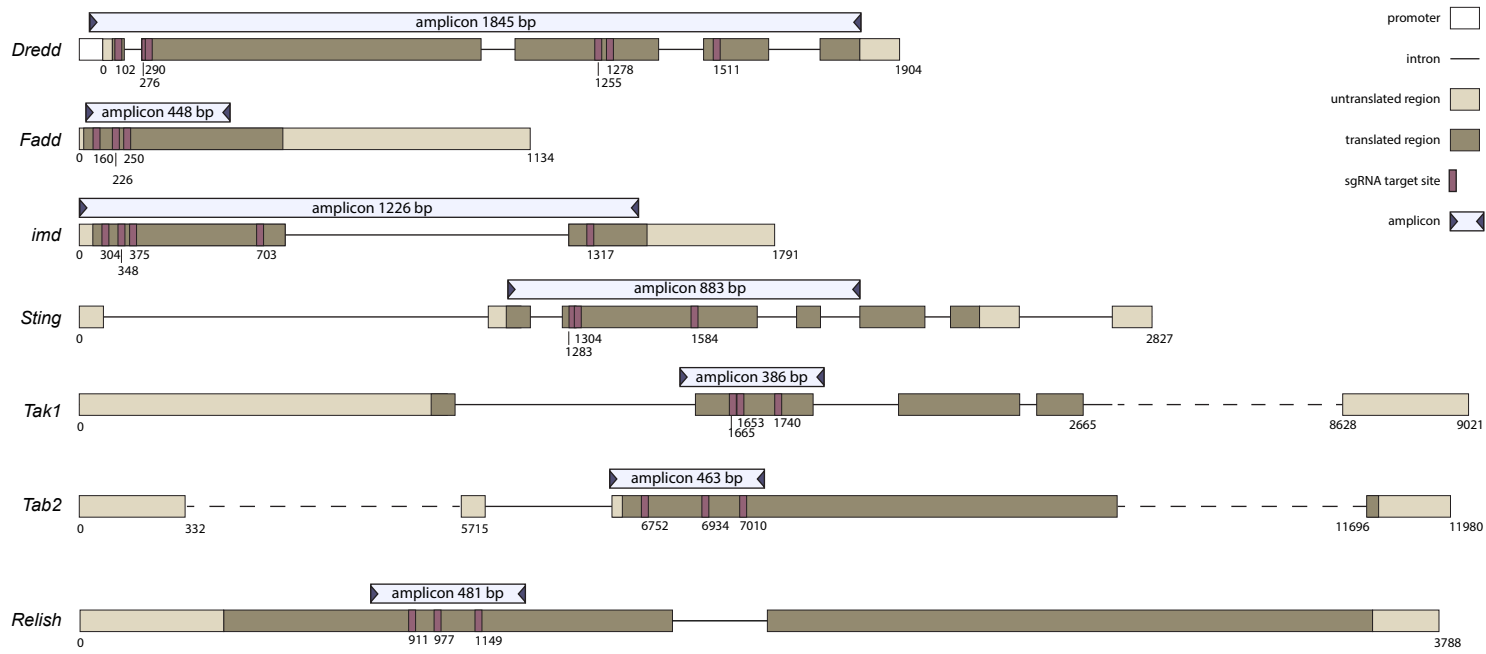
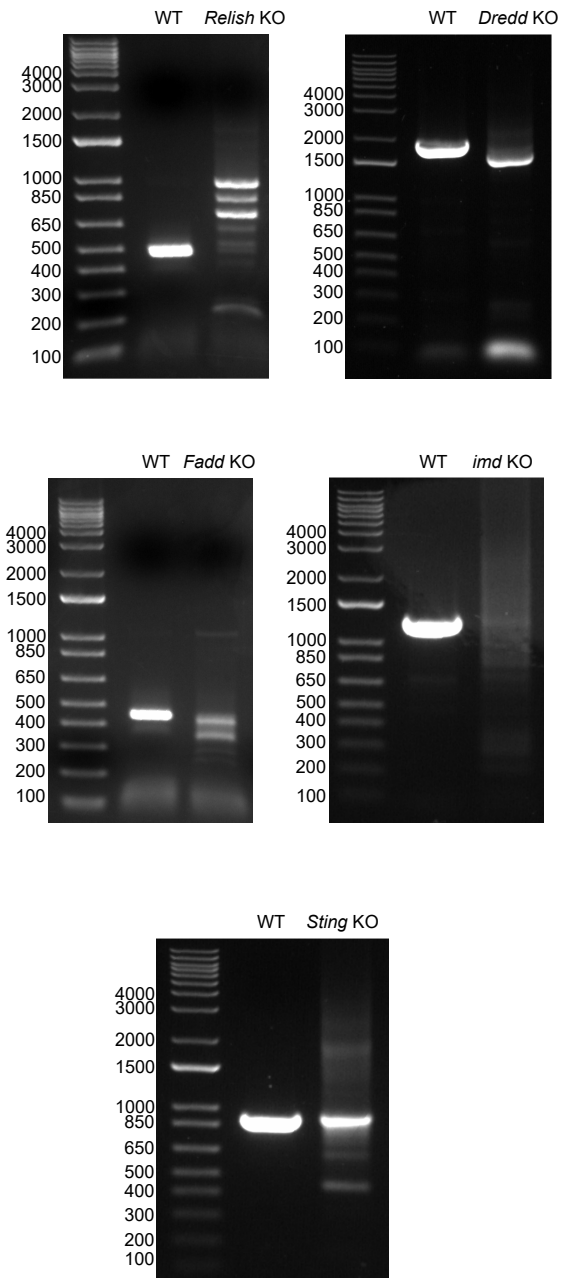


