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Scientists discover special class of natural fats stimulates immune cells to fight diseases

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An international research team led by scientists from Singapore Immunology Network (SIgN) under the Agency of Science, Technology and Research (A*STAR) discovered that a special class of fatty molecules is essential for activating a unique group of early-responding immune cells. This study sheds light on how recognition of fatty molecules by immune cells could protect from infection, allergic reactions, autoimmune diseases and cancer. More importantly, it offers new opportunities to exploit the use of these stimulatory fatty molecules in therapeutic interventions, such as the development of new vaccines and drugs targetted for autoimmune diseases.

The early-responding immune cells investigated in this study, called the invariant natural killer T (iNKT) cells, are important as first line of defence against infectious and foreign agents. When stimulated, iNKT cells secrete large amounts of biological chemicals, and are capable of influencing the responses of other immune cells in the body.

It is well established that iNKT cells recognise and are activated by fatty molecules from various sources, including those from diseases-causing bacteria and those that are naturally produced in the thymus. This study identifies for the first time, the actual type of fatty molecules that stimulates the development of iNKT cells in the thymus. This discovery came about through systematic biochemical and structural analysis of fatty molecules extracted from the thymus.

The team, co-led by Professor Gennaro De Libero and Dr Lucia Mori,

Senior Principal Investigators at SIgN, found that the fatty molecules produced in the thymus which were able to stimulate iNKT cells all have the chemical linkage called ether bonds.

To validate the stimulatory activity of these special class of self-generated fatty molecules, the scientists artificially manufactured ether-bonded fatty molecules through synthetic chemistry, and found that they were similarly able to activate iNKT cells, promoting their development in the thymus.

In addition, the scientists uncovered that these ether-bonded fats were the same type of fatty molecules which are produced by the peroxisome, a sub-compartment that specialises in fat metabolism, found within all cells of the body. Using a mouse strain that is lacking in the peroxisomal enzyme, and hence unable to make ether-bonded fatty molecules, the scientists found that such mice could not produce the complete repertoire of fully functional iNKT cells.

Dr Mori said, "We are very excited to have identified the type of fatty self-molecules that stimulates T cells. This discovery sets a new paradigm for understanding the rules that govern development and activation of frontline immune cells of the body."

Professor De Libero added, "With fresh insights from this study, we now have new tools to explore novel therapeutic strategies for autoimmune and inflammatory diseases where such fatty molecules are key to disease development."

Scientific Director of SIgN, Professor Paola Castagnoli said, "Our focus and mission at SIgN has always been to study human immunology, in particular the underlying mechanisms of inflammatory responses in human diseases. This discovery is a breakthrough for the field of lipid immunity, a new niche area in immunology that SIgN has recently been

developing. I would like to congratulate Gennaro and Lucia for this excellent piece of work that has done SIgN, A*STAR proud at the international scientific level. I am confident that with more in-depth understanding of the role of lipid immunity in human diseases, we will find novel ways to cure many types of immune diseases, from autoimmune to infectious diseases, for the benefit of patients in the future"

Provided by Agency for Science, Technology and Research (A*STAR)