Characterization of innate lymphoid cells with an advanced cytometric technique yields surprising insights

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From left to right: Michael Fehlings, Yannick Simoni, Evan Newell. Credit: A*STAR Singapore Immunology Network

A family of cells key to the immune system's frontline defenses has been described in greater detail than ever before. A*STAR researchers hope their analysis will help those seeking to target them to treat disease.

Innate lymphoid cells (ILCs) are a class of immune cells which include natural killer (NK) cells, which target tumor and virally-infected cells, and non-cytotoxic, helper-type ILC1s, ILC2s and ILC3s.

Research groups have defined and sub-divided ILCs in various ways, partly because of technical limitations, and because much of the work has been done on mouse cells.

Yannick Simoni and Evan Newell of the A*STAR Singapore Immunology Network used a more advanced technique to profile the ILCs in a range of human tissue types in greater detail than previously possible.

Other groups have studied ILCs using a technique called flow cytometry. This involves labeling cell parts with fluorescent tags and observing variations in light they emit under a laser beam.

Instead, Newell's team used mass cytometry in which single-isotope heavy metals are used to tag cells that are then ionized with inductively charged plasma. A mass spectrometer is used to identify and quantify cell components. The technique offers more detailed and accurate analysis.

The group measured levels of surface markers and transcription factors in nine different healthy tissues, lung and colorectal tumor samples, and diseased adipose tissue.

Newell explained they were surprised not to find any ILC1 cells at all, and speculated that those previously identified by others to be ILC1 cells could in fact be T cells or other immune cells in contaminated samples.

For instance, a 2013 study described cells within the surface layer of mucosal tissue called intraepithelial ILC1s. Yet Newell's team found cells with similar properties in non-mucosal tissue in their diseased samples, and defined them as NK cells.

Their results highlight the inadequacy of current definitions of ILC2s

and ILC3s based solely on the presence of certain transcription factors. Overall, the group found high levels of ILC heterogeneity between different individuals and tissues and proposed new ways to describe and identify them.

ILCs have been identified by others as possible mediators of inflammatory bowel disease and obesity, leading to the possibility of developing new treatments for these conditions.

"We hope those seeking to target ILCs pharmacologically can use our work to better understand which tissues to find them in and what types of variation they might have to deal with," says Newell.

More information: Yannick Simoni et al. Human Innate Lymphoid Cell Subsets Possess Tissue-Type Based Heterogeneity in Phenotype and Frequency, *Immunity* (2017). DOI: 10.1016/j.immuni.2016.11.005

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