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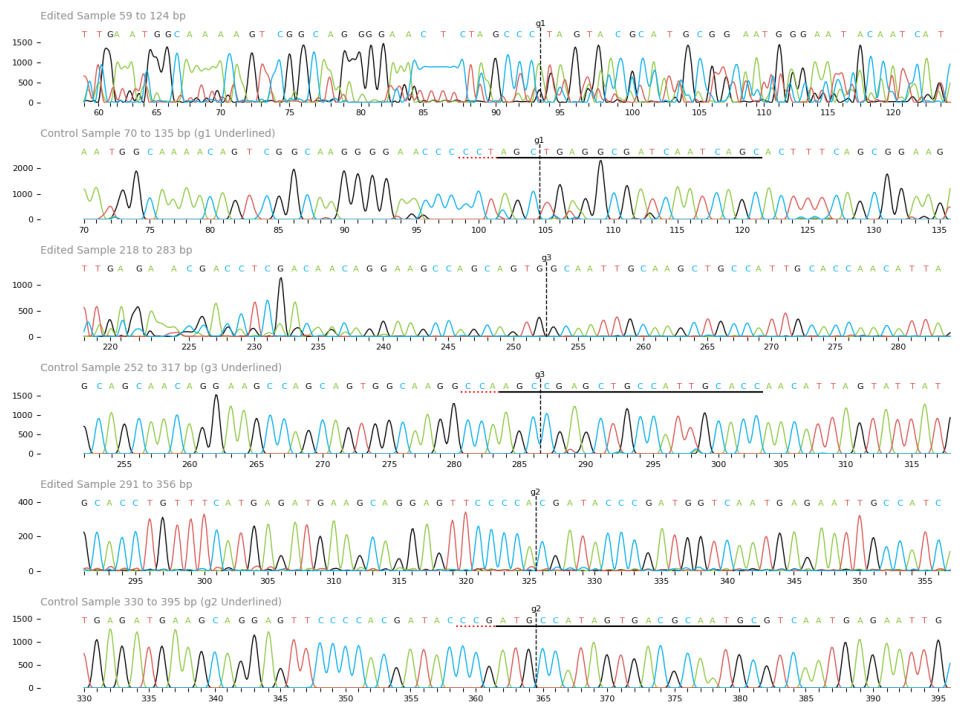
FADD is recruited to activated STING oligomers to initiate caspase-mediated NF- κ B activation in *Drosophila melanogaster*

