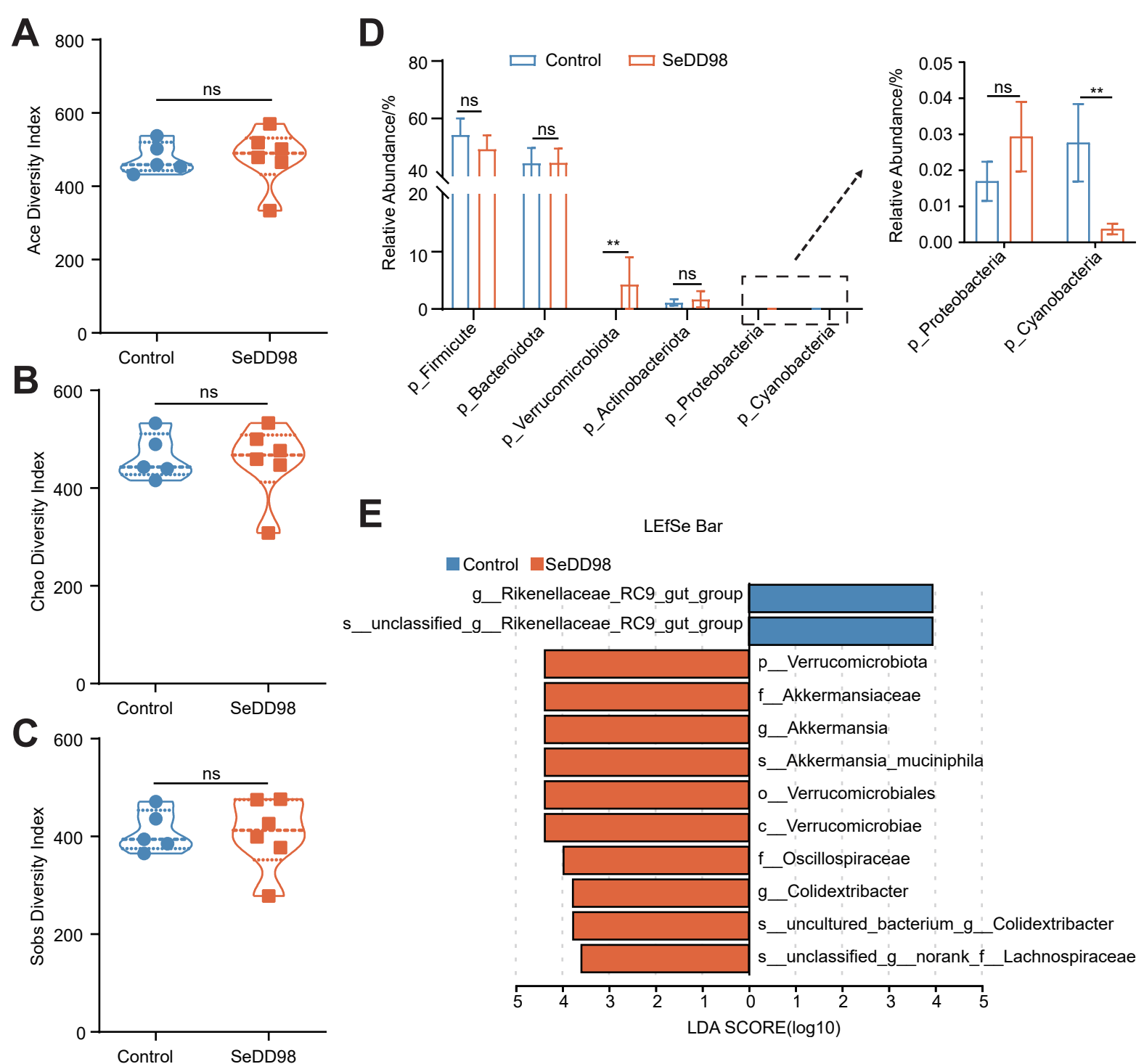
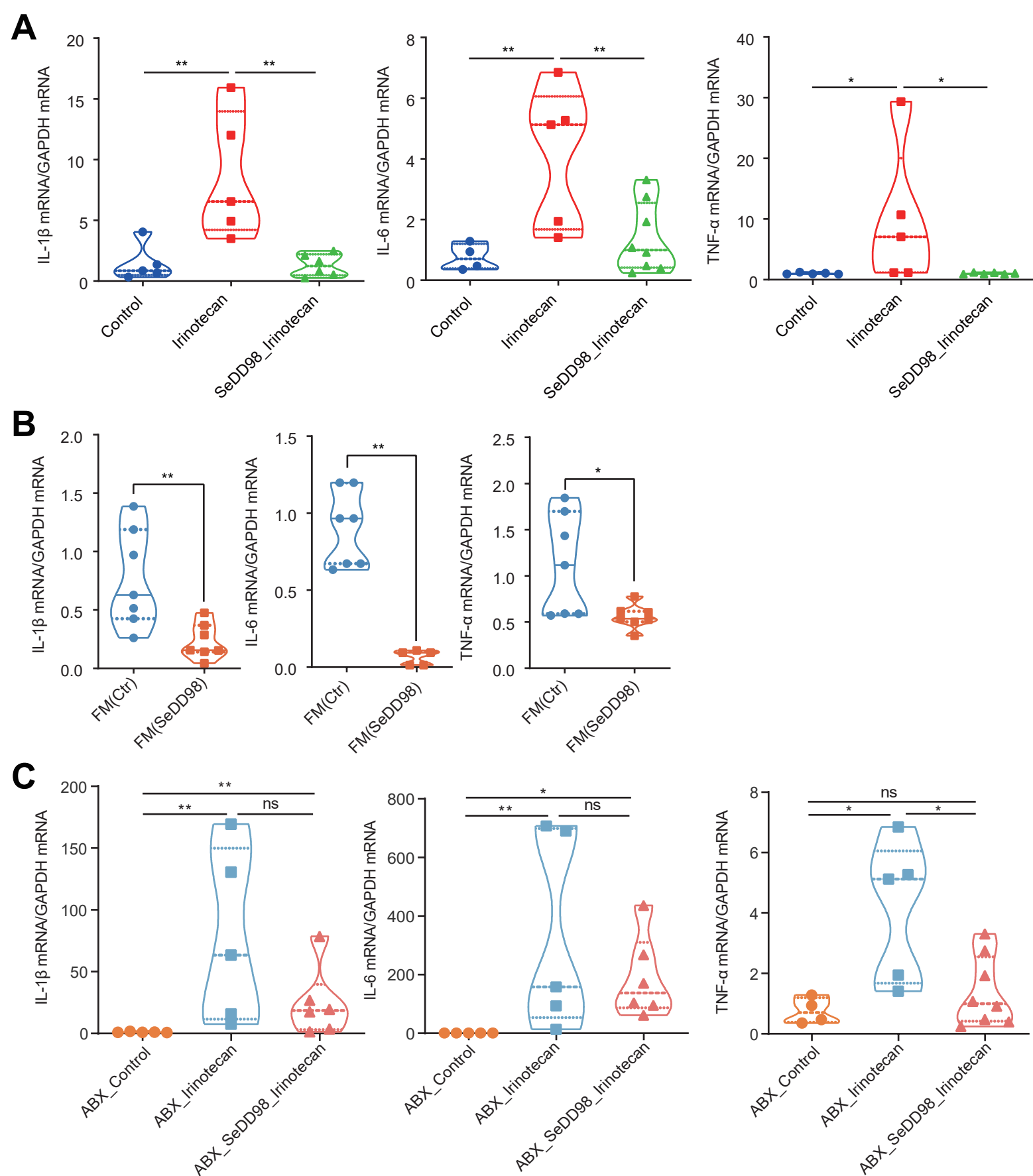
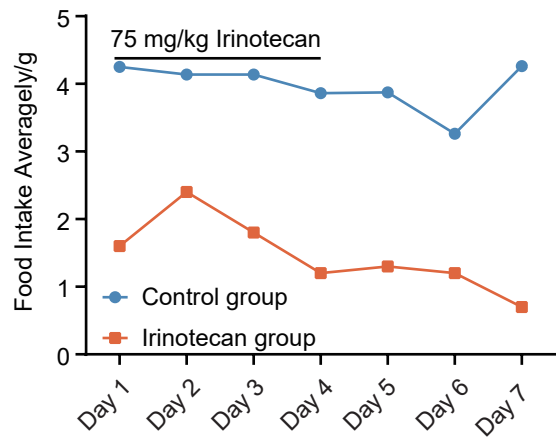




