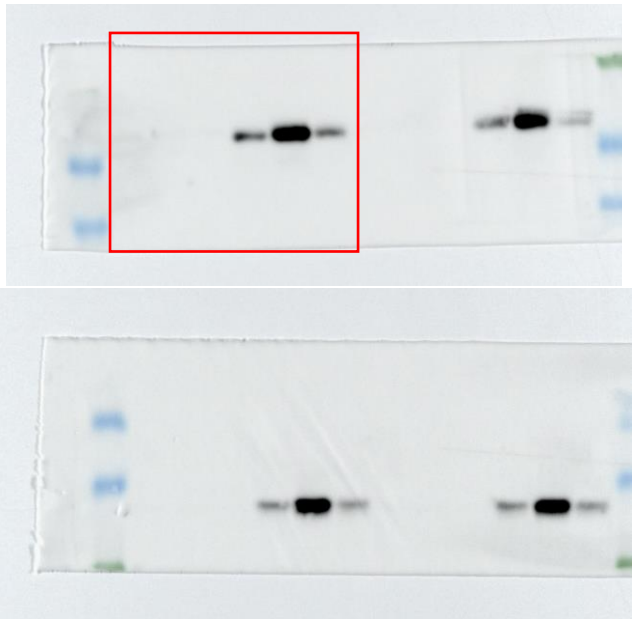


Fig. 9G

TNF- $\alpha$



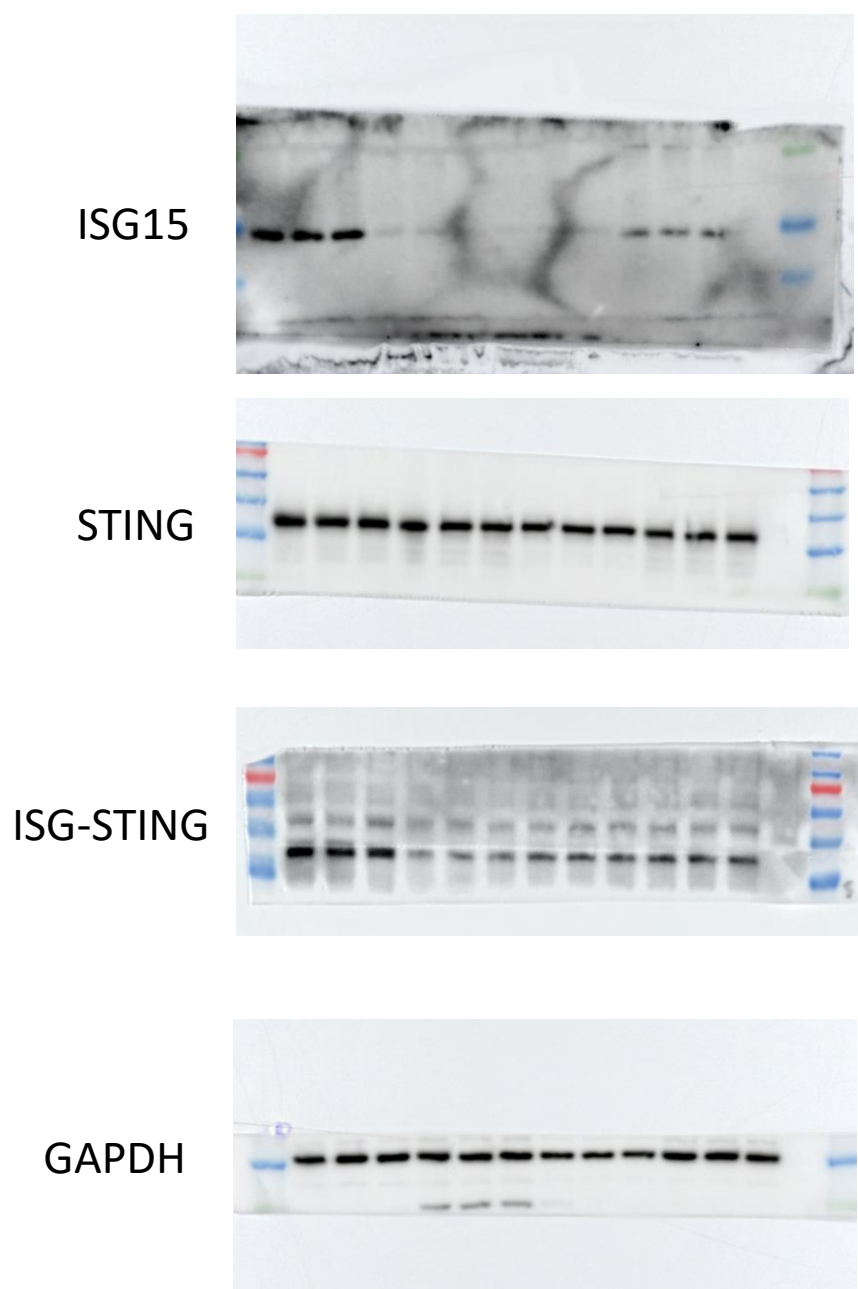
$\alpha$ -syn



GAPDH



**Fig. S1**

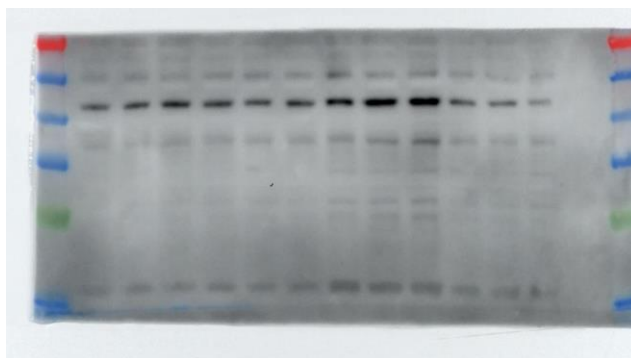


**Fig. S2**

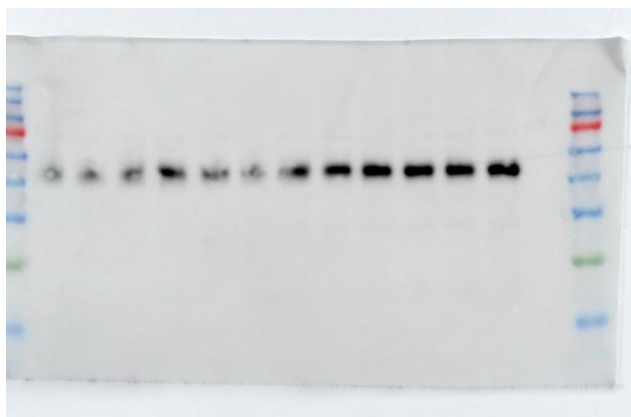
