Understanding the biology behind resurrection of anti-inflammatory gene IRGM

The group of Dr Santosh Chauhan at DBT's Institute of Life Sciences (ILS), Bhubaneswar, reported that Immunity-Related GTPase family M (IRGM) is a master suppressor of the inflammatory response, including the interferon response. For achieving this, IRGM utilizes a process called autophagy. Autophagy is a cell self-cleaning process that removes or degrades the old and worn-out organelles and proteins from the cells. Accumulation of dysfunctional organelles (or proteins) is toxic to the cells. For example, the accumulation of obsolete mitochondria may release toxic substances that can induce inflammatory signaling leading to cell death and tissue damage. Therefore, the removal of mitochondria by autophagy (called mitophagy) is an essential process to keep cells healthy. In addition, autophagy can selectively degrade certain proteins to control several cell biological processes. The IRGM suppresses inflammation by degrading the proteins involved in inducing inflammation and also, by removing worn-out mitochondria. Thus, IRGM maintains a healthy and non-inflammatory condition in the cell. Literature suggests that during the course of evolution, IRGM protein was present in mice and then remain dead (inactive) for 20 million years of evolution. It resurrected back in ancestors of human. A prominent role of IRGM in suppressing inflammation and autoimmune diseases presented by the group of Dr Chauhan, justify why IRGM protein, might have revived back. This study defines IRGM as a strong potential target for new therapeutic interventions against autoimmune diseases and viral diseases.

Overzealous inflammation plays a significant role in the pathogenesis and progression of several autoimmune and auto-inflammatory diseases. One of such inflammatory response is named as interferon (IFN) response. IFN response where one side is first-line of defense against pathogens (esp. viruses including SARS-COV2), on the other side, its uncontrolled activation can lead to several autoimmune diseases. The knowledge of the master switches and the mechanisms that can suppress the IFN responses will be beneficial for generating therapeutics against autoimmune and viral diseases. IRGM protein is genetically and functionally associated with several inflammatory and autoimmune diseases including ankylosing spondylitis, autoimmune thyroid diseases, Graves ' disease, Sjogren's syndrome, Crohn's disease, experimental autoimmune encephalomyelitis, hepatic steatosis, NAFLD and severe sepsis. The presence of IRGM in humans and mice is shown to be protective against the autoimmune disorders, however, how IRGM performs this function is not clear.

Link: http://www.scisoup.org/article/2020/biology-behind-resurrection-of-anti-inflammatory-IRGM-gene.html

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