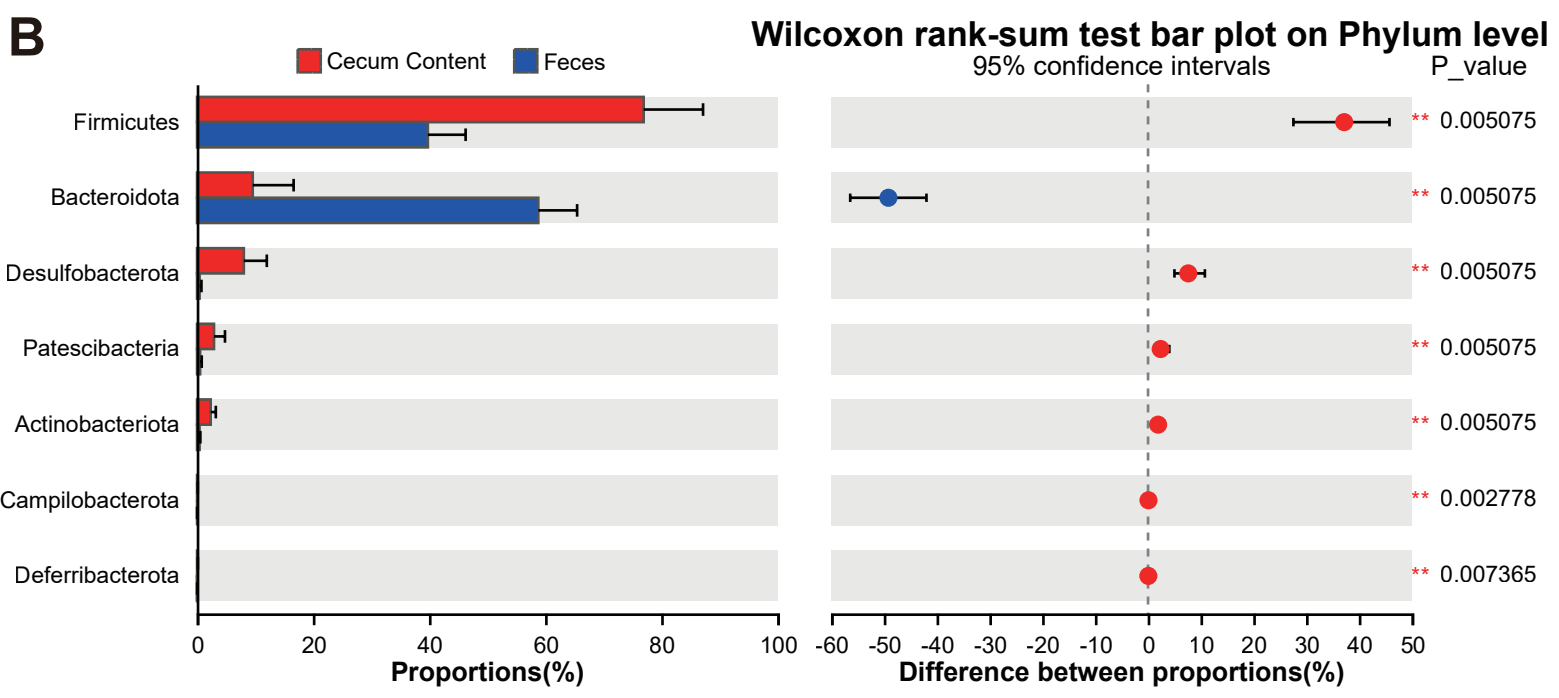
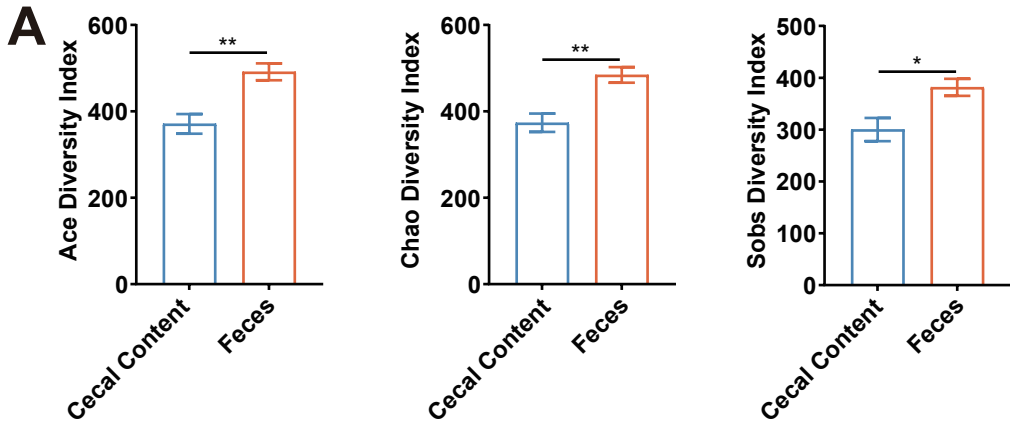
Supplementary Figure 1. Pretreatment with SeDD98 impacted the gut microbiota. (A-C) Alpha diversity indexes based on OTUs (Ace, Chao and Sobs). (D) The bar graph of the relative abundance at the phylum level. (E) LEfSe analysis depicted taxonomic association between microbiome communities from the Control and SeDD98 groups, with the LDA score (the criteria for feature selection was log LDA score > 3.5). Mean $\pm$ SEM values are presented. And p values were calculated using unpaired t tests, and ns means not significant. n = 5 ~ 6 mice per group. Mean $\pm$ SEM values are presented. And p values were calculated using unpaired t tests, **p < 0.01, and ns means not significant.



