The Human BioMolecular Atlas Project "HuBMAP"

Robert Carter, MD, NIAMS

on behalf of the trans-NIH HuBMAP WG

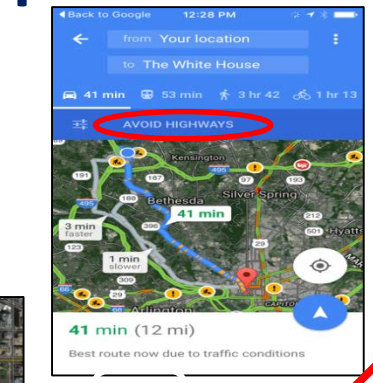
HuBMAP NIH Working Group

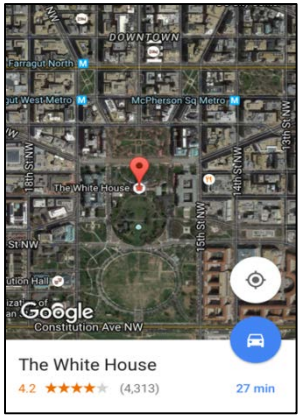
- **Common Fund Program Lead:** Ananda Roy, Ph.D. Office of Strategic Coordination (OSC)

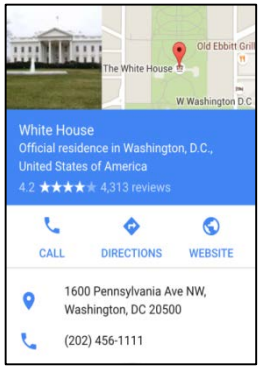
Members representing:

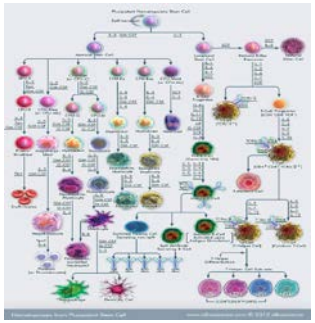
- **Center for Scientific Review (CSR)-** David Balasundaram, Ph.D
- **Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)** - Reiko Toyama, Ph.D.
- **National Cancer Institute (NCI) -** Jennifer Couch, Ph.D., J. Randy Knowlton, Ph.D., Jerry Li, Ph.D.
- **National Heart, Lung, and Blood Institute (NHLBI)** - Zorina Galis, Ph.D. , Pothur Srinivas, Ph.D., Sara Lin, Ph.D.
- **National Institute of Aging (NIA) -** Jose Velazquez, Ph.D.
- **National Institute of Allergy and Infectious Diseases (NIAID) -** Elizabeth Church, Ph.D., Katarzyna Bourcier, Ph.D**.**
- **National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)** - Robert Carter, M.D.
- **National Institute of Biomedical Imaging and Bioengineering (NIBIB) -** Richard Conroy, Ph.D.
- **National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)** - Deborah K. Hoshizaki, Ph.D., Krystyna Rys-Sikora, Ph.D
- **National Institute of General Medical Sciences (NIGMS) -** Sarah Dunsmore, Ph.D., Joseph G. Gindhart, Ph.D
- **National Human Genome Research Institute (NHGRI) -** Ajay Pillai, Ph.D**.,** Jeff Schloss, Ph.D.
- **National Institute of Mental Health (NIMH) -** Andrea Beckel-Mitchener, Ph.D., Yong Yao, Ph.D.
- **National Institute of Neurological Disorders and Stroke (NINDS) -** Francesca Bosetti, Ph.D**.**
- **Office of Strategic Coordination (OSC) -** Jessica Smith, Ph.D., Tony Casco

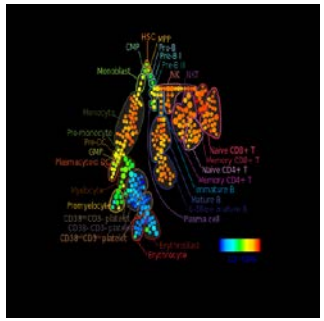
Aspiration: Building from Single Cells to Context to Organizational Principles Across the Human Body

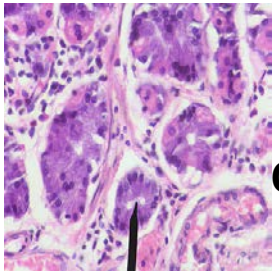












Distance

BODY

Understand Principles

Tissue

Understand Patterns

Neighborhood

Understand Relations

Cell in-situ

Amount of data

Reality check..