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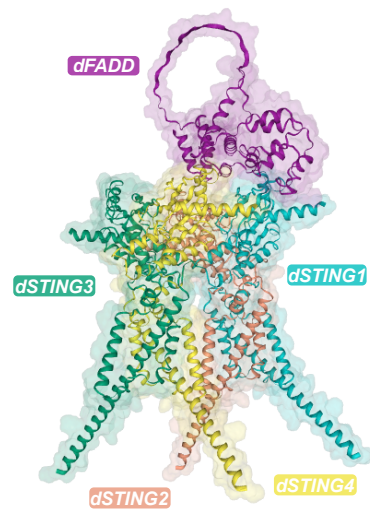
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A**B****C**

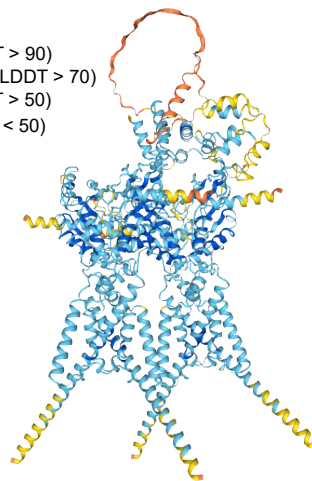
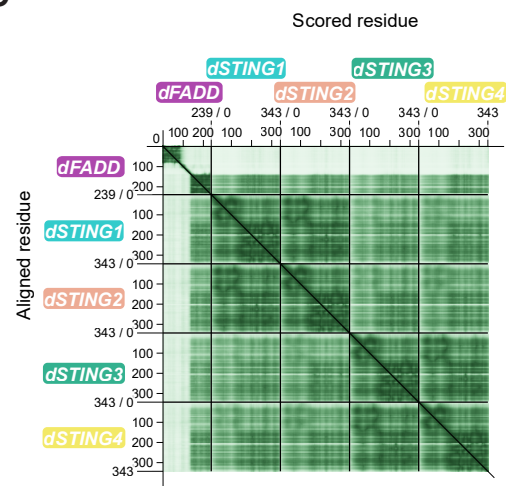
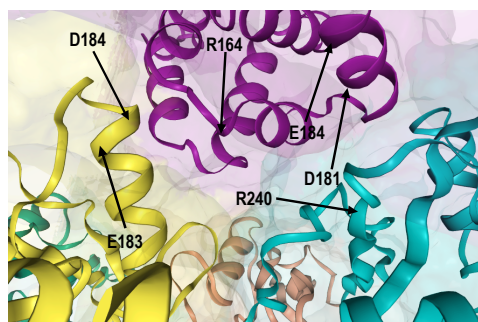
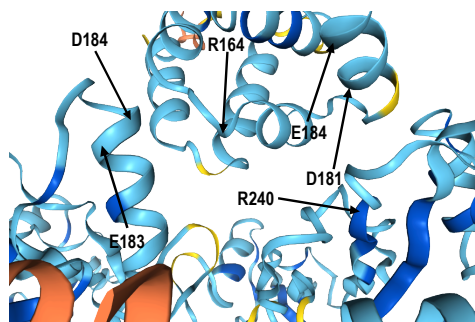
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1582	59	T	Reference: T. Reads: G (1), T (4)	K	conflict
1588	65	C	Reference: C. Reads: A (1), C (4)	M	conflict
1626	103	T	Reference: T. Reads: C (1), T (4)	Y	conflict
1630	107	T	Reference: T. Reads: A (1), T (4)	W	conflict
1649	126	G	Reference: G. Reads: G (2), T (1)	K	conflict
1742^1743	220	C	Reference: -. Reads: - (2), C (2)	C	conflict
1743	221	A	Reference: A. Reads: A (2), G (2)	R	conflict
1745	223	C	Reference: C. Reads: C (2), T (2)	Y	conflict
1746	224	A	Reference: A. Reads: A (2), G (2)	R	conflict
1748^1749	227	G	Reference: -. Reads: - (2), G (2)	G	conflict
1750	229	A	Reference: G. Reads: A (2), G (2)	R	conflict
1751^1752	231	A	Reference: -. Reads: - (2), A (2)	A	conflict
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1752^1753	235	G	Reference: -. Reads: - (2), G (2)	G	conflict
1752^1753	236	T	Reference: -. Reads: - (2), T (2)	T	conflict
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D