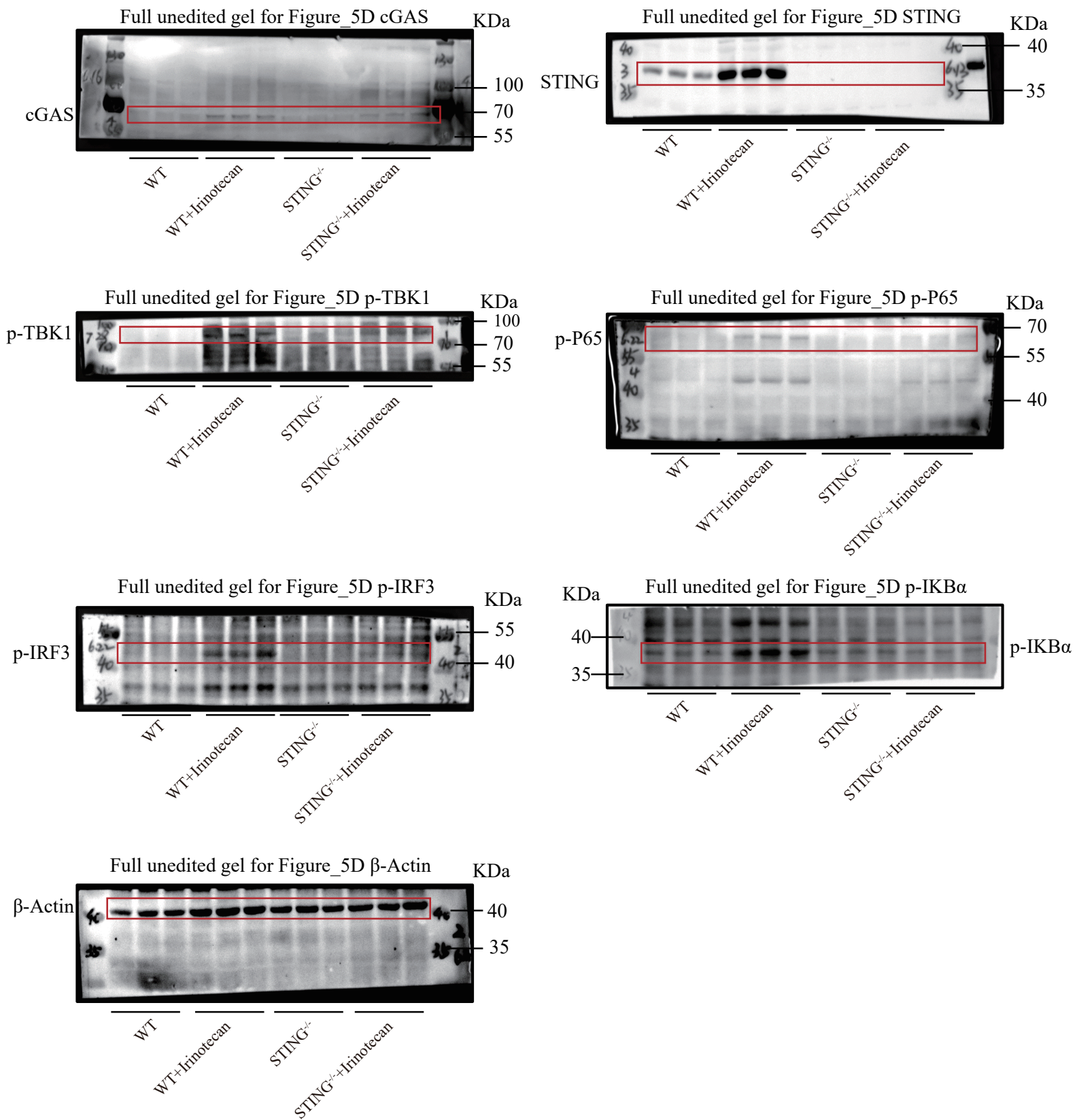
Supplementary Figure 2. The expression of the proinflammatory cytokines in intestinal tissues determined by qPCR was impacted. (A) SeDD98 decreased the expression of cleaved IL-1 β , IL-6 and TNF- α induced by irinotecan, $n = 5 \sim 8$ mice per group. (B) Fecal microbiota from SeDD98-treated mice decreased the expression of these proinflammatory cytokines, $n = 6 \sim 7$ mice per group (C) SeDD98 partly alleviated irinotecan-induced high expression of these proinflammatory cytokines in ABX mice, $n = 5 \sim 8$ mice per group. Mean $\pm$ SEM values are presented. And p values were calculated using unpaired t tests, * $p < 0.05$, ** $p < 0.01$, ns means not significant.



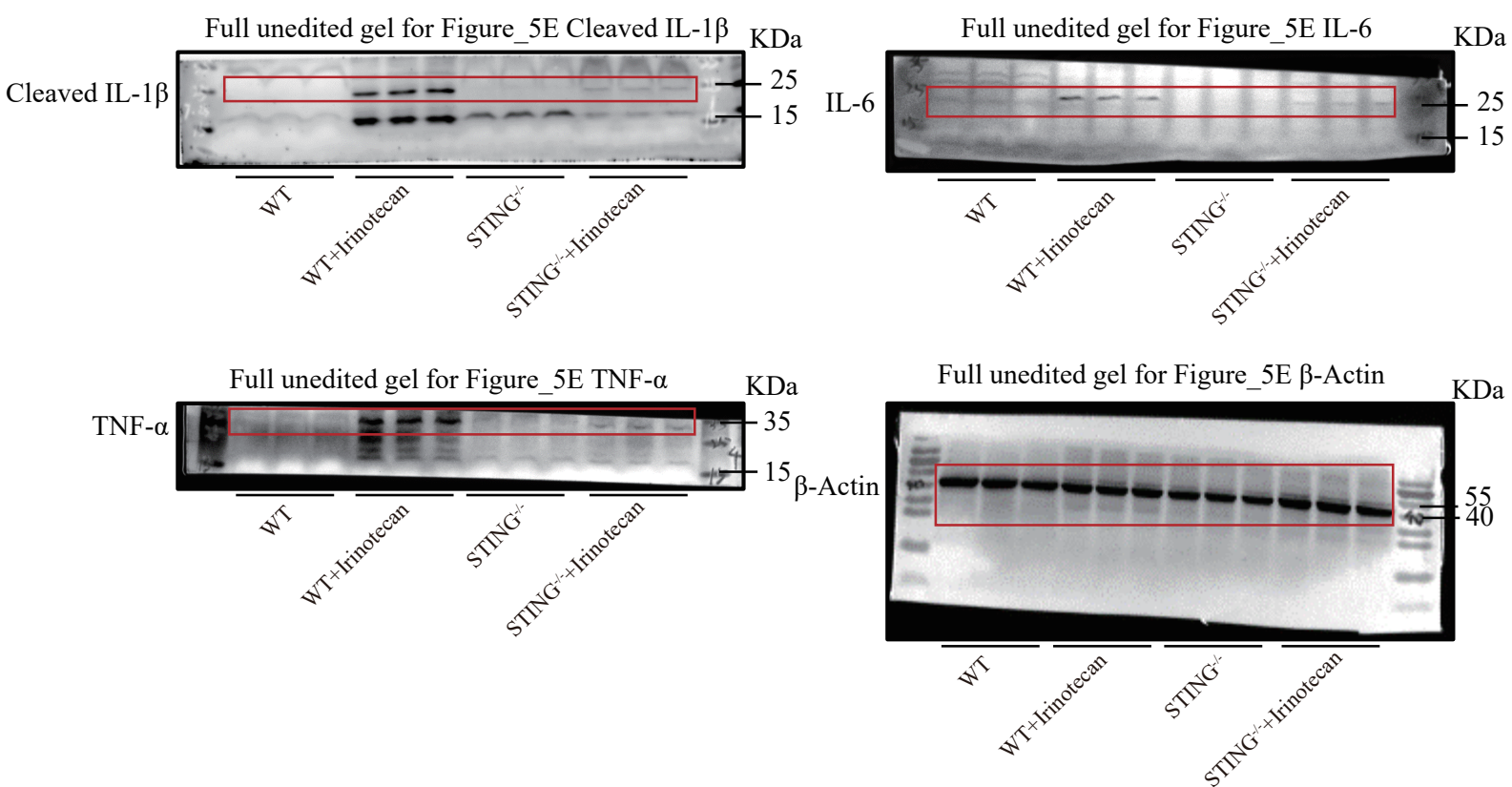
Supplementary Figure 3. The average daily food intake per mouse in each group was calculated by dividing the total daily food consumption of the group by the number of mice.



Supplementary Figure 4. The comparisons between fecal and cecal microbiota were conducted. (A) Alpha diversity indexes based on OTUs (Ace, Chao and Sobs). (B) Wilcoxon rank-sum test bar graph for microbial composition on the phylum level. The results are expressed as the mean $\pm$ SEM, n = 6. And p values were calculated using unpaired t tests, *p < 0.05, **p < 0.01.

