Linking genome instability to innate immune activation

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Aicardi-Goutières syndrome (AGS) is a genetic mimic of congenital viral infections (CMV/Rubella/Zika). It provides a monogenic model of nucleic acid-mediated inflammation relevant to the pathogenesis of systemic autoimmunity. Mutations that impair ribonuclease (RNase) H2 enzyme function are the most frequent cause of this autoinflammatory disorder of childhood, and are also associated with systemic lupus erythematosus.

My lecture will describe our work over last decade - from identifying these genes RNase H2, implicating it as an essential genome stability enzyme, demonstrating its substrate, genome-embedded ribonucleotides

(rNs) to be the most common aberrant nucleotides in the mammalian genome and our work to link the resulting DNA damage to innate immune-mediated inflammation that drives the pathology in AGS.