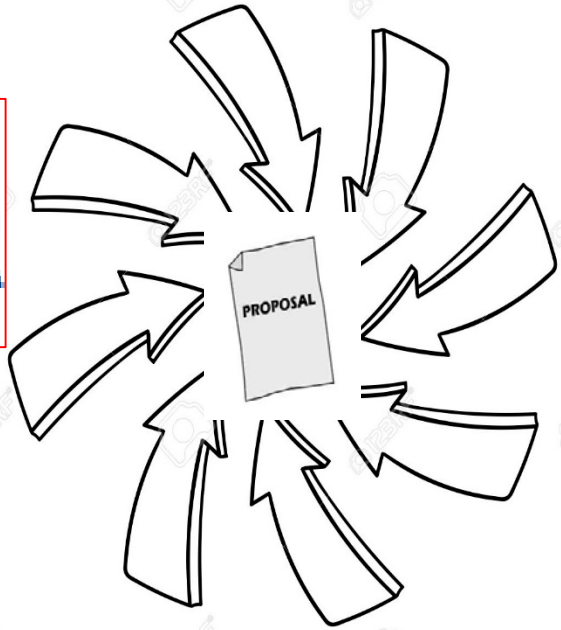
Identifying Key Areas in a Human BioMolecular Atlas (HuBMAP) WS, June 15, 2016