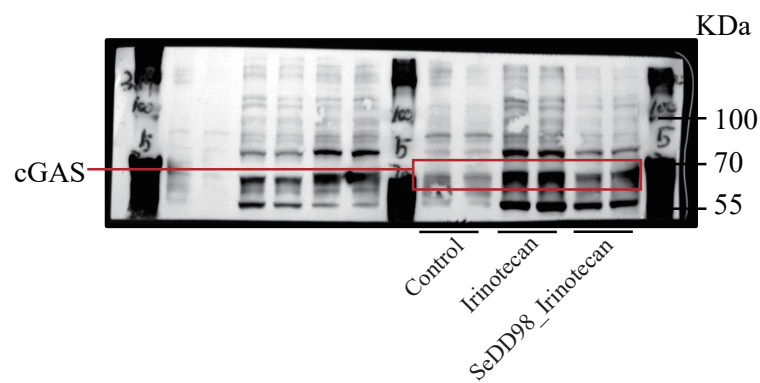


Supplementary Figure 5. STING mutation inhibited the STING-NF-κB pathway activated by irinotecan.

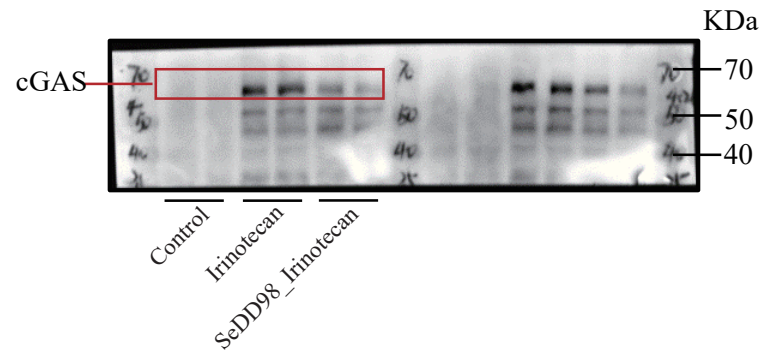


Supplementary Figure 6. STING mutation inhibited the expression of Cleaved IL-1 β , IL-6 and TNF- α in intestinal tissues induced by irinotecan.

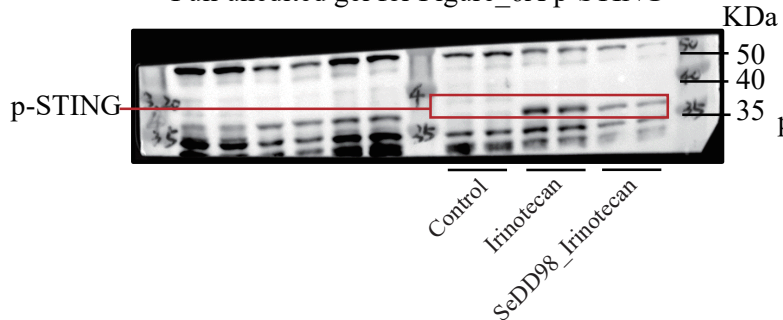
Full unedited gel for Figure_6A cGAS



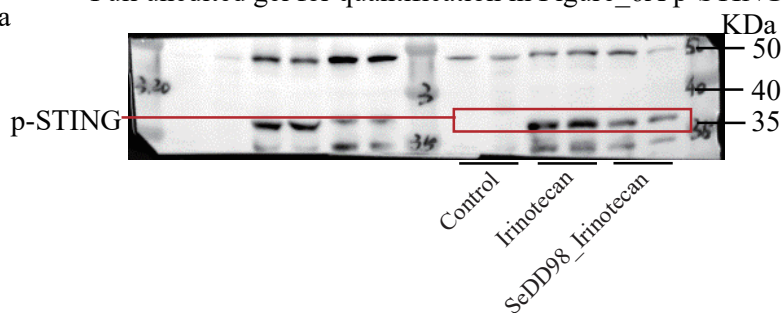
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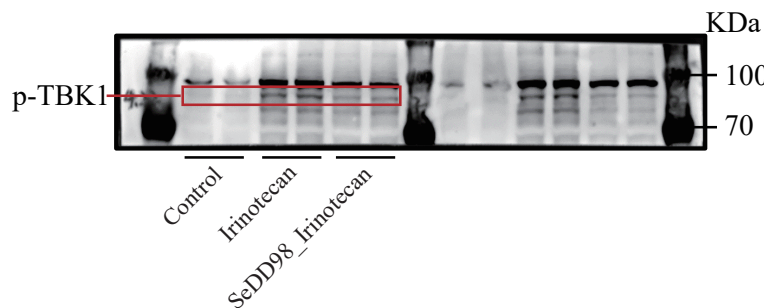
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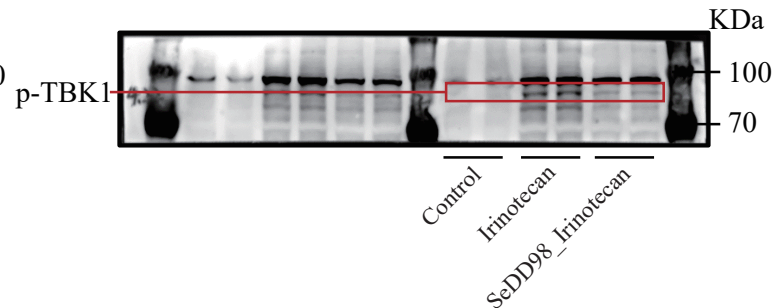
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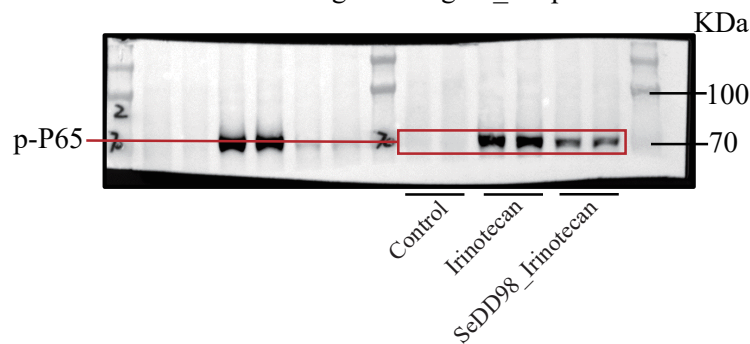
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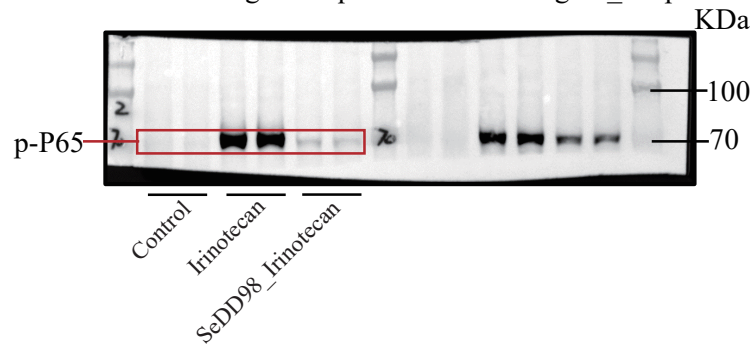
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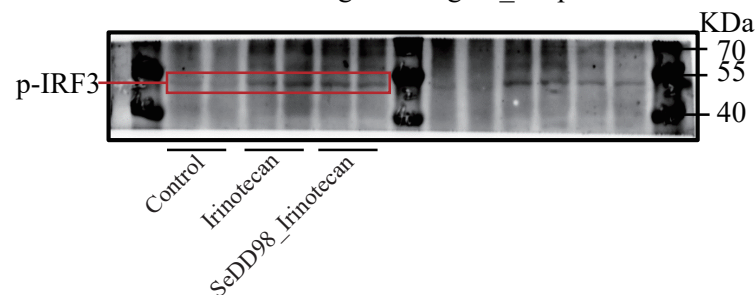
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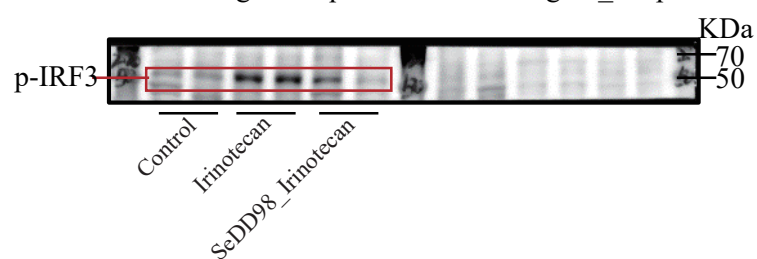
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Full unedited gel for Figure_6A p-IRF3

