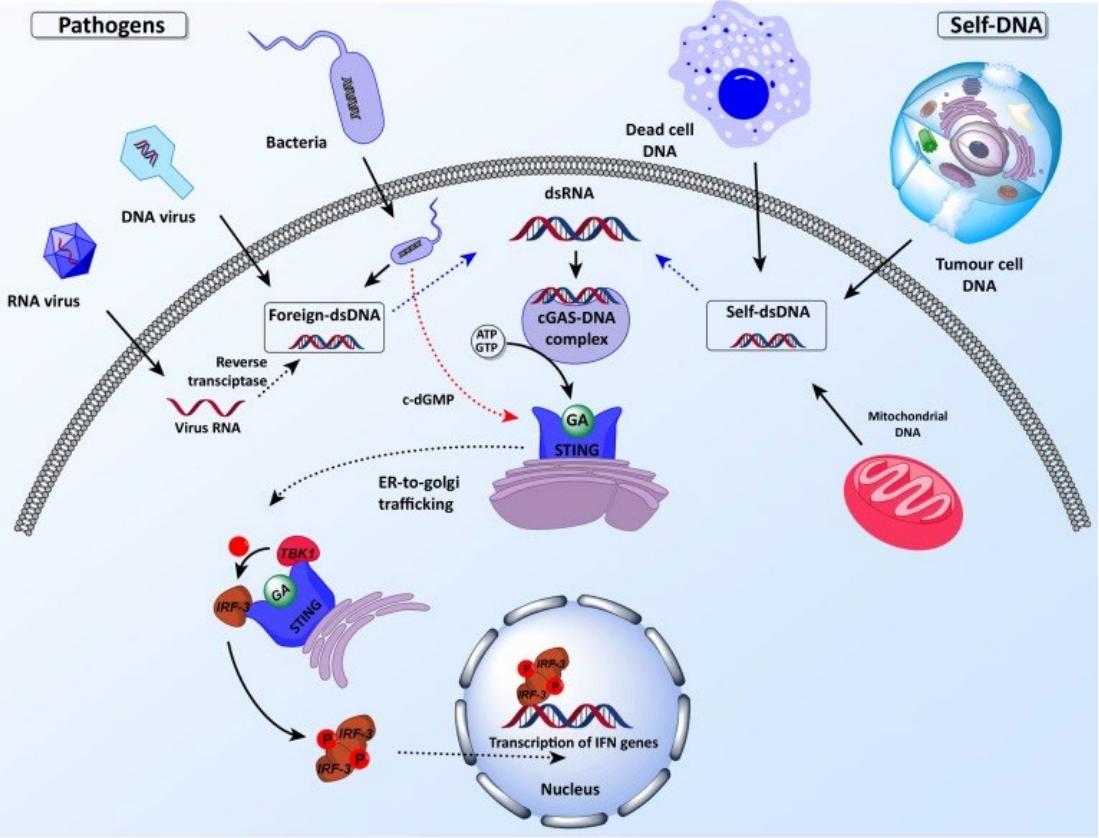
CD3 | CENTRE FOR DRUG DESIGN AND DISCOVERY

cGAS – STING antagonists for treating auto-immune disorders

cGAS-STING antagonists (type I interferonopathies)

BACKGROUND

- cGAS-STING is a cytosolic DNA sensor pathway which activates innate immune response (pathogens, tumor-derived DNA, self DNA)
- **Gain-Of-Function mutations cause rare type I IFN auto-immune disorders**.
- **Hyper-activation** of cGAS-STING in **more common type I interferonopathies** (Lupus, RA, …)
- **Emerging role in age-related disorders associated with chronic sensing of cytosolic DNA** (myocardial infarction, lung inflammation, neurodegeneration/neuro-inflammation, and tumorigenesis/metastasis)



Trends in Molecular Medicine

cGAS-STING antagonists (type I interferonopathies)

STATUS

- STING HTS performed
  - Initial hit compounds and analogs (re)tested → Selection of Hit series ongoing
  - Orthogonal confirmation studies ongoing

- cGAS
  - HTS finalised

→ Select most promising approach for H2L by Q3, 2019