the WHITE HOUSE
BRAIN INITIATIVE
BRAIN RESEARCH THROUGH ADVANCING INNOVATIVE NEUROTECHNOLOGIES

GTEx

LungMAP
Molecular Atlas of Lung Development Program

NIH RePORTER



GUDMAP

PubMed.gov

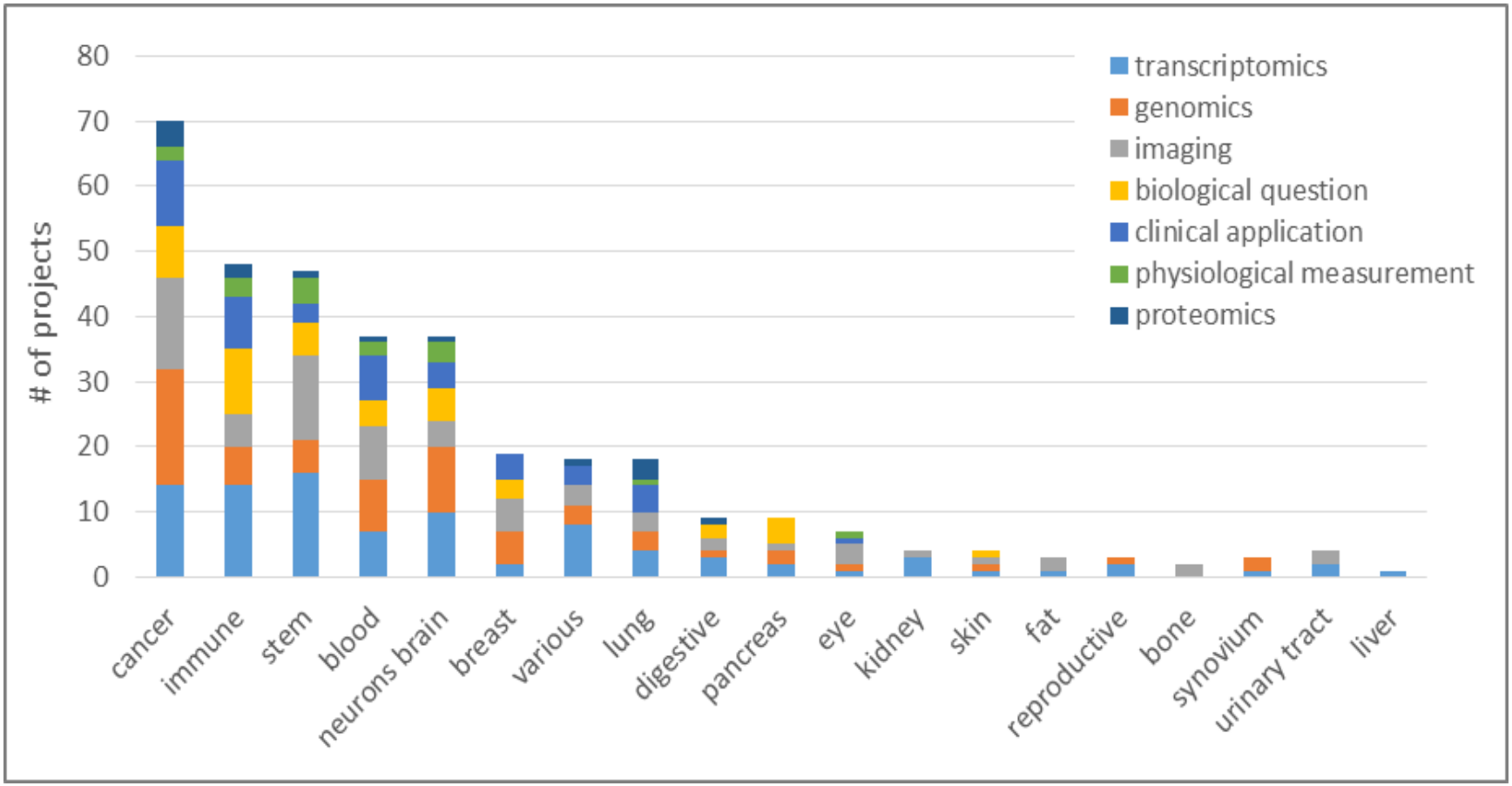
THE HUMAN PROTEIN ATLAS

CellFinder

Request for Information (RFI): Characterizing and Understanding the Organization of Individual Cells within Human Tissues

Notice Number: NOT-RM-16-025

Current Landscape of NIH-Funded Research



Cell or Tissue Type and Project Focus or Technology

NIH Query, View, and Report (QVR), June 28th, 2016
169 projects, 17 IC's. Total investment of $97M.

Why the HuBMAP?

	HuBMAP	GTEx	GUDMAP	LungMAP	BRAIN	SGMAP	HPA
Primary Species	**Human**	Human	Mouse moving to Human	Human / Mouse	Mouse	Mouse	Human
Tissues	**Phase 1: ~10 Phase 2: ~40**	~53	Kidney / Prostate	Lung	Brain	Salivary glands	~44
Focus	**Inter-individual variability**	eQTLs	Early development	Early development	Cell census	Early development	Proteome
Tech	**FISH, RNA-Seq, IMS**	RNA-Seq	FISH, RNA-Seq	FISH, RNA-Seq, MS, CT	RNA-Seq	Microarray / RNA-Seq	60,000+ Antibody
Single cell focus?	**Yes**	No	Yes	Yes	Yes	No	Moving towards
Spatial?	**Yes**	No	Yes	Yes	No	No	Yes
Across Body?	**Yes**	**Yes**	**No**	**No**	**No**	**No**	**Yes**

Opportunities

Synergistic Collaborations

GUDMAP

SHOGoiN
Human Omics database for the Generation of iPS and Normal Cells

CellFinder

THE HUMAN PROTEIN ATLAS

LungMAP

GTEx

THE BRAIN INITIATIVE

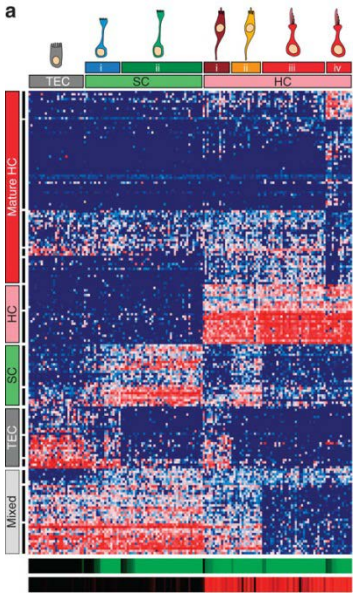
Accelerating Medicines Partnership
Rheumatoid Arthritis
Type 2 Diabetes

