A new technique dramatically enhances profiling and classification of cells involved in innate immunity

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A*STAR researchers used an algorithm to map 38-dimensional phenotypic profiles of myeloid cells derived from eight different mice tissues. Each dot represents an individual cell; cells close to each other have similar properties and cells with less similar characteristics are plotted further from each other. The colors roughly represent cell types: neutrophils (green), monocytes (blue), macrophages (orange), dendritic cells (red) and innate lymphocytes (black). Credit: A*STAR Singapore Immunology Network

A new method developed by A*STAR researchers to comprehensively quantify and classify mouse cells responsible for detecting pathogens invading the body could revolutionize our ability to study innate immunity and inflammatory diseases.

Myeloid cells are the first line of defense against disease as they detect pathogens and then trigger immune responses. Until now, however, analysis of the myeloid system had been limited, because previous analysis techniques did not fully account for the high complexity of myeloid cells.

"The problem with myeloid cell types is that everyone has a different way of classifying them, and these classifications can be difficult to reconcile," explains Evan Newell, one of the A*STAR Singapore Immunology Network researchers who worked on the project with other scientists in Singapore and Switzerland. "This new analysis will help people speak the same language when referring to different types of mouse myeloid cells."

Existing methods for analyzing myeloid cells rely on traditional markers and historical naming systems. These are problematic, not least because some cell subpopulations do not express the markers and inflammation can cause phenotypic changes, which are not picked up by traditional techniques.

The new method uses mass cytometry coupled with machine learning technology to map the myeloid system of mice (see image). "Mass cytometry works by tagging cellular probes with heavy metal elements," says Newell. "The probes are usually antibodies and can be used to quantify the abundance of proteins present in cells."

Crucially, mass cytometry has more available tags than other methods, reducing the likelihood that tags will bind to more than one cell component. This allows more detail about individual cells to be uncovered.

A key concern for the researchers was limiting 'batch effects'—problems arising from analyzing many different samples on different days. Mass

cytometry allowed the team to run all their samples simultaneously, enabling them to examine as many as eight tissue samples from up to six different mice in parallel. The researchers then used machine learning approaches to interpret the results and identify different cell types.

"This approach gives a complete snapshot of the myeloid composition of each individual tissue, and hopefully differences between experimental settings or mouse genetics will not be overlooked," explains Newell. "The approach is useful for analyzing blood and tissue from mice or humans."

The technique will allow detailed profiling of human myeloid cells and help uncover how innate immune cells behave in a wide range of diseases.

More information: "High-dimensional analysis of the murine myeloid cell system." *Nature Immunology* 15, 1181–1189 (2014). dx.doi.org/10.1038/ni.3006

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