Resolving the heterogeneity of human circulating innate lymphoid cells via simultaneous, high-dimensional analysis of protein and gene expression.

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Cancer treatment has been revolutionized with the development of immunomodulatory therapies. These therapies have primarily focused on enhancing T-cell responses: whether it is unleashing T cells through blockade of regulatory checkpoint inhibitors or generation of chimeric antigen receptor (CAR) T cells. However, there has been recent interest in harnessing the immunotherapeutic potential of other cytotoxic cells such as Natural Killer (NK) cells. Similar to NK cells, innate lymphoid cells (ILCs) may offer another target of these immunotherapy approaches. Before the potential of these cells can be realized, there is a need for better understanding of these recently described cell populations. ILCs act as the immune system's first responders and have been shown to play a key role in tissue homeostasis, chronic inflammation and cancer. Three main groups of non-cytotoxic ILCs (ILC1, ILC2 and ILC3) have been broadly defined based on developmental trajectories and function, driven by expression of specific transcription factors. Deeper characterization of these cells through either high parameter protein analysis or single cell RNA sequencing has revealed a more complex and heterogeneous nature of ILCs across different tissues and donors. Therefore, the identity of ILCs is still elusive and controversial.

In this study, we developed a comprehensive approach to further refine the signatures of human circulating ILC subsets. Total ILCs (Lineage- CD127+ cells) were enriched from 4 normal donors by flow sorting using the BD FACSAria™ Fusion cell sorter and processed for downstream single-cell multiomic characterization. BD® AbSeq reagents and a targeted BD Rhapsody™ Immune Response Panel were used to enable simultaneous detection of 42 proteins and 399 genes using the BD Rhapsody™ Single-Cell Analysis System. Differential protein and gene expression analysis in addition to combinatorial expression of CD294 and CD117 confirmed 3 conventional ILC populations as well as the signatures of three distinct subsets within ILC1. This discovery approach provided information about relative expression of a small selection of proteins or surface marker-coding genes that enable the discrimination of these ILC subsets. These data were used to design high-parameter flow cytometry panels for high-throughput analysis of different healthy donors. ILC subsets differentially distributed across donors were detected and defined using unsupervised computational analysis confirming the result of multiomic analysis.

Biography

Christian Aguilera-Sandoval has a passion for immunology and analysis—after obtaining his Ph.D. in Immunology from UCLA and a productive immunology post-doctorate at UNC-Chapel Hill focusing in immunotherapy testing and development in, In Vivo models, he continues building his career helping researchers ask and answer the difficult questions through flow cytometry and multiomics. Currently, a Scientific Advisor with BD, focusing on providing scientific advice to Fortune 500 companies, fostering strong networks to facilitate and streamline the discovery process and to present/publish current scientific breakthroughs achieved in High Dimensional Biology through the partnership of KOLs in immunology, Immuno-oncology, and immunotherapy.

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