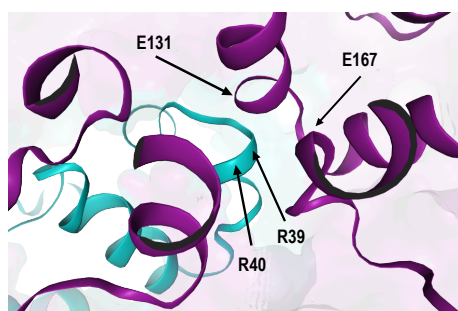
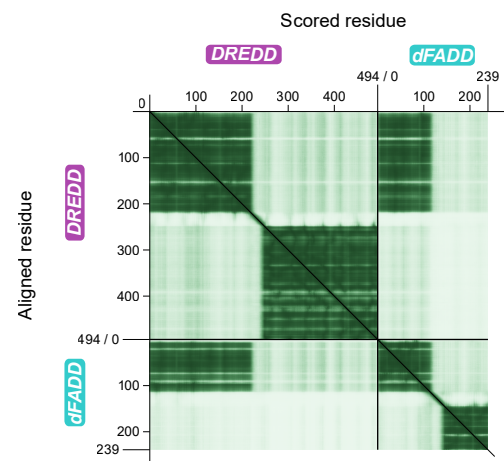
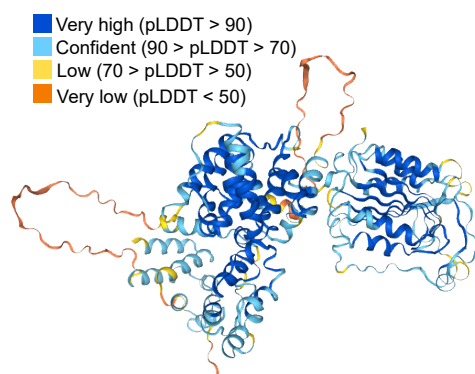
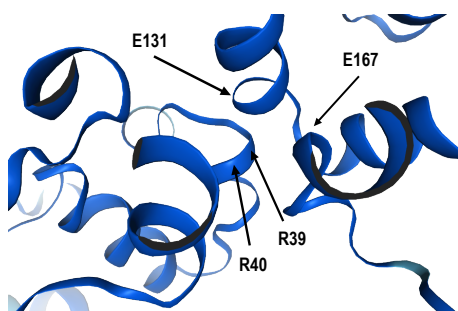
Appendix Figure S1. Editing of S2 cell KO pools. **A**, Figure shows an overview of genes edited in S2 cells by CRISPR/Cas9 including sgRNA target sites and expected amplicon sizes **B**, Genomic DNA from WT and edited polyclonal S2 cells was purified and the indicated regions in **A** were amplified by PCR and analysed by gel electrophoresis. **C-D**, The PCR products from *Tab2* and *Tak1* KO cells were sanger sequenced either directly (*Tab2*, panel d) or after cloning (*TAK1*, panel c).

