

MURDER MYSTERY: UNRAVELLING CELL DEATH IN NATURAL KILLER (NK) CELLS

Jadie Acklam, Alex J. Hogg, Nathan G.F. Leborgne, Max E. Noble, Frances E. Pearson, Alison M. Layton, Ian S. Hitchcock, Dave Boucher, Jillian L. Barlow

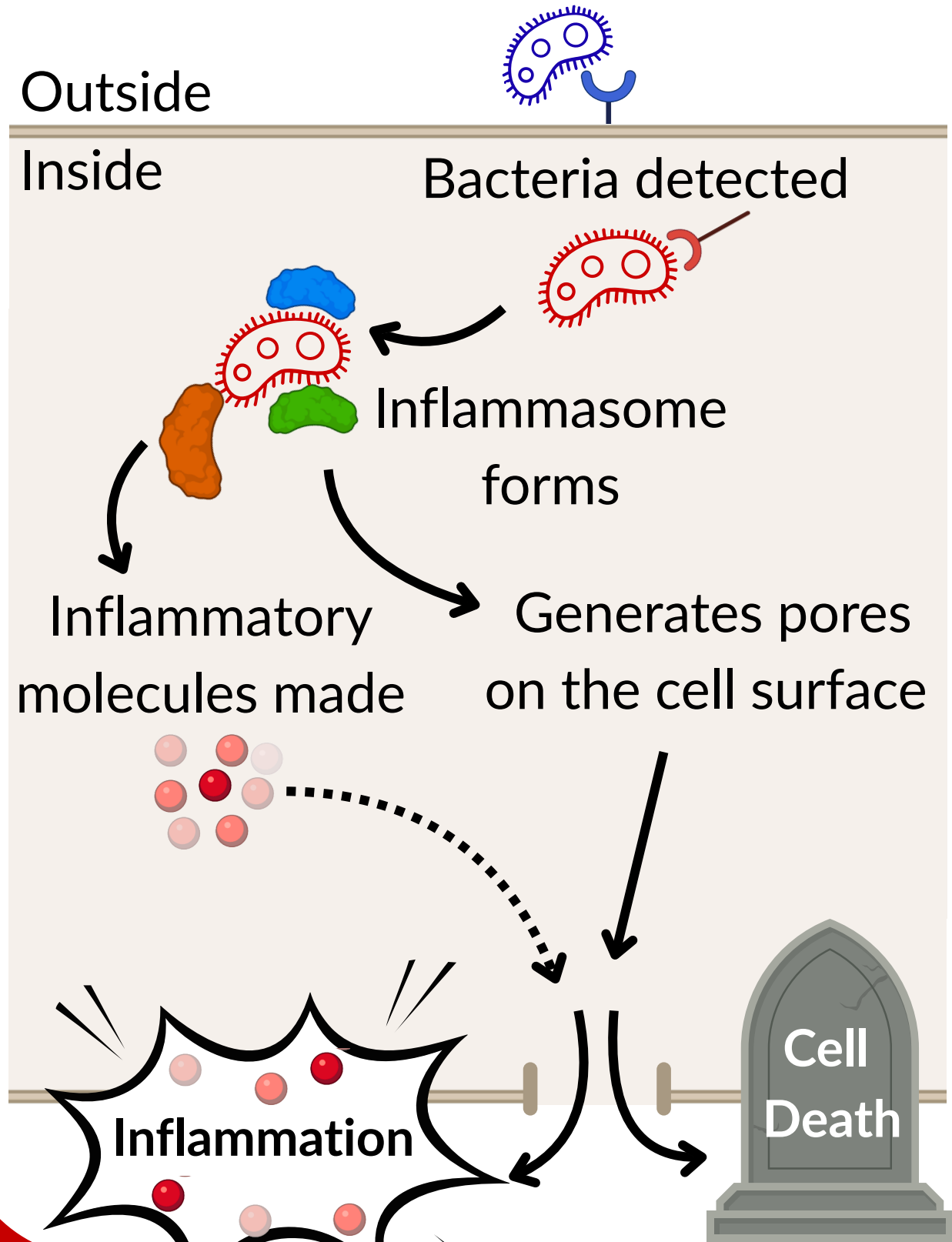


1

CRIME SCENE: THE INFLAMMASOME

The inflammasome is a group of proteins that assemble inside the cell once bacteria are detected, resulting in cell death and inflammation.

