MedicalXpress

FAMIN or feast? Newly discovered mechanism influences how immune cells 'eat' invaders

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A new mechanism that affects how our immune cells perform - and hence their ability to prevent disease - has been discovered by an international team of researchers led by Cambridge scientists.

To date, researchers have identified hundreds of genetic variants that increase or decrease the risk of developing diseases from cancer and diabetes to tuberculosis and mental health disorders. However, for the majority of such genes, scientists do not yet know how the variants contribute to disease - indeed, scientists do not even understand how many of the genes function.

One such gene is C13orf31, found on chromosome 13. Scientists have previously shown that variants of the gene in which a single nucleotide - the A, C, G and T of DNA - differs are associated with risk for the infectious disease leprosy, and for the chronic inflammatory diseases Crohn's disease and a form of childhood arthritis known as systemic juvenile idiopathic arthritis.

In a study published today in the journal *Nature Immunology* and led by the University of Cambridge, researchers studied how this gene works and have identified a new mechanism that drives energy metabolism in our immune cells. Immune cells help fight infection, but in some cases attack our own bodies, causing inflammatory disease.

Using mice in which the mouse equivalent of the C13orf31 gene had been altered, the team showed that the gene produces a protein that acts as a central regulator of the core metabolic functions in a specialist immune cell known as a macrophage (Greek for 'big eater'). These cells are so named for their ability to 'eat' invading organisms, breaking them down and preventing the infection from spreading. The protein, which the researchers named FAMIN (Fatty Acid Metabolic Immune Nexus), determines how much energy is available to the macrophages.

The researchers used a gene-editing tool known as CRISPR/Cas9, which acts like a biological 'cut and paste' tool, to edit a single nucleotide in the risk genes within the mouse's genome to show that even a tiny change to our genetic makeup could have a profound effect, making the mice more susceptible to sepsis (blood poisoning). This showed that FAMIN influences the cell's ability to perform its normal function, controlling its capacity to kill bacteria and release molecules known as 'mediators' that trigger an inflammatory response, a key part of fighting infection and repairing damage in the body.

Professor Arthur Kaser from the Department of Medicine at the University of Cambridge, who led the research, says: "By taking a disease risk gene whose role was completely unknown and studying its function down to the level of a single nucleotide, we've discovered an entirely new and important mechanism that affects our immune system's ability to carry out its role as the body's defence mechanism."

Dr Zaeem Cader, the study's first author, adds: "Although it's too early to say how this discovery might influence new treatments, genetics can provide invaluable insights that might help in identifying potential drug targets for so-called precision medicines, tailored to an individual's genetic make-up."

More information: Cader, MZ et al. C13orf31 (FAMIN) is a central

regulator of immunometabolic function. *Nature Immunology*; 1 Aug 2016; DOI: 10.1038/ni.3532