3'2'-cGAMP is a novel nucleotide second messenger in *Drosophila melanogaster*

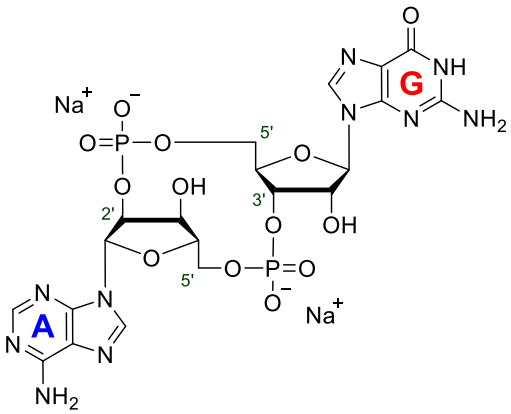
Kailey Slavik and Philip Kranzusch
Harvard Medical School
Dana-Farber Cancer Institute
Boston, MA - USA

Two recent studies reveal 3'-5' / 2'-5' cyclic GMP-AMP (3'2'-cGAMP, Biolog Cat. No. C 238) as a new nucleotide second messenger that controls immune activation in *Drosophila melanogaster* (1, 2).

In *Drosophila*, the enzyme cGAS-like Receptor 1 (cGLR1) functions as a pattern recognition receptor that senses foreign double-stranded RNA and synthesizes 3'2'-cGAMP to induce activation of the receptor STING and downstream NF-κB-dependent signaling. 3'2'-cGAMP more potently activates Drosophila STING than the human cGAS product 2'3'-cGAMP, and 3'2'-cGAMP is resistant to viral nucleases called poxins that degrade 2'3'-cGAMP and disrupt STING-dependent immunity.

3'2'-cGAMP has also been identified as a signaling product produced by the bacterial CD-NTase enzyme *Asticcacaulis sp.* CdnG (3), suggesting broad roles for 3'2'-cGAMP signaling pathways in nature.

Cat. No. C 238
3'2'-cGAMP /
c[A(2',5')pG(3',5')p] /
3',5'-2',5'-cGAMP



References:

1 Slavik, K.M.; Morehouse, B.R.; Ragucci, A.E.; Zhou, W.; Ai, X.; Chen, Y.; Li, L.; Wei, Z.; Bähre, H.; König M.; Seifert, R.; Lee, A.S.Y.; Cai, H.; Imler, J.L.; Kranzusch, P.J., *Nature*, **597**(7874), 109 - 113 (2021): "cGAS-Like Receptors Sense RNA and Control 3'2'-cGAMP Signalling in *Drosophila*"

2 Holleufer, A.; Winther, K.G.; Gad, H.H.; Ai, X.; Chen, Y.; Li, L.; Wei, Z.; Deng, H.; Liu, J.; Frederiksen, N.A.; Simonsen, B.; Andersen, L.L.; Kleigrewe, K.; Dalskov, L.; Pichlmair, A.; Cai, H.; Imler, J.L.; Hartmann, R., *Nature*, **597**(7874), 114 - 118 (2021): "Two cGAS-Like Receptors Induce Antiviral Immunity in *Drosophila*"

3 Fatma, S.; Chakravarti, A.; Zeng, X.; Huang, R.H.: "Molecular Mechanisms of the CdnG-Cap5 Antiphage Defense System Employing 3',2'-cGAMP as the Second Messenger", BioRxiv, doi: https://doi.org/10.1101/2021.08.31.458341

Copyright October 2021 by Biolog Life Science Institute