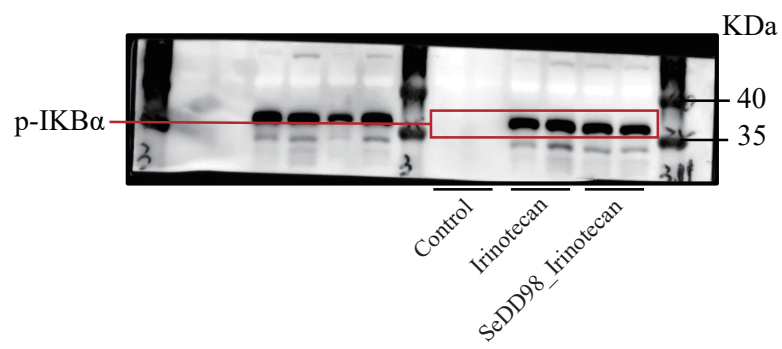


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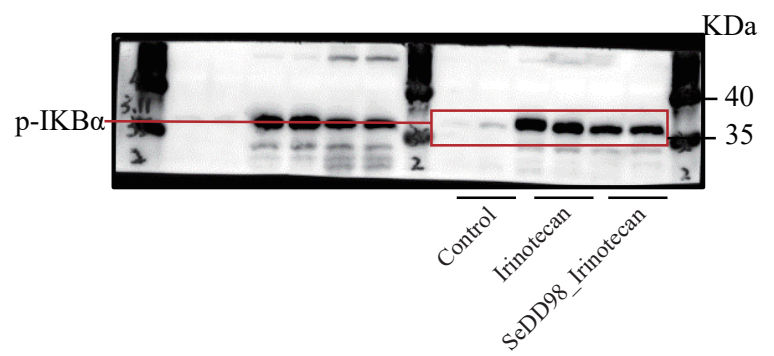


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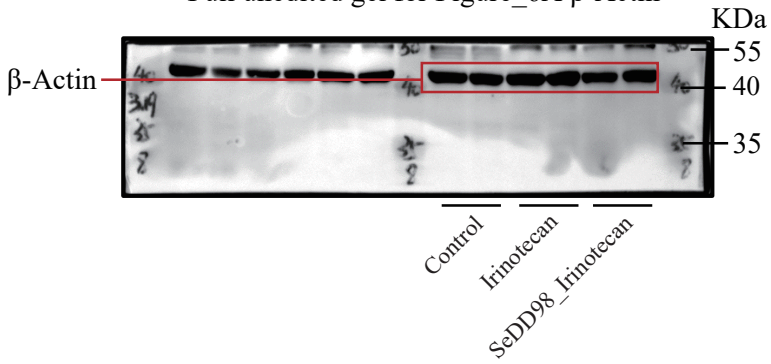
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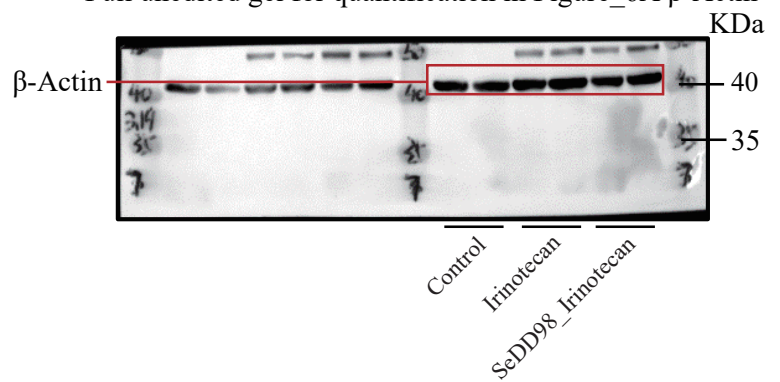
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Full unedited gel for Figure_6A β -Actin

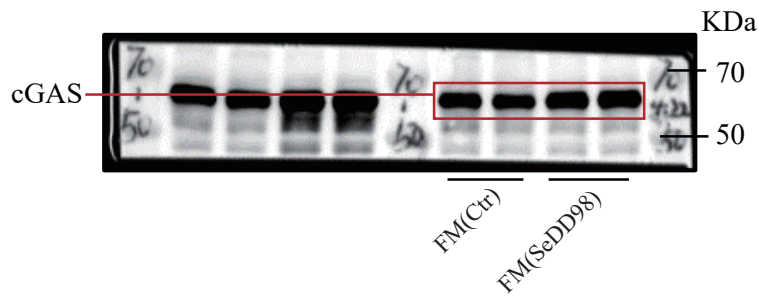


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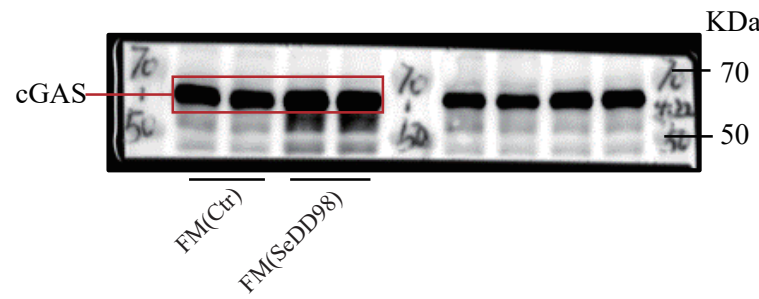


Supplementary Figure 7. Pretreatment with SeDD98 inhibited the STING-NF- κ B pathway in irinotecan-induced intestinal mucositis.