The inflammasome has been implicated in autoimmune and inflammatory diseases.



There are two types of inflammasome:

- 1. Canonical**
Detects bacteria **outside** the cell
- 2. Non-canonical**
Detects bacteria **inside** the cell



Hmm, NK cells have been dying around here!
The main suspect is the inflammasome, let's follow the evidence...

2

CATCHING THE INFLAMMASOME PERPETRATOR

Isolate NK cells from healthy human blood

+/- infection with different bacteria

+/- inflammasome inhibitor (VX)

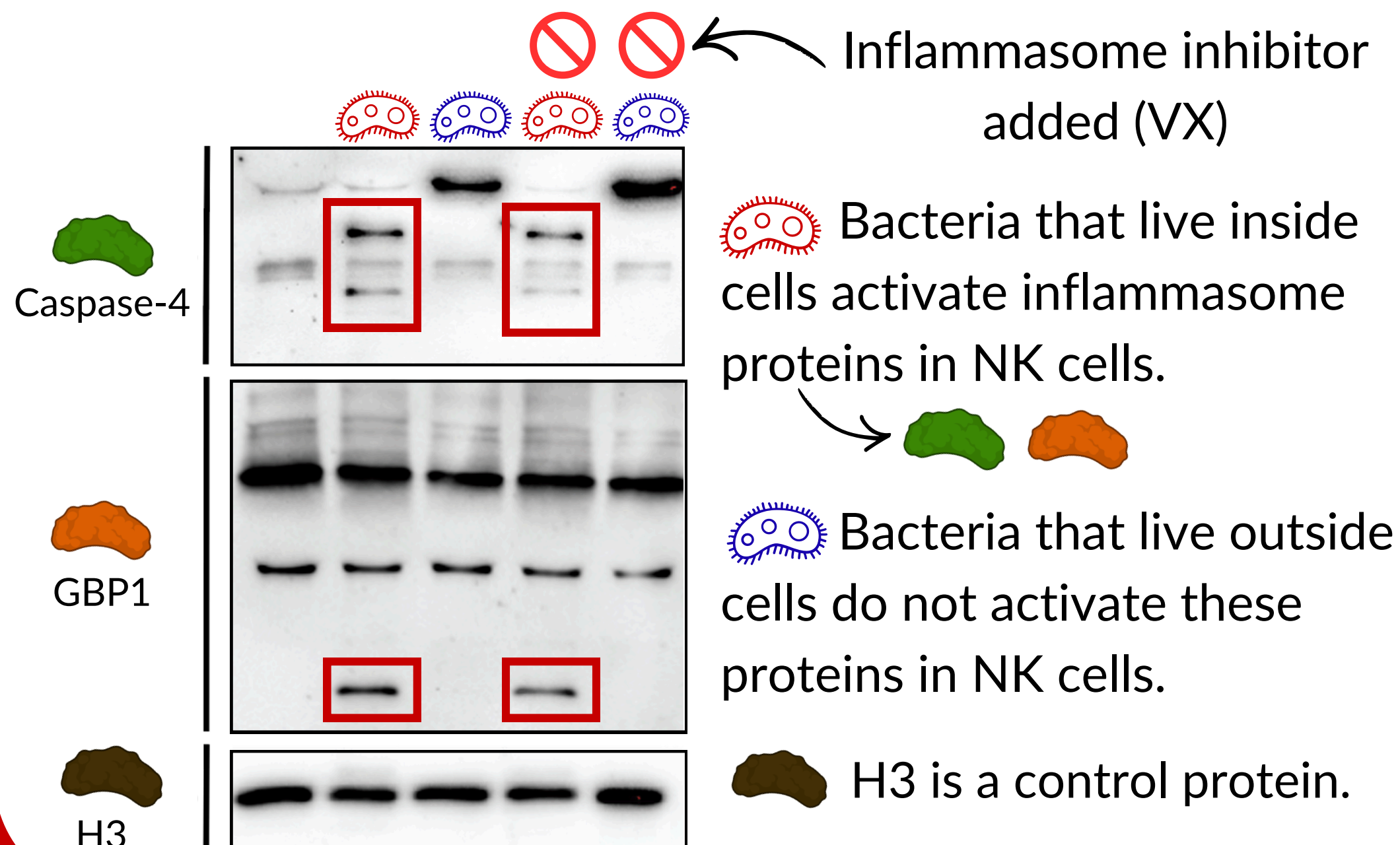
Western blot: Are inflammasome proteins present/active?

