Online resources from the Allen Institute for Immunology: longitudinal profiling of multiple myeloma treatment and the Human Immune System Explorer platform

Abstract No. 1071

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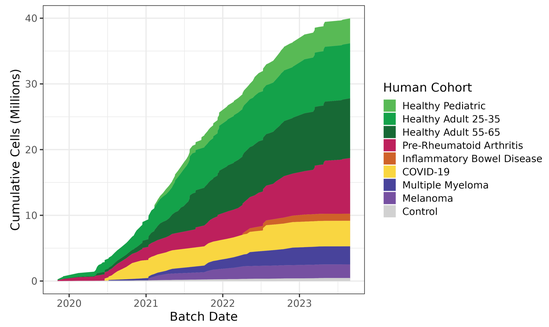
We have *a lot* of data from human cohorts

We developed high throughput, high quality, multimodal pipelines to deeply profile the peripheral immune system. Over the last 5 years, we've brought this scale and quality to 8 human health and disease cohorts.



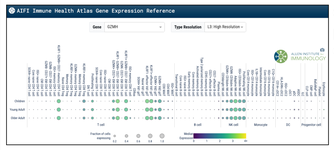
Totals from our scRNA-seq Pipelines as of August 22, 2024:

460 subjects **2,302 samples** **55,519,418 single cells**

Now, we're completing initial studies and working towards releasing this trove of high quality data to the scientific community.

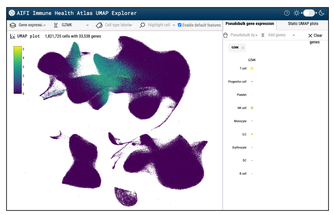
A suite of rich exploration tools

To support the release of our ***Immune Health Atlas***, we built tools to enable scientists to refer to and explore this resource generated from 108 healthy subjects from 11 to 65 years old.

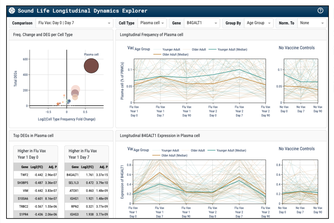


Quickly see which PMBC populations express a gene with our **Gene Expression Reference**.

Explore cell type annotations and gene expression with our dynamic **UMAP Explorer** which interactively displays **> 1.8 million single cells**.



Our ***Dynamics of Immune Health and Age*** project explores how age, CMV infection, and flu vaccine responses alter our peripheral immune cells. To elucidate these dynamic changes over time, we developed visualization tools that chart longitudinal and pairwise changes found in our dataset from 96 healthy adults, with 868 samples and **> 13.7 million single cells**.



Longitudinal Dynamics Viewer enables visualization of changes to population frequency and gene expression over time and in response to flu vaccination.

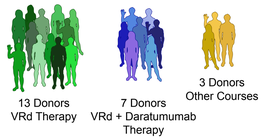
Differential Gene Explorer displays specific comparisons related to CMV infection status, age group, and biological sex, and enables exploration of changes to specific genes.

Connecting induction and ASCT through longitudinal deep immune profiling

In collaboration with the Fred Hutchinson Cancer Center, we followed a cohort of Newly Diagnosed Multiple Myeloma (NDMM) patients over the course of induction therapy, autologous stem cell transplant (ASCT), and Post-ASCT recovery for up to 2 years, obtaining peripheral blood, plasma, and bone marrow biopsies.

Fred Hutch Cancer Center

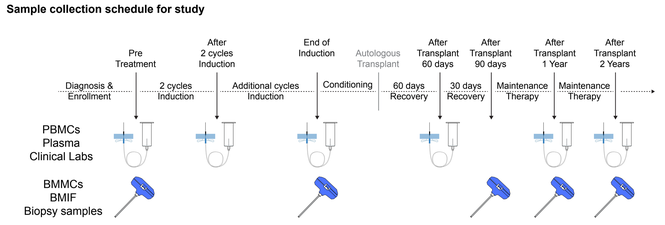
NDMM therapy administration, cohort recruitment, and sample collection



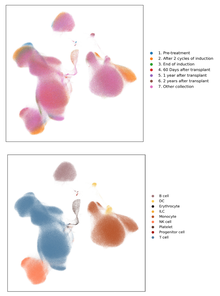
Plasma and bone marrow interstitial fluid (BMIF) were profiled using the Olink Proteomics platform.