ALLEN INSTITUTE for CELL SCIENCE

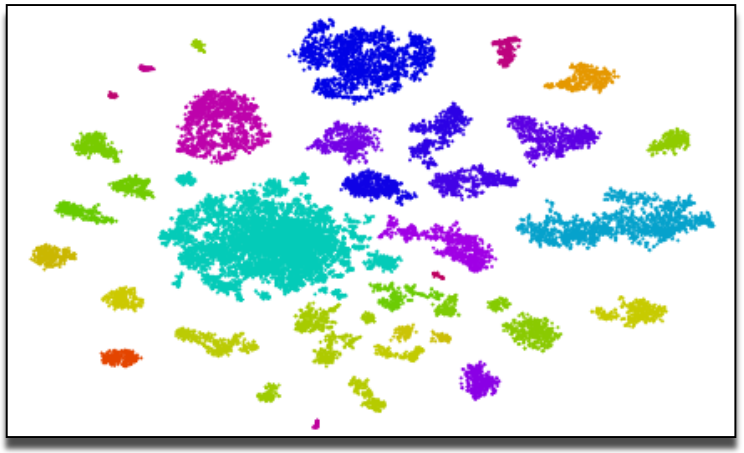
NIH LINCS PROGRAM

The Society for Single-Cell Surveyor
Understanding Life at the Molecular Level

Single Cell Technologies

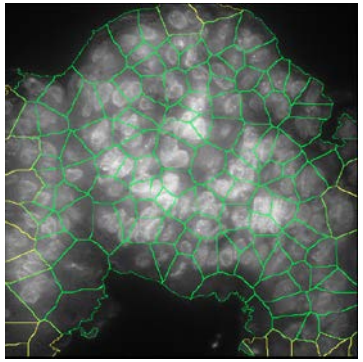


RNA-Seq identifies unique cell types in mouse utricle (Kelley Lab)

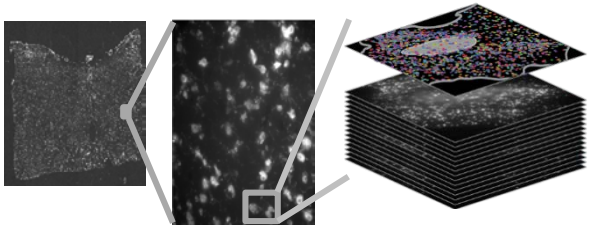


Retina Drop-Seq (48,808 cells) – 3 new cell types identified (Regev Lab)

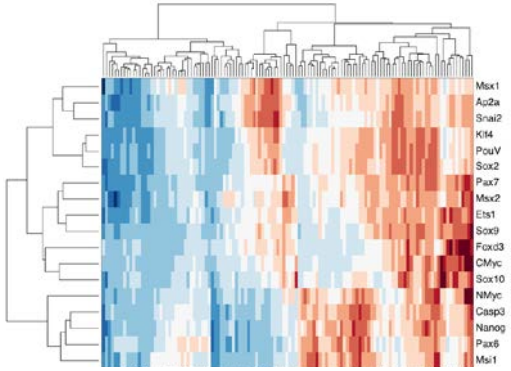
Emerging In-situ Technologies



FISH Imaging

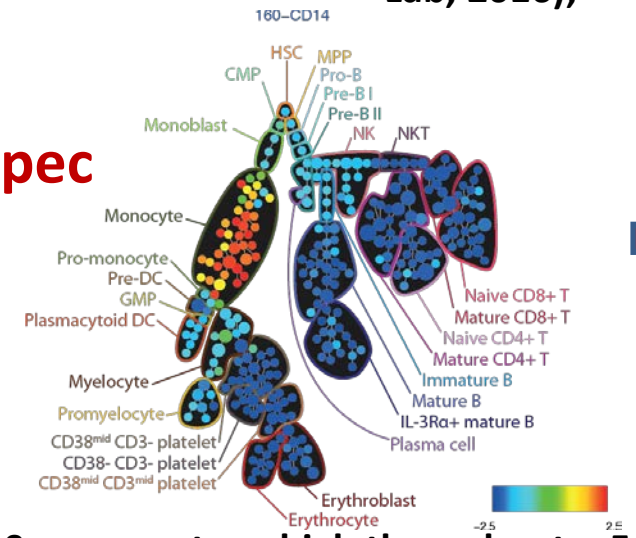


MERFISH – Imaging 1000+ genes in tissue (Zhuang Lab, 2016);

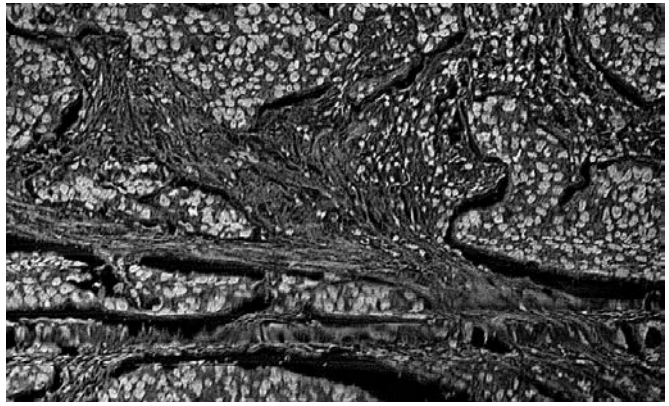


SeqFISH– Sequential barcoding, 100+ parameters, single molecule sensitivity (Cai Lab)

