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Investigation of the neuroinflammatory basis of human type I interferonopathies (Neuro-IFN)

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Aicardi-Goutières syndrome (AGS) is a childhood-onset brain disease. The associated neurological damage results from an inflammatory process involving the production of the major anti-viral cytokine, type I interferon. In normal circumstances interferon is produced following a viral infection. In AGS, however, a primary genetic defect leads to the accumulation of excess interferon, which causes brain dysfunction and possible permanent neurological damage. Given the severity of the condition there is an urgent need to develop new treatments for AGS. To do so, a better understanding of how the genetic changes responsible for AGS drive interferon production is essential.

Neuro-IFN will use the latest technologies to understand how brain cells are damaged by inflammation in AGS. We will study pathology samples from AGS patients, make use of state-of-the-art methods for creating 'brain cells' in a test-tube (derived from the cells of AGS patients), and analyse a mouse strain which has undergone changes in one of the AGS-related genes.

Although AGS is rare, the study of the genes and the proteins related to the disease has become highly important. The same molecules affecting AGS are also involved in the response to HIV-1 infection. There is also an overlap between AGS and so-called autoimmune diseases, a situation in which the body attacks itself. Our work, therefore, will not only be relevant to children and families directly affected by AGS, it may also have implications for a much wider set of human medical disorders.