Peripheral blood mononuclear cells (PBMCs) and Bone marrow mononuclear cells were profiled using Flow Cytometry, scRNA-seq, and CITE-seq.

Sample collection schedule for study



scRNA-seq of 1.7M PBMCs from 131 samples

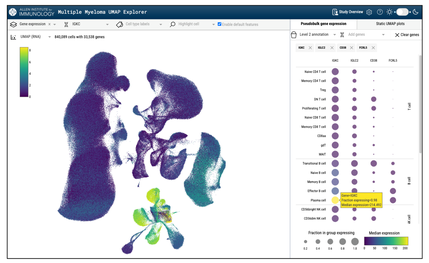


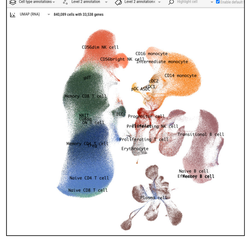
Interactive tools for NDMM treatment course analysis

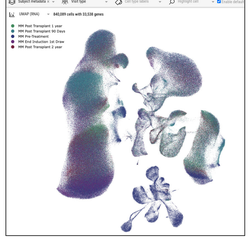
To enable exploration of our BMMC CITE-seq data, we developed a UMAP explorer that displays **> 800,000 BMMCs** across treatment and transplant.

Right: Individual gene expression can be viewed, along with summaries of expression per cell type.

Below: Metadata related to cell type labels, longitudinal visits, and other subject and sample metadata can be easily visualized.





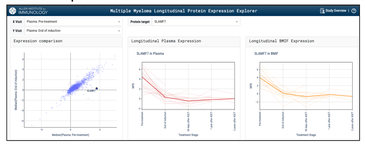


Protein profiling from both plasma and bone marrow interstitial fluid (BMIF) enable investigation of cross-tissue and longitudinal patterns of protein expression.

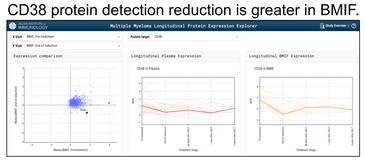
We developed an interactive viewer to enable rapid comparison and plotting of our protein expression data.

Right: Several examples of expression patterns identified across plasma and BMIF are displayed, including critical tumor cell markers and drug targets.

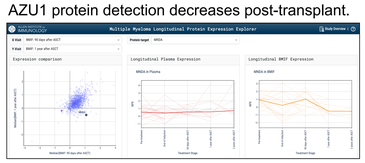
SLAMF7 protein detection is reduced after induction.



CD38 protein detection reduction is greater in BMIF.

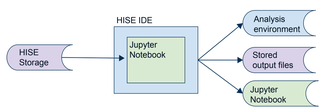


AZU1 protein detection decreases post-transplant.



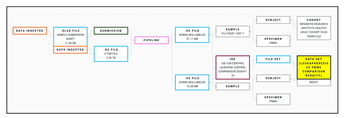
Proactive tracing to ensure reproducibility

The Human Immune System Explorer (HISE) platform was developed from conception to proactively track our analyses, from raw data to published results, using the **Certificate of Reproducibility** framework. This enables inspection and interactive re-analysis by anyone, whether you're at the Allen Institute or an external user. Additional details are available in our publication in Royal Society Open Science.



Left: The anatomy of a proactively traced analysis step in the HISE platform. Storage of not only the data and code, but also the *exact analysis environment* used, ensures reproducibility.

