Review of: "[Review] Cyclic GMP-AMP synthase- Stimulator of Interferon Genes Signaling and their Agonistic / Antagonistic Values"

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Potential competing interests: No potential competing interests to declare.

Cyclic GMP-AMP synthase- Stimulator of Interferon Genes Signaling and their Agonistic / Antagonistic Values

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The manuscript by A.K., according to the statement in the title, should review the progress in the cGAS/STING pathways and, as understood by this reviewer, the potential benefits of activating or antagonizing this nucleic acid sensing pathway.

The manuscript summarizes many different observations, but it lacks a clear structure, so that it is difficult to read and understand. The reader bumps across many information, in some instances also contradictory ones, but no help is provided by the author to guide him through this confusing territory. It would definitively be very interesting if the author could suggest some hypothesis on the significance of the many existing DNA sensing pathways, their relation with and importance compared to the cGAS/STING pathway. Finally, I am convinced that the reader would really appreciate to learn about the progress of therapeutically targeting the different DNA sensors and which of these pathways hold the highest potential.

My suggestion would be to rewrite the manuscript, focussing the discussion around cGAS/STING, whilw systematically comparing it with other dsDNA sensors: starting from molecular mechanism and ending with therapeutic potential.

The author should also pay attention to many incorrect statements:

for example cGAS, the Cyclic GMP-AMP synthase is named cGAMP:…. *“Ablasser A et al. 2013, described the catalytic reaction of cGAMP (cGAS) in -vivo…”*.

Do *RRRs really activate STING*? cGAMP activates STING

Localization of *STING at the mitochondrial membrane* might just be an artifact of immunostaining or do data exit that show/suggest a specific function for STING at the mitochondrial membrane

4 DNAases are mentioned, but this reviewer could find three of them.