A switch for autoimmunity

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When a virus or bacteria comes calling, protein "sensors" in your cells can detect the invader's DNA and activate inflammatory responses to prevent infection. One such sensor is cGAS (cyclic GMP-AMP synthase).

Normally, cGAS is an asset – something you definitely want to be working for you. However, abnormal responses to intracellular DNA can lead to hyper-inflammatory or autoimmune disorders such as lupus. Turning cGAS off may actually help treat this disease.

Manuel Ascano Jr., Ph.D., and colleagues now report the discovery of a class of compounds that can inhibit cGAS. One "chemically improved" compound, RU.521, showed potent and selective inhibition of cGAS activity and lowered inflammatory signaling molecules in immune cells in a mouse model of an autoimmune disease.

Reporting Sept. 29 in the journal *Nature Communications*, the researchers concluded that RU.521 will help scientists learn more about the biological roles of cGAS and as a "molecular scaffold" may pave the way for development of future therapies for autoimmune disorders.

More information: Jessica Vincent et al. Small molecule inhibition of cGAS reduces interferon expression in primary macrophages from autoimmune mice, *Nature Communications* (2017). DOI: 10.1038/s41467-017-00833-9