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
Reality check..

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

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?

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

Synergistic Collaborations

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
## Proposed HuBMAP Budget

<table>
<thead>
<tr>
<th>Initiatives</th>
<th>Lead IC</th>
<th>Phase 1</th>
<th>Phase 2</th>
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<tbody>
<tr>
<td></td>
<td>FY18</td>
<td>FY19</td>
<td>FY20</td>
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<tr>
<td>Initiative 1: Tissue Core</td>
<td>TBD</td>
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<td>Initiative 2: Census of Human Cell Types</td>
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<td>Initiative 3: Deep Profiling of Human Tissues</td>
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<td>Initiative 4: Technology Development for in situ Analysis</td>
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<td>Initiative 5: Data Coordination Center</td>
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<td>2.0</td>
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<td>Initiative 6: Organizational Hub</td>
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<td>Initiative 7: Visualizing and Modelling Large-Scale Cell Networks</td>
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<td>Initiative 8: Tissue Perturbation Mapping</td>
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<td>RMS:</td>
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<tr>
<td>TOTAL</td>
<td></td>
<td>20.5</td>
<td>21.5</td>
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THANK YOU.

QUESTIONS?