A**B**

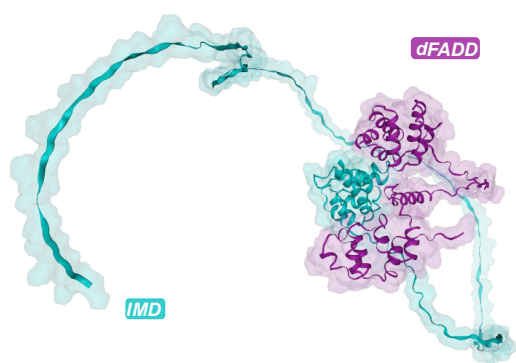
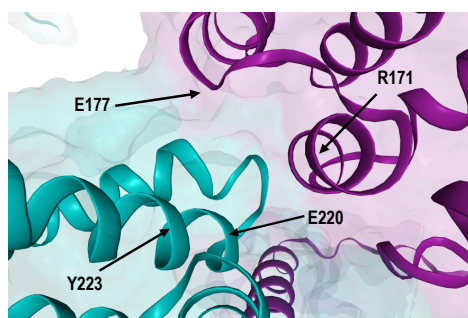
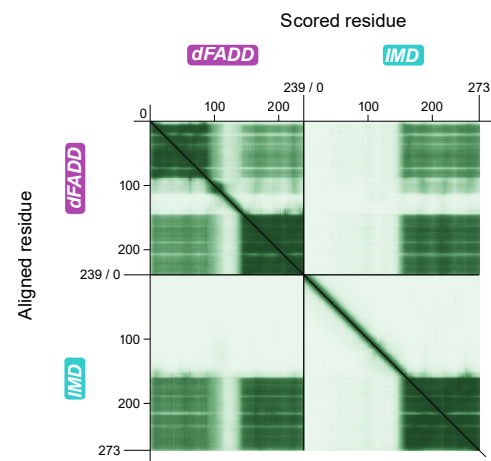
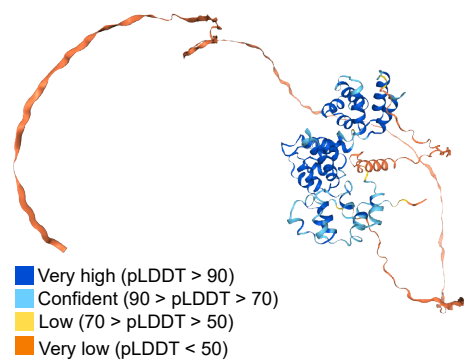
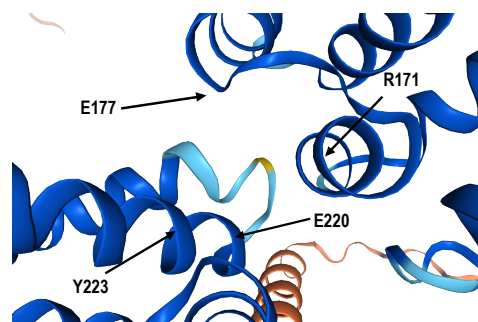
Very high (pLDDT > 90)
 Confident (90 > pLDDT > 70)
 Low (70 > pLDDT > 50)
 Very low (pLDDT < 50)