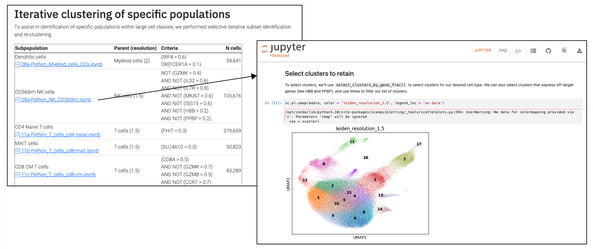
Right: An example Certificate of Reproducibility for a simple analysis step to generate a result that can be shared online.



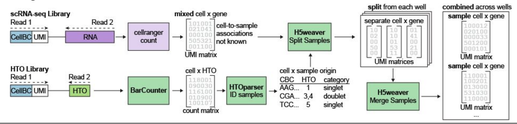
Meijer P, Howard N, Liang J, Kelsey A, Subramanian S, Johnson E, *et al*. Provide proactive reproducible analysis transparency with every publication. R Soc Open Sci. 2025;12: 241936. doi:10.1098/rsos.241936
tinyurl.com/repro-article

Direct connection to analysis methods

In addition to the Certificate of Reproducibility framework, the rich descriptive context we can supply through our Data Apps websites enables us to connect readers *directly with the exact analysis code* that they're reading about so we can go beyond the Methods Section to reveal exactly how analysis was done.



We're also releasing all of the code and tools from our high-throughput pipelines so that external scientists can utilize the same methods we did for generating our large-scale data resources.



Where to learn more at AACR

Advancing multiple myeloma research: patient-derived 3D Organ-on-a-Chip models to reveal immunological mechanisms influencing cancer growth and resistance

Abstract No: **3970**
Presented by: **Medbh Dillon**
Tuesday, 9 AM - Noon
Poster Section: **6** | Board Number: **14**

Longitudinal Analysis of Multiple Myeloma: Therapeutic Response and Immune Microenvironment Dynamics in the Context of Tumor Heterogeneity

Abstract No: **4540**
Presented by: **Imran McGrath**
Tuesday, 9 AM - Noon
Poster Section: **28** | Board Number: **11**

For additional information, links to relevant web resources, and access to **special previews of our interactive visualizations** for AACR 2025, visit our conference landing page at:

tinyurl.com/allen-aacr-2025

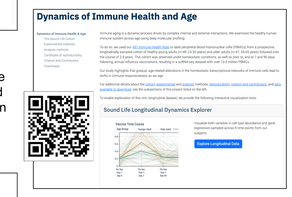
Public resources available now

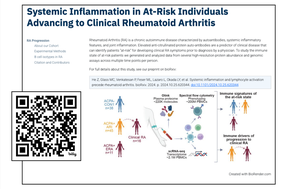
Our first HISE Data Apps are available now. These focus on the release of deeply characterized and longitudinally profiled healthy peripheral immune cells and progression to rheumatoid arthritis:

An atlas of PBMC populations from 108 pediatric, young adult, and older adult healthy subjects

Interactive tools and cell type labeling models

Longitudinal profiling and extensive analyses of changes over time and across age, sex, and CMV infection in healthy subjects





Subjects at-risk for rheumatoid arthritis (RA) were longitudinally profiled over two years.

~30% of subjects developed clinical symptoms of RA. Comparisons between subjects with progressive RA to non-progressive at-risk subjects, early RA, and healthy controls characterize progression in at-risk patients.

In total, we're releasing scRNA-seq data from **~16 million** peripheral blood mononuclear cells, along with extensive documentation and visualizations.

Watch us grow at ***explore.allenimmunology.org***

Acknowledgments

All sample and data collection from NDMM patients were performed under the Fred Hutchinson Cancer Center IRB protocol #10265.

With thanks to the patients and clinical staff at the Fred Hutchinson Cancer Center that have contributed samples and managed patient enrollment and sample collection for study.

We wish to thank the Allen Institute founder, Paul G. Allen, for his vision, encouragement, and support.