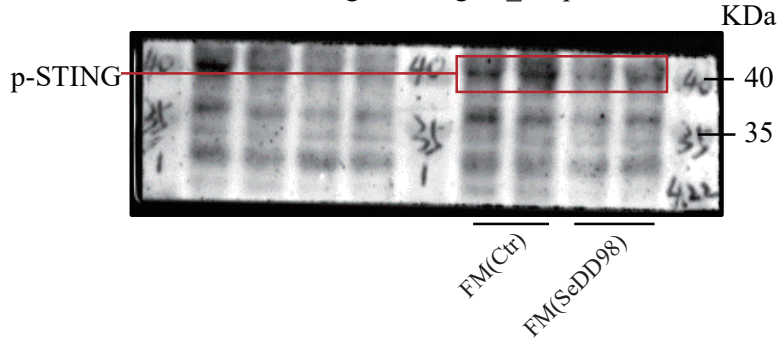
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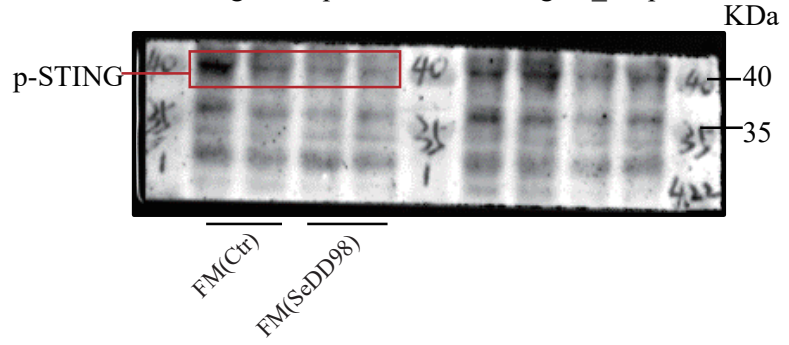
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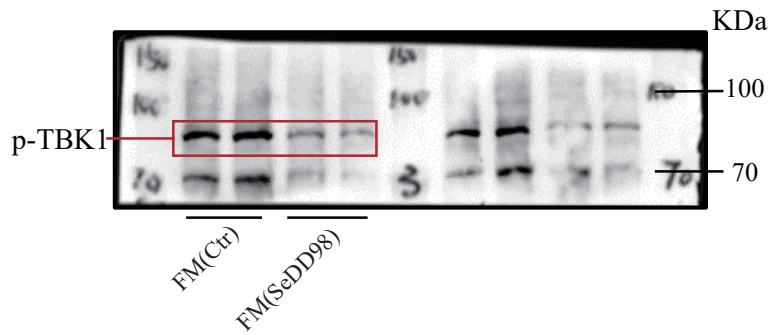
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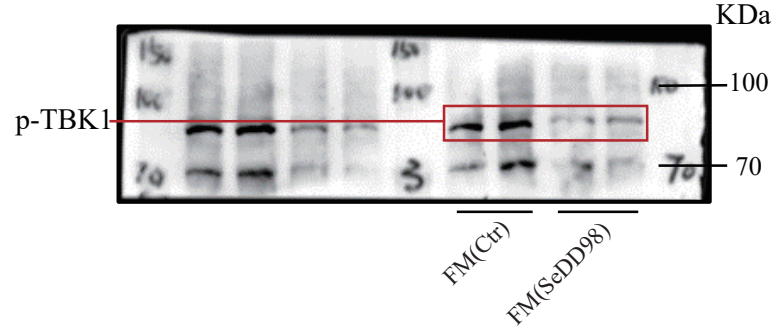
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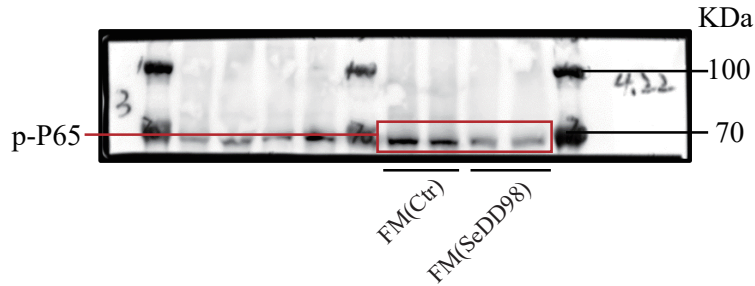
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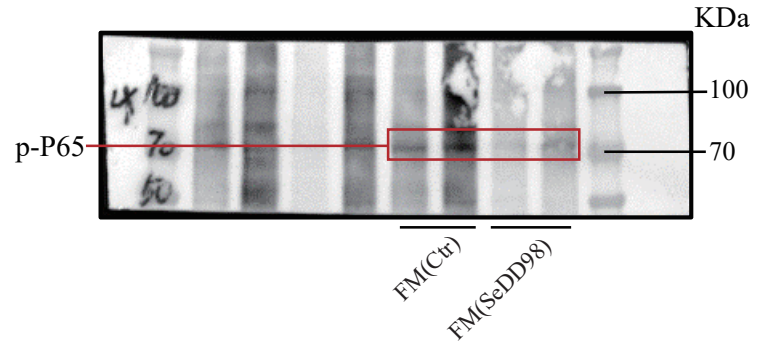
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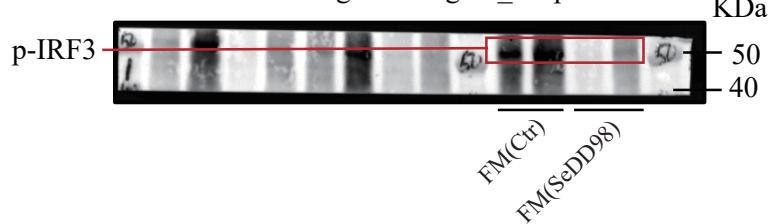
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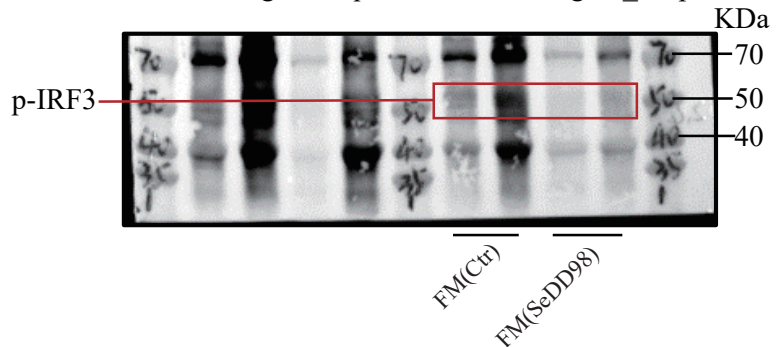
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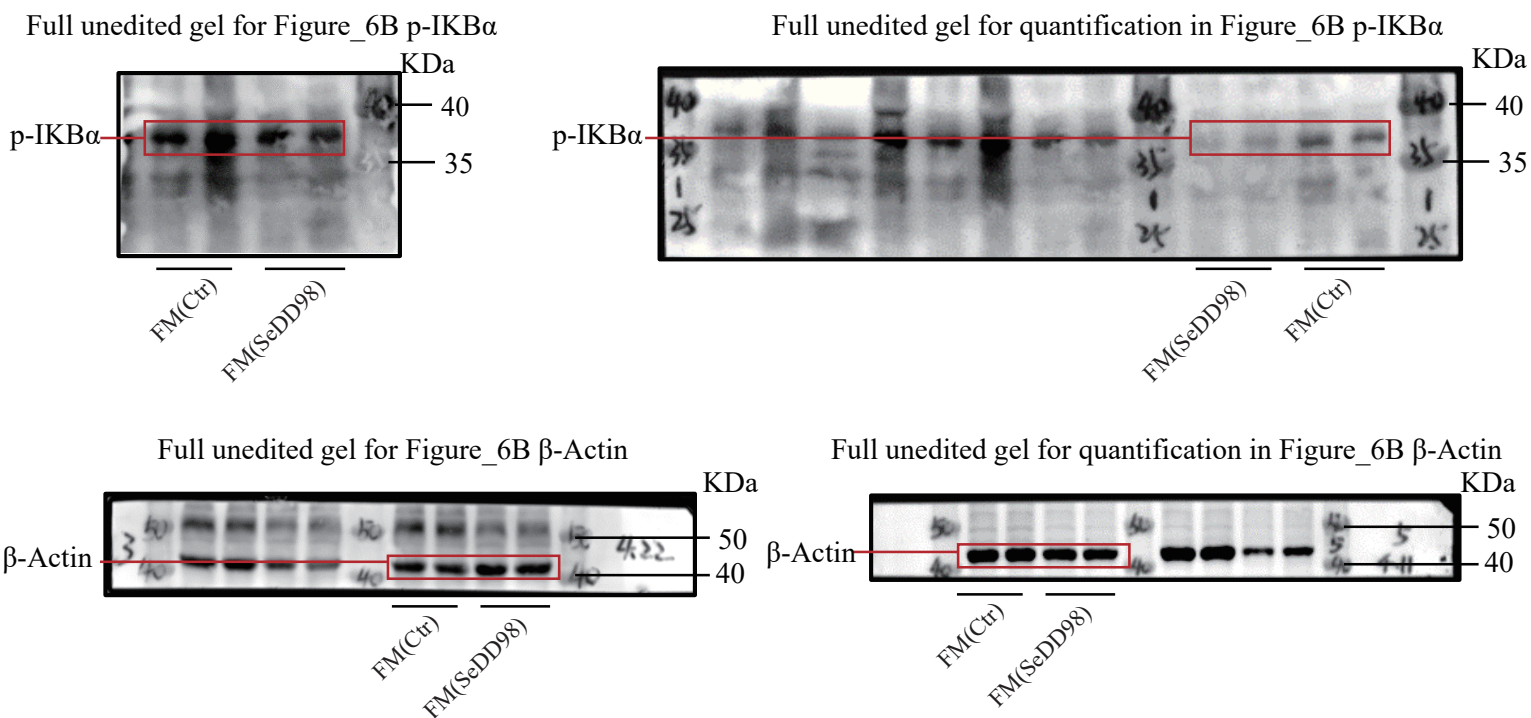
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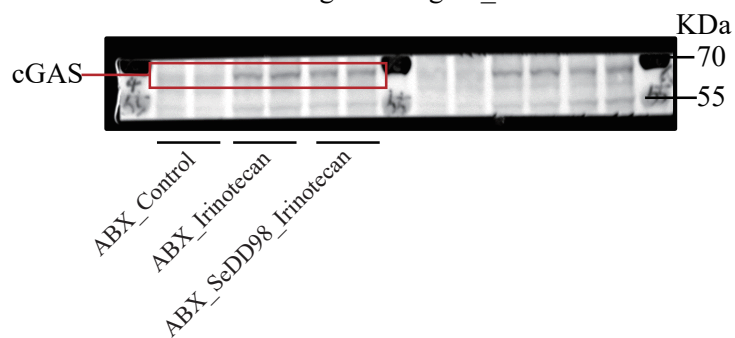


