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ImmGenMaps, an open-source cartography of the immune system

The Immunological Genome Project Consortium (ImmGen) is announcing the launch of ImmGenMaps (https://www.immgen.org/ImmGenMaps/), a project designed to spatially profile every immune cell across the mouse anatomy. This community project builds upon the bulk and single-cell profiling efforts of ImmGen to characterize the genetic regulation of all cells of the mouse immune system. Using state-of-the-art spatial transcriptomics technology, ImmGenMaps goes one step further by profiling immune cells within their natural environments across all major organs, at baseline or under challenge. In addition to capturing transcriptional profiles and a subset of landmark protein markers of immunocytes, ImmGenMaps will also profile non-immune cells (stroma, epithelia, connective tissue), whose key roles in orchestrating immune function is increasingly recognized. By capturing the pieces of the immune game (immune cells) and the playing board (tissue structures and non-immune cells), and determining the rules that govern the immune game (environmental signals and cellular interactions), we expect to provide a key resource to the scientific community. In line with ImmGen's previous 'OpenSource' projects[1,2], the intent is to leverage the broader community's expertise by welcoming the participation of immunology and computational biology labs beyond the core ImmGen membership.

ImmGenMaps aims to broach several initial questions aimed at deepening our understanding of cellular dynamics across tissues. It seeks to profile the frequency of all immune and non-immune cell types, including those, like granulocytes, that are typically lost during tissue dissociation-based profiling. In addition, the project aims to define discrete cellular niches, spatial domains and the relevant gradients of organ function, while also unraveling the connectivity between immune cells and their surrounding cells. Further objectives include mapping the sources of key signals — such as chemokines and cytokines — in both health and disease, assessing the link between cellular location and phenotype, and conducting a rigorous evaluation of how cell types and phenotypes correlate with tissue type and location.

Although the spatial transcriptomics approach has been around for a few years, the development and commercialization of technologies that can simultaneously measure thousands of genes at single-cell resolution has provided a breakthrough in our ability to probe complex gene programs in situ[3]. The advantages of these single-cell technologies compared with single-cell transcriptomics approaches (such as single-cell RNA sequencing) that require tissue dissociation include retention of the original spatial context, creation of minimal perturbations to the normal functioning of cells, rich optical profiling of cell shapes and cellular contacts, and the potential to be combined with the profiling of proteomes, metabolomes and other layers of biological information. At the same time, spatial transcriptomics still has several incompletely resolved issues: non-standardized tissue processing, cell segmentation inaccuracies, signal sparsity and targeted gene panels not covering the full transcriptome. Thus, we expect that the scope of ImmGenMaps will feed technological and computational progress and that it will serve as a complement to more classic profiling technologies that ImmGen uses.

The potential of these technologies to generate new insights is fueling the generation of other spatial atlases, such as the Brain Map initiative (https://portal.brain-map.org/) led by the Allen Institute or the Spatiotemporal Omics Consortium (https://sto-consortium.org). To enable interoperability with other initiatives, all datasets will be processed following a unified spatial omics analysis pipeline that considers the latest advances and guidelines developed by the community[4]. ImmGenMaps will utilize an optically read spatial transcriptomics platform, the Xenium Analyzer (commercialized by 10x Genomics), to capture the expression of 5,106 genes, 100 of which have been expertly curated to enhance the detection and profiling of subsets and states of immunocytes. Importantly, spatial transcriptomics profiling with Xenium is compatible with formalin-fixed paraffin-embedded samples and provides enough tissue coverage to profile entire mouse organs. The transcriptome profiling, centralized at the Broad Institute, will be complemented by 15 protein stains using the Orion Microscope (RareCyte), as well as hematoxylin and eosin, performed on the same tissue sections after Xenium at the La Jolla Institute for Immunology. Obtaining protein information for a highly curated selection of protein markers will support accurate cell type detection and aid in cell segmentation approaches.

The first phase of ImmGenMaps will generate a comprehensive survey of healthy tissues to be used as a baseline. To do this, we will generate high-quality spatial transcriptomics datasets for 26 organs at homeostasis for male and female mice. The second phase of the project will map immune responses to immune challenges such as infection, cancer, allergy and autoimmunity. These perturbations represent clinically relevant disease settings with pressing unmet needs. To this end, ImmGenMap participating labs will be organized in focus groups around particular tissues or cell types to design and execute experiments, and prepare samples strictly following shared standard operating procedures and standards.

ImmGen's OpenSource collaborative format hopes to tap into the decades-long experience of participants across the globe to design and execute this comprehensive immune cartography project. As usual, participants who contribute to the entire resource are also free to use their data for their own purposes. Do you want to participate? Do you have unique experimental models, or specialized histopathological expertise, or are you interested in novel computational strategies for data integration and data visualization strategies? Expressions of interest and proposed experiments should be entered via the form available on the project website (https://www.immgen.org/ImmGenMaps/contact).

With ImmGenMaps, we aim to provide a usable and expandable resource that offers highly curated, free-to-use data, accessible

computational frameworks, and visualization tools for studying and exploring immune cell populations within tissues. Ultimately, our goal is to create a foundational dataset that will underpin further studies and enhance our understanding of immunological processes.

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Competing interests

The authors declare no competing interests.

Additional information

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