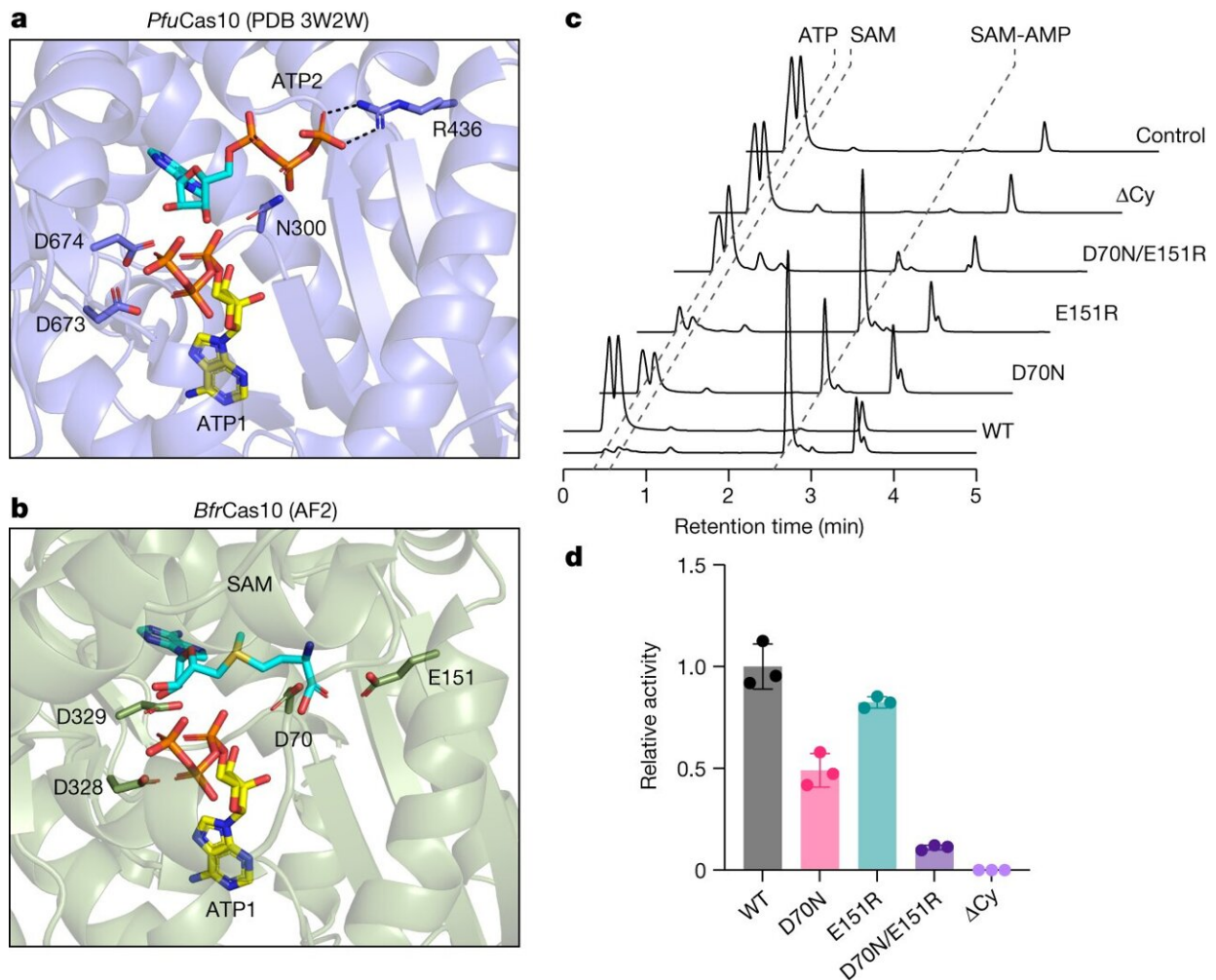


Scientists discover new molecule that combats viral infection in bacteria

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Changes in the active site of Cas10 during synthesis of SAM-AMP. a, The crystal structure of the *P. furiosus* (*Pfu*) Cas10 subunit with 2 bound ATP molecules. Side chains for the two metal binding aspartate residues of the DD motif, together with residues N300 and R436 that interact with ATP2, are

shown. b, Equivalent view of the AF2 model of the *B. fragilis* (Bfr) Cas10 structure with ATP1 from the *P. furiosus* Cas10 structure and ATP2 replaced by SAM. The precise conformation and position of SAM is unknown. The conserved acidic residues D70, E151, D328 and D329 are shown. c, In vitro SAM-AMP synthase activity of wild-type and variant *B. fragilis* Cmr, analyzed by HPLC following incubation of 2 μ M Cmr with 0.5 mM ATP and SAM for 30 min. d, Relative SAM-AMP synthase activity of Cmr variants. Three independent experiments; data are mean \pm s.d., calculated using GraphPad Prism 9. Credit: *Nature* (2023). DOI: 10.1038/s41586-023-06620-5

A Ph.D. researcher at the University of St Andrews studying microbes in the human gut has discovered a new molecule that acts as a "distress signal" when viruses are detected. The research is [published](#) in the journal *Nature*.

The discovery paves the way to a new class of bioactive molecules that could lead to drugs with applications in [human health](#) and antimicrobial therapy.

The community of microbes that inhabit the [human body](#) is known as the "microbiome." The health of the microbiome is crucial to our own well-being. Just like us, microbes are often infected by viruses and just like us they have immune systems to prevent viruses running amok in the population.

Haotian Chi, from the School of Biology, discovered [new molecule](#) SAM-AMP, previously unknown to science, which is made by joining two of the most widespread chemicals present in all living things, SAM and ATP, in a completely new way.



Credit: University of St Andrews

Once made, SAM-AMP causes pores in the [cell surface](#) to open, making cells leaky. This can lead to "altruistic suicide" of infected cells to protect neighbors from infection—a type of defense also seen in human cells.

Haotian Chi identified SAM-AMP while trying to understand how the cells' defense system worked. As it was new to science, this involved a lot of perseverance and detective work using a technique known as [mass spectrometry](#) to break the molecule into tiny pieces and then identifying

all the parts.

She said, "The existence of SAM-AMP was completely unexpected, showing us there is much we still don't understand about bacterial immune systems."

Professor Malcolm White, who led the research, said, "As viruses are constantly infecting bacteria, SAM-AMP is being made in all of us, every day. It will be fascinating to explore how it affects bacteria and whether our own cells can sense this distress signal too. Now that we know how to make this molecule, we can manipulate the component parts to generate a whole family of novel compounds with potential applications in biomedicine."

More information: Haotian Chi et al, Antiviral type III CRISPR signalling via conjugation of ATP and SAM, *Nature* (2023). [DOI: 10.1038/s41586-023-06620-5](https://doi.org/10.1038/s41586-023-06620-5)

Provided by University of St Andrews

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