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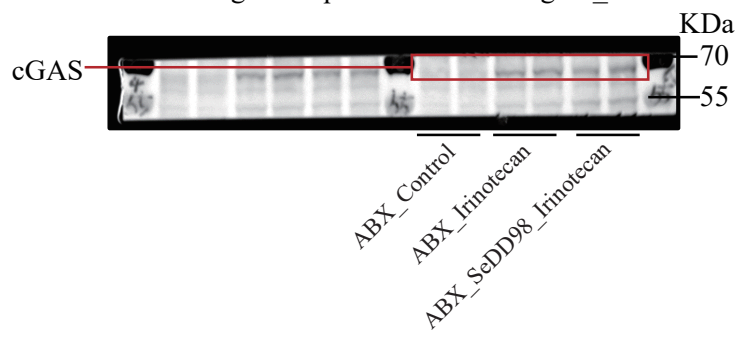


Supplementary Figure 8. Fecal microbiota from SeDD98-treated mice inhibited the STING-NF- κ B pathway in irinotecan-induced intestinal mucositis.

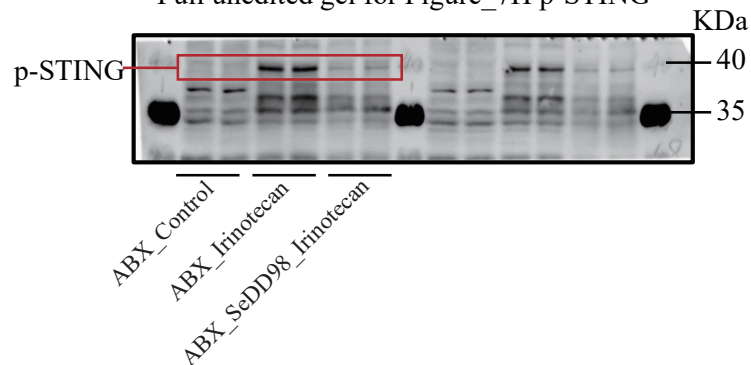
Full unedited gel for Figure_7H cGAS



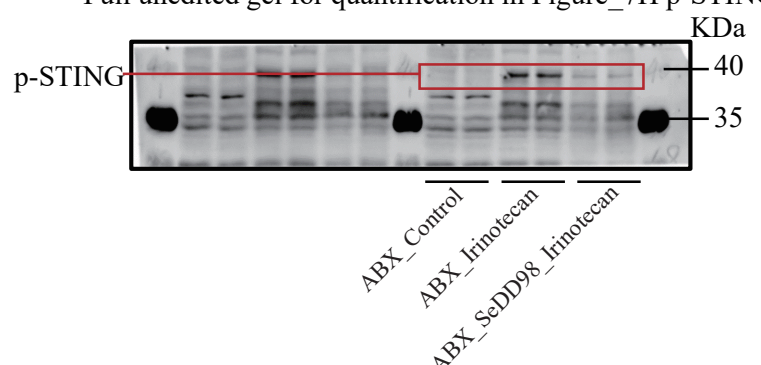
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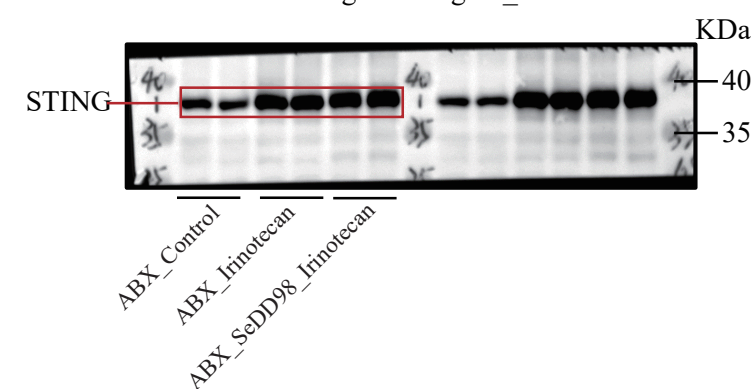
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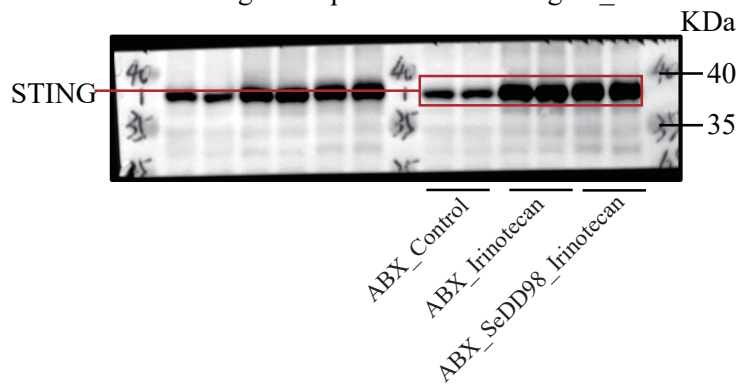
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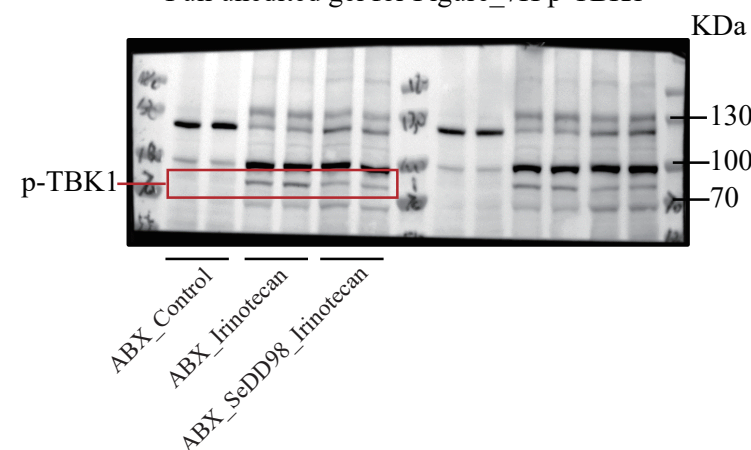
