Researchers create 'lipidomic map,' offering insights into immunology

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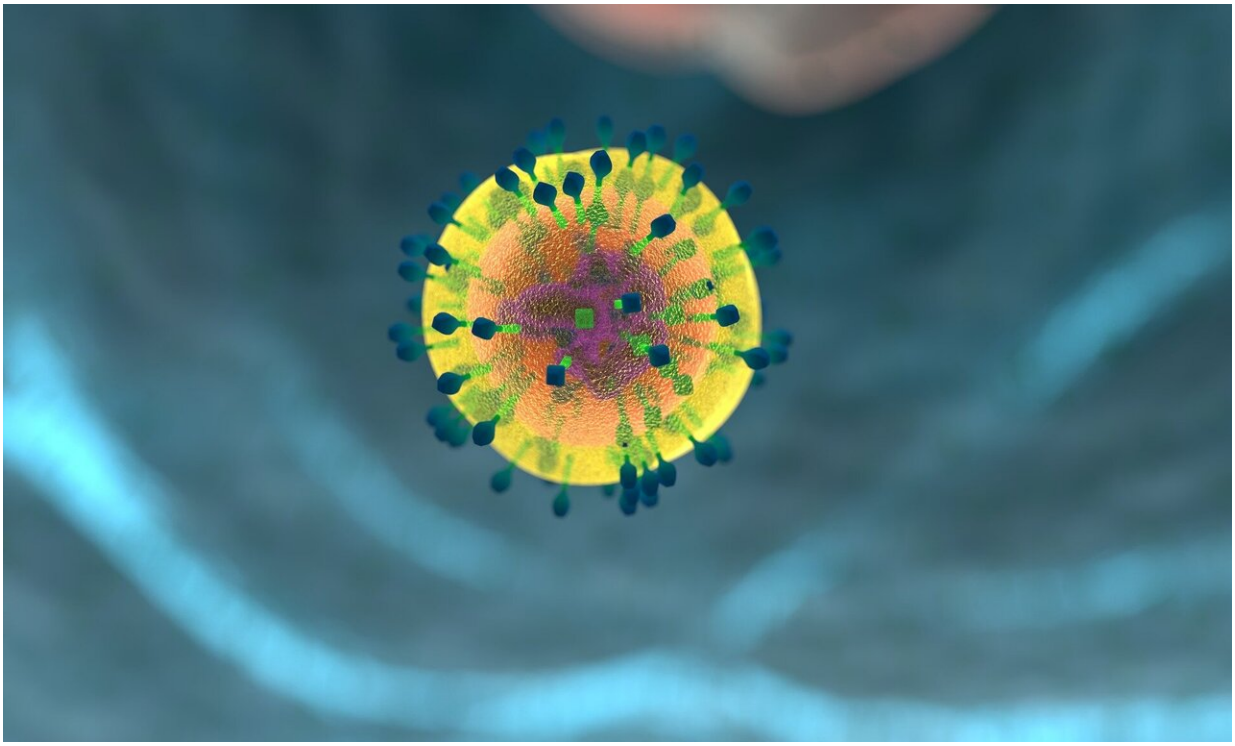

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An international team of scientists has developed a method for simultaneously detecting thousands of lipid molecules that are displayed to T cells in the human immune system.

The study, co-led by D. Branch Moody, MD, of the Division of

Rheumatology, Immunity and Inflammation at Brigham and Women's Hospital, a founding member of the Mass General Brigham health care system, represents a collaboration among researchers from Oxford, United Kingdom, Melbourne, Australia and Groningen, Netherlands. Results are published in *Cancer Cell*.

The team developed a new and sensitive method to detect more than 2,000 lipids bound to CD1 antigen-presenting molecules, which display antigens to the human immune system. While scientists have long known that T cells recognize antigens, until the 1990s, it was thought that these antigens were always peptides derived from proteins.

Because lipids are not encoded by genes and are instead made by enzymes and form into membranes, they have entirely different functions and positions in the cell. The ability to measure many lipid antigens at one time will allow future researchers to cross-check any disease-related lipid of interest to the list of candidate lipid antigens from this map and potentially make connections to diseases.

Their efforts yielded the first integrated CD1 lipidomic map, which could help guide the investigation and discovery of lipid blockers and antigens for T cells and support the view that lipids normally influence immune responses.

The research builds on earlier methods that separate cellular lipids in one chromatographic system, which provided only a limited perspective. The new structural biology work, undertaken in the lab of Jamie Rossjohn, Ph.D., FRS, showed how lipids fit inside proteins using size-based mechanisms. Combined, the structures and biochemistry detail rules about the size, shape, and chemical content of the kinds of lipids that can bind CD1 and cause a T cell response—either activation or deactivation. It is the latest in a series of studies that date back to the 1990s, when Brigham scientists discovered that T cells can recognize lipid antigens.

"I applaud the tenacity of the researchers for building the critical mass of technology needed to develop this multi-stage system that allows large numbers of lipids to be identified, solved individually, and then grouped in patterns," said Moody.

"The Brigham provides an environment where physicians and scientists from differing fields can collaborate. This multidisciplinary effort involved biophysical techniques related to mass spectrometry and biological techniques related to lipid chemistry. The lipids informed immunological outputs, and the mode of lipid recognition is proven through X-ray crystallography."

More information: Catherine J Wu, ZNF683 marks a CD8+ T cell population associated with anti-tumor immunity following anti-PD-1 therapy for Richter syndrome, *Cancer Cell* (2023). DOI: 10.1016/j.ccell.2023.08.013. www.cell.com/cancer-cell/fullt … 1535-6108(23)00306-9

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