STING



ISG-STING



ubiquitin

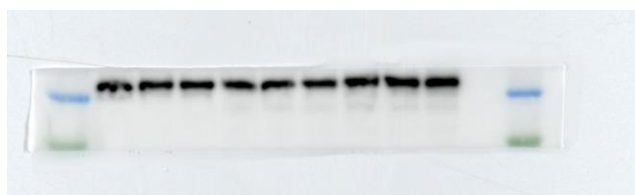


GAPDH

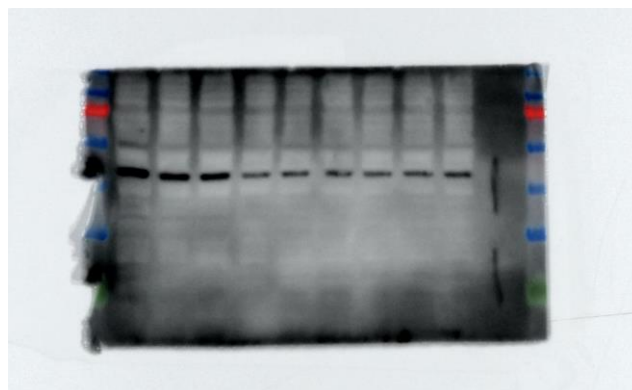


**Fig.S3**

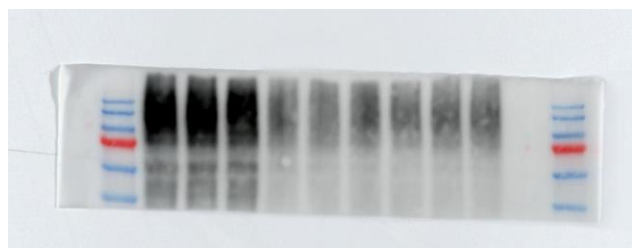
STING



ISG-STING



ubiquitin



GAPDH