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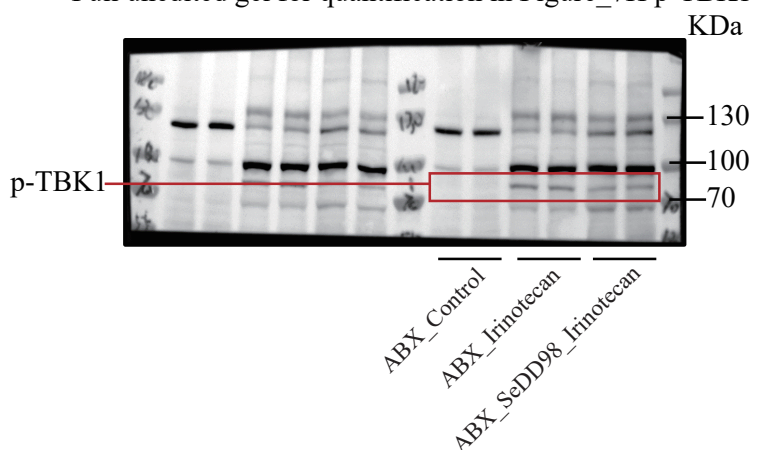
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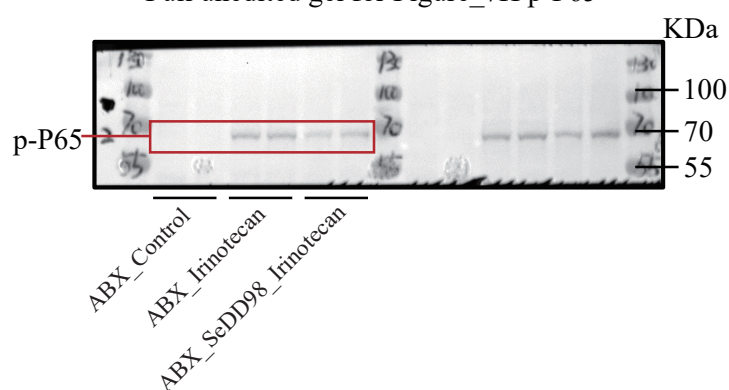
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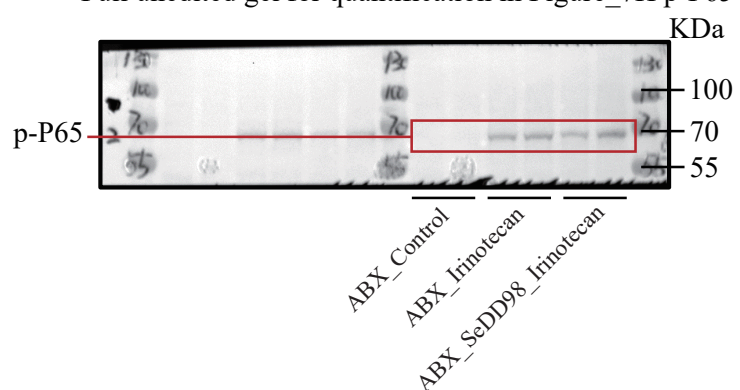
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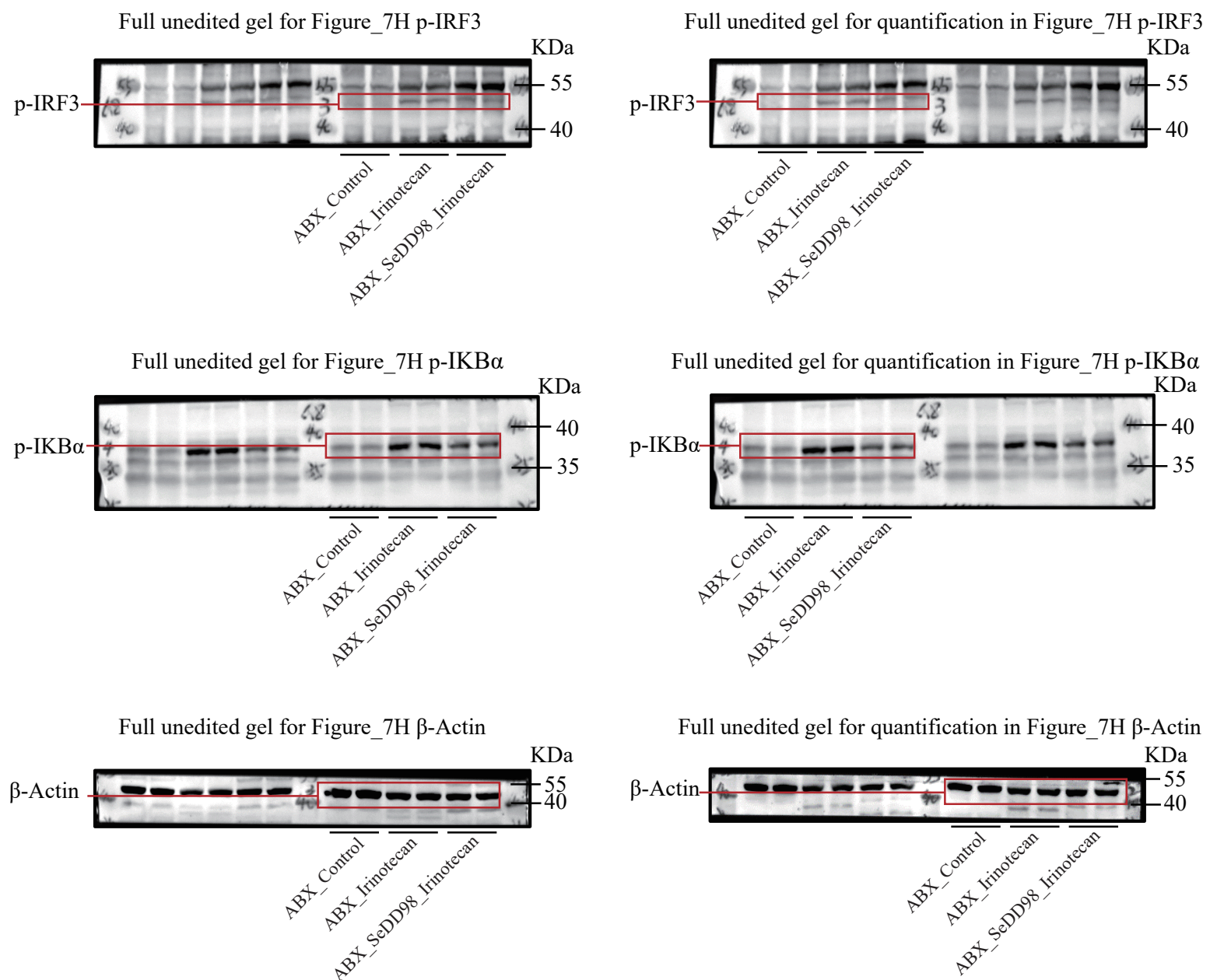


Full unedited gel for Figure_7H p-P65



Full unedited gel for quantification in Figure_7H p-P65





Supplementary Figure 9. Depletion of gut microbiota by a broad-spectrum antibiotic cocktail (ABX) blunted the inhibitory effect of SeDD98 on the STING-NF- κ B pathway.