**C****D****E**

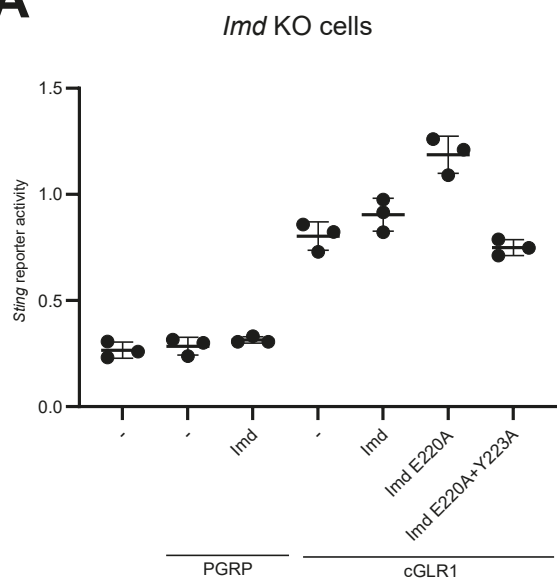
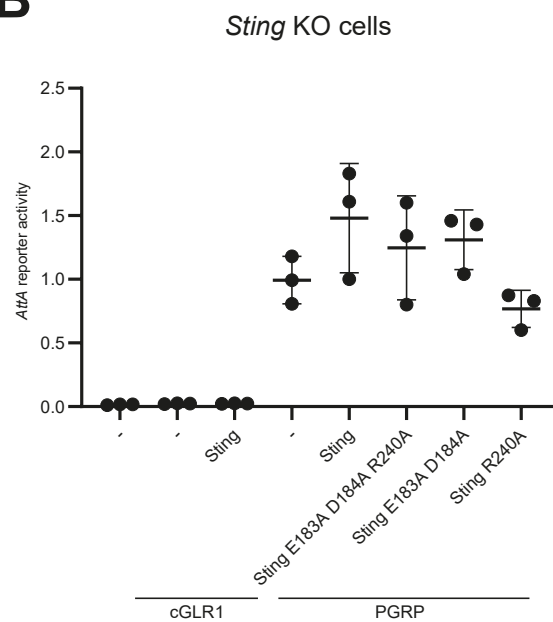
Appendix Figure S2. AlphaFold model of dFADD in complex with dSTING. **A**, Predicted structure of the complex between dFADD and a dSTING tetramer colored according to chains. **B**, Predicted structure of the complex between dFADD and a dSTING tetramer colored according to pLDDT score. The complex is predicted with high confidence (scores >70) except for some less ordered regions. **C**, The PAE plot for the complex. Protein chains are indicated by different colors. **D-E**, Zoom of the predicted interaction site between dFADD and dSTING colored by **D**, chains and **E**, pLDDT score. Showing that the interaction site is predicted with high confidence (pLDDT scores > 70). Mutated residues are indicated.

A**B****C****D****E**

Appendix Figure S3. AlphaFold model of dFADD in complex with DREDD. **A**, Predicted structure of the complex between dFADD and DREDD colored according to chains. **B**, Zoom of the predicted interaction site between dFADD and DREDD colored by chains. Mutated residues are indicated. **C**, The PAE plot for the complex. Protein chains are indicated by different colors. **D**, Predicted structure of the complex between dFADD and a DREDD colored according to pLDDT score. The complex is predicted with high confidence (scores >70) except for some less ordered regions. **E**, Zoom of the predicted interaction site between dFADD and DREDD colored by pLDDT score. Showing that the interaction site is predicted with very high confidence (pLDDT scores > 90). Mutated residues are indicated.

A**B****C****D****E**

Appendix Figure S4. AlphaFold model of dFADD in complex with IMD. **A**, Predicted structure of the complex between dFADD and IMD colored according to chains. **B**, Zoom of the predicted interaction site between dFADD and IMD colored by chains. Mutated residues are indicated. **C**, The PAE plot for the complex. Protein chains are indicated by different colors. **D**, Predicted structure of the complex between dFADD and a IMD colored according to pLDDT score. The complex is predicted with high confidence (scores >70) except for the N-terminal part of IMD and the loop between the N- and C-terminal of dFADD which is predicted with very low confidence (pLDDT score < 70). **E**, Zoom of the predicted interaction site between dFADD and IMD colored by pLDDT score. Showing that the interaction site is predicted with very high confidence (pLDDT scores > 90). Mutated residues are indicated.

A**B**

Appendix Figure S5. Luciferase assay of dSTING and Imd mutants. **A**, mutating E220A alone or both E220A and Y223A in IMD does not impact dSTING signalling (*Sting* reporter activity) in *Imd* KO cells. **B**, Likewise, the dSTING E183A/D184A/R240 mutant, or the respective single mutants, have no or little effect on IMD signalling (*AttA* reporter activity) in *Sting* KO cells. **A-B**, data from one independent experiment performed in biological triplicates, are shown with mean and bars indicating standard deviation ($n = 3$).