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## **HCT116** Apoptosis



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HCT116 Pyroptosis



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## DLD1 Pyroptosis

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**DLD1** Pyroptosis



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Fig.5 | Oligomerization of NT-GSDMD, NT-GSDME and p-MLKL triggers PANoptosis after co-treatment of IFN- $\gamma$  + TNF- $\alpha$ .

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## Sensors of Cytoplasmic DNA fragments

а b 293T 293T 293T HT29 HT29 HT29 DLD1 HCT116 DLD1 HCT116 DLD1 HCT116 68KD ZBP1 **40KD AIM2** 62 KD cGAS 25KD ASC •38 KD AIM2 62KD cGAS 68KD ZBP1 25 KD ASC 38KD ZBP1 110 KD ATP **110KD ATP** 35 KD GAPDH **35 KD GAPDH** 15 KD p-H2A.X 68 KD Lamin B1 45 KD Cleaved Lamin B1

Fig.6 | DNA sensors for DNA fragments in Cancer cells with dMMR are in the nucleus, not in the cytoplasm.





Fig.7 | Hyperactivation of PANoptosis effective moleculars by AIM2-ZBP1-RIPK1-RIPK3-ASC-CASP8-CASP1 signal pathway.



Fig.10 | *Mlh1* knockout CT26 and CMT93 undergo natural hyperactivation of GSDMD, GSDME and p-MLKL.



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