Cell death assay: Are the cells dying?

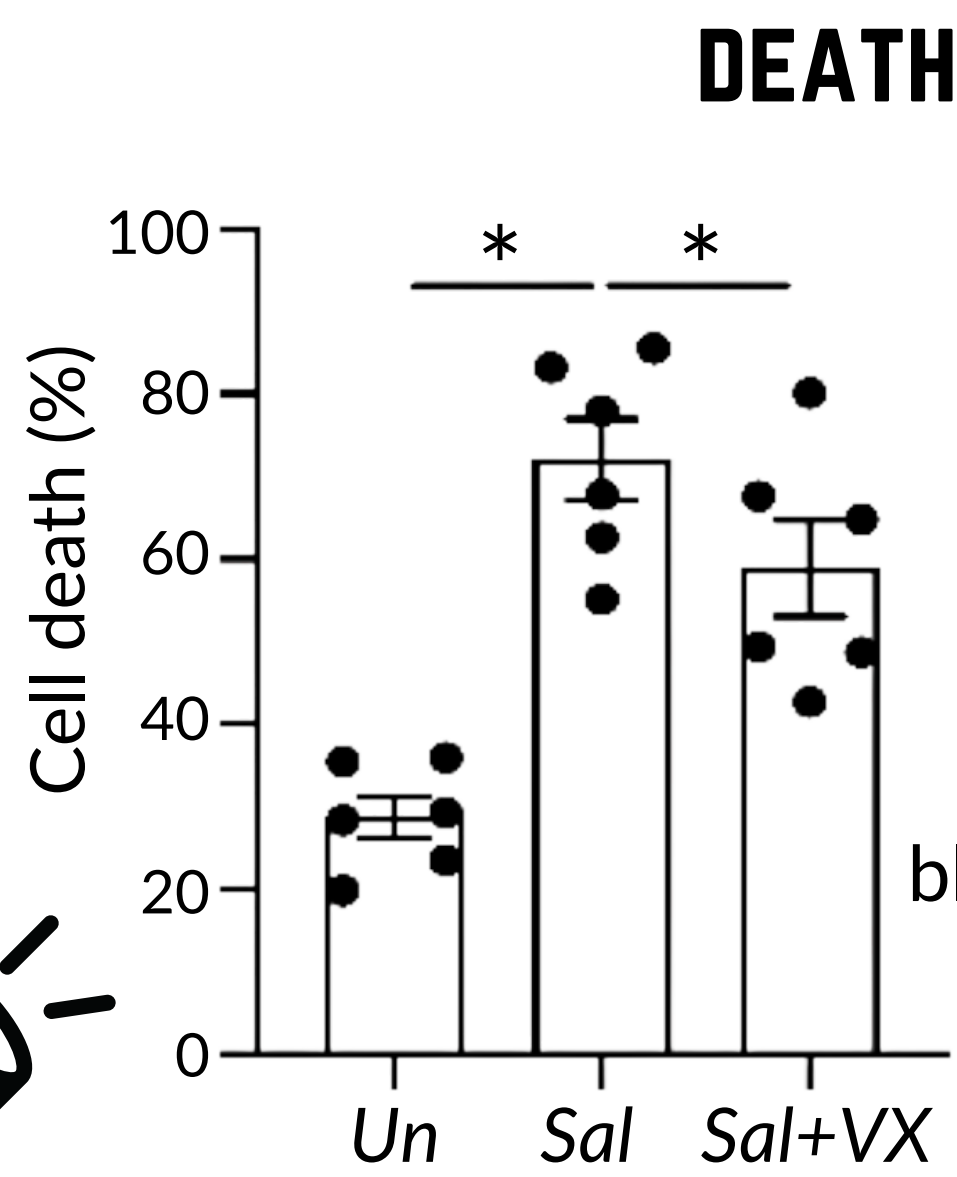
Microscopy: Are the bacteria inside the cells?

3

EVIDENCE 001: NON-CANONICAL INFLAMMASOME PROTEINS ARE PRESENT AND ACTIVATED



4 EVIDENCE 002: INFECTION WITH BACTERIA THAT LIVE INSIDE CELLS INCREASES CELL DEATH



Salmonella (Sal) is a bacterium that lives inside cells.

