Second DNA-sensing pathway in humans discovered

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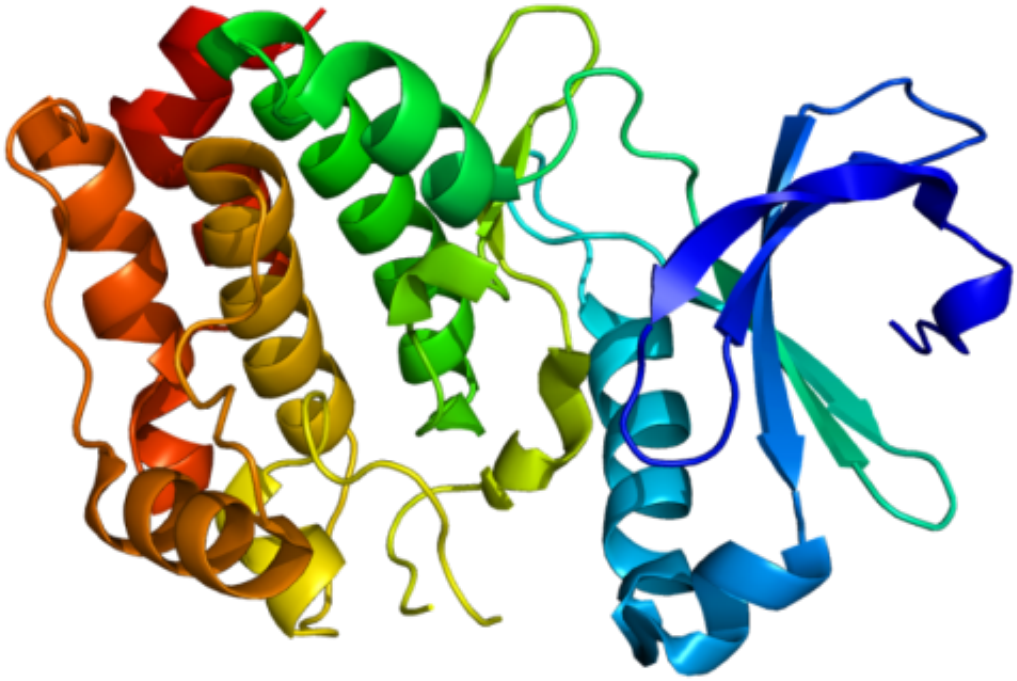

Structure of the Aurora A kinase protein. Based on PyMOL molecular visualization system rendering of Protein Data Bank (PDB) 1mq4. Credit: Created by Emw, Wikimedia CC BY-SA 3.0.

A team of researchers at Washington State University has discovered a second DNA-sensing pathway that initiates an antiviral response to foreign genetic material in human cells. In their paper published in the journal *Science Immunology*, the group describes their study of the

protein kinase and what they found.

Seven years ago, medical researchers found that a protein called stimulator of interferon genes (STING) could detect the presence of DNA in a foreign body—an indication of an infection. Once detected, a process was initiated that led to an immune response. A year later, researchers found that STING also responds to tumor cells. The discovery of STING led to research by pharmaceutical companies eager to develop drugs to fight off infections and to treat cancer patients —most of which was carried out on mice because STING operates in nearly the same way in the rodents. In this new effort, the researchers have found a second DNA-sensing pathway in humans called DNA protein kinase (DNA-PK) that could lead to changes in how DNA sensing pathway research is conducted because it is not present in mice.

The team describes their discovery of DNA-PK as accidental—they were studying STING responses to tumor-promoting viruses and were surprised to find an immune response even after disabling STING. A closer look showed that a different enzyme was behind the response—one that had been seen before but never identified as a primary DNA-sensing pathway. Researchers had studied the enzyme but had concluded that it was an offshoot of STING. The new research showed that it was independent of STING and also initiated antiviral responses differently. Both findings are likely to set off a host of research efforts both in the academic community and in pharmaceutical labs.

The researchers also found DNA-PK in other primates and rats but not in mice—a finding that could have a profound impact on the way DNA sensing research is conducted. Up until now, mice have played a central role in such research. They note that their findings could also have implications for research aimed at modulating innate immune responses in people with autoimmune diseases.

More information: Katelyn Burleigh et al. Human DNA-PK activates a STING-independent DNA sensing pathway, *Science Immunology* (2020). DOI: 10.1126/sciimmunol.aba4219