Mass Spec & CyTOF



CyTOF – 30+ parameters, high throughput, <5 Ab sensitivity (Nolan Lab)



MIBI-TOF – up to 50 parameter imaging, down to 20nm (Angelo Lab, 2016)

Proposed Goals for the HuBMAP

To understand:

1) The principles behind the organization of cells in human tissues across the body
2) The role of this organization in orchestrating short and long-range communication between individual cells

Will lead to better understanding:

1) The role played by specific individual variations and changes across the lifespan and health/disease continuum

Outputs of the HuBMAP

Phase 1:

1. A standardized pipeline to create multiscale multidimensional molecular maps
2. Next generation tools (high-resolution, high-content and high-throughput) to map tissue organization
3. Census of major cell types in multiple tissues to understand inter-individual variability
4. Characterization and mapping of the 3D biomolecular architecture of all cells in ~10 human tissues / systems
5. Understanding of “normal” inter-individual variation

Phase 2:

1. Extension of cell census and mapping projects to lifespan and health / disease continuum
2. Validated models of organizational / functional relationships in tissue
3. Next generation tools to explore tissue dynamics (4D)

Initiatives

Phase 1 & 2

1. **Tissue Core:** Human tissue from multiple donors (>20) and multiple sites (>20) to 1) study inter-individual variability, 2) changes in development & disease
2. **Cell Census and Deep Profiling:** High-throughput single cell RNA-seq and FISH imaging, chemistry, validation and benchmarking. Accelerate the development, validation and dissemination of in situ analysis. Mapping the organizational and functional relationship between tissue-specific cells of each organ and immune cells, progenitor cells, endothelial/vascular cells, and the stroma.
3. **Data Coordination and Organizational Hub:** Track, store, and display all data generated by the HuBMAP and assist with development of ontologies, metrics, standards and analytical tools. Integrate with complementary programs to make data interoperable. Promote cross-site interactions, managing working groups and committees of the consortium (e.g. the Steering Committee), the website, meetings and outreach

Phase 2 Only

1. **Visualizing and Modeling:** Build statistical and analytic techniques and models of cellular organization and communication in tissues. Compare signatures of tissues from healthy individuals to those with different diseases
2. **Tissue Dynamic Mapping:** Accelerate the development of technologies and systematic approaches for mapping spatio-temporal changes within human tissues

Next steps

- Refine boundaries based on continued community input
- Decide which components will be prioritized by peer review
- Build synergies with ongoing similar NIH and international programs
- Continue gathering best practices for management and evaluation of the HuBMAP consortium in phase I and phase II
- Develop detailed implementation plans for the HuBMAP program

Backup Slide

Proposed HuBMAP Budget

Initiatives		Phase 1			Phase 2				
	Lead IC	FY18	FY19	FY20	FY21	FY22	FY23	FY24	FY25
Initiative 1: Tissue Core	TBD	1.0	1.0	1.0	1.5	1.5	1.5	1.5	1.5
Initiative 2: Census of Human Cell Types	TBD	6.0	6.0	6.0	10.0	10.0	10.0	10.0	10.0
Initiative 3: Deep Profiling of Human Tissues	TBD	6.0	6.0	6.0	10.0	10.0	10.0	10.0	10.0
Initiative 4: Technology Development for in situ Analysis	TBD	5.0	5.0	5.0	3.0	3.0	3.0	3.0	3.0
Initiative 5: Data Coordination Center	TBD	1.0	2.0	3.0	3.0	3.0	3.0	3.0	3.0
Initiative 6: Organizational Hub	TBD	1.0	1.0	1.0	1.5	1.5	1.5	1.5	1.5
Initiative 7: Visualizing and Modelling Large-Scale Cell Networks	TBD				3.0	3.0	3.0	3.0	3.0
Initiative 8: Tissue Perturbation Mapping	TBD				5.0	5.0	5.0	5.0	5.0
RMS:	TBD	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
TOTAL		**20.5**	**21.5**	**22.5**	**37.5**	**37.5**	**37.5**	**37.5**	**37.5**

THANK YOU.

QUESTIONS?