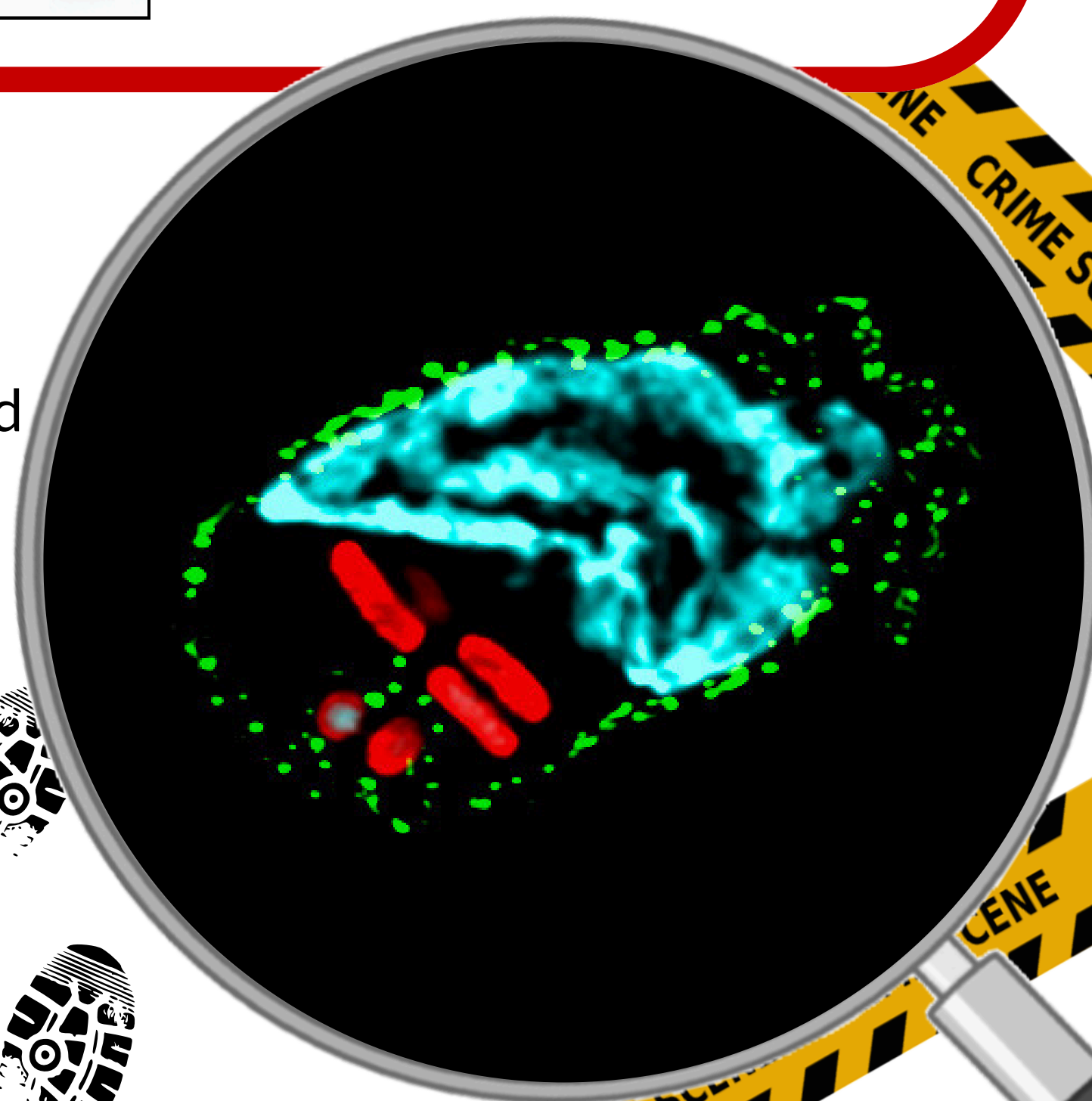
VX inhibits the inflammasome by blocking inflammasome proteins.

Salmonella infection increases inflammasome cell death in NK cells compared to the untreated (Un) controls.

5

EVIDENCE 003: MICROSCOPY

Human NK cells are infected with *Salmonella* (red)
Cell surface (green)
DNA (blue)



6

THE VERDICT

We find that the non-canonical inflammasome is guilty of causing inflammatory cell death in human NK cells. Future work will investigate changes in NK cells from patients with disease.