

Novel targets for treatment of autoimmune disease

Researchers at Hudson Institute of Medical Research are developing a molecular understanding of the cGAS-STING pathway and how it can be targeted for treatment of autoimmune disease.

Activation of the cGAS-STING pathway leads to the rapid stimulation of a potent inflammatory response, and has been implicated in autoimmune diseases such as systemic lupus erythematosus (SLE).

Summary

The cGAS-STING pathway is involved in the sensing of DNA within cells, which is a signal of cellular damage or infection. In response to this DNA signal, expression of inflammatory genes is triggered – leading either to senescence or to activation of the immune response and inflammation. However, aberrant, chronic activation of the cGAS-STING pathway has been linked with autoimmune diseases, such as systemic lupus erythematosus.

Blocking activation of the cGAS-STING pathway could be a target for treatment of autoimmune diseases like lupus. However, direct inhibition of cGAS or STING activation presents risk of systemic immunosuppressive functions, or effects on cellular capacity to enter senescence. To circumvent these risks, our team propose another route to modulating the cGAS-STING pathway.

Our team have identified novel cell:cell interactions that subsequently lead to pathway activation and a positive feedback loop that results in increased inflammation. They have demonstrated that blocking these interactions can stop this feedback loop and limit inflammation.

Their finding provides an opportunity to develop composition of matter targeted to this purpose, for the treatment of autoimmune diseases such as lupus.

Team

This project is led by Dr Michael Gantier PhD, ARC Future Fellow and head of the Nucleic Acids and Innate Immunity research group at Hudson Institute. Over the past decade, his work has contributed to our understanding of how cells selectively identify pathogenic RNA and toxic DNA; and more recently, how immune responses could be engaged in damaged cells, with implications in infection, immunity and cancer.

IP position

PCT application filed.

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