Concept Clearance for Two Additional Initiatives
for the Production Phase of the
Common Fund Human BioMolecular Atlas Program (HuBMAP)

SUMMARY

Program Title:	**Human BioMolecular Atlas Program (HuBMAP)**
Program Goal:	*To catalyze the development of a framework for mapping the human body at single cell resolution.*
IC Director(s) or Senior IC Staff:	*Gary Gibbons (NHLBI), Jill Heemskerk (NIBIB), Robert Star (NIDDK)*
Program Coordinator(s) and Leads:	*Technology Development: Jerry Li (NCI), Pothur Srinivas (NCI)* *Tissue Mapping Centers: Zorina Galis (NHLBI)* *HIVE Collaboratory*: Tyler Best (OD), Ajay Pillai (NHGRI) *Demonstration Projects:* Ajay Pillai (NHGRI) *OSC Staff:* Richard Conroy, Dena Procaccini
Proposed Concepts:	*2 initiatives to augment the Production Phase:* • HuBMAP Integration, Visualization, and Engagement (HIVE) Collaboratory [Reissue] • Data Mining and Demonstration Projects [New]

BACKGROUND INFORMATION

Over the past decade there has been an explosion of new techniques for studying single cells in a high throughput manner. These techniques have unleashed the opportunity to study the composition, spatial organization, and temporal dynamics of cells, although in the process they generate more data than we currently have capabilities to fully understand. While we broadly understand how cells are organized in most tissues, we lack an understanding of organizational motifs, networks, and dependencies that exist between cells, cells and their extracellular matrix, as well as within the natural tissue milieu. The Human BioMolecular Atlas Program (HuBMAP) was launched in Fall 2018 to address this need. A better understanding of tissue organizing principles will have a transformative impact on tissue remodeling, aging and accompanying disease progression processes, as well as how tissue-specific, molecular pathways may enable more targeted therapies.

The goal of HuBMAP is to catalyze the development of a framework for mapping the human body down to the level of single cell resolution. The key components of this framework, and the strengths of HuBMAP, are: 1) 3D spatial mapping of tissue at high resolution, and 2) *in situ* analysis of multiple classes of biomolecules (DNA, RNA, proteins, lipids) to produce high-quality reference datasets for normal human tissues; 3) development of computational techniques for integrated analysis of data across spatial scales and molecular classes and discovery of organizing principles, and 4) a platform that adheres to FAIR principles, including tools that allow cross-referencing HuBMAP outputs with contemporary information, to build a comprehensive mapping system that can be easily adapted and adopted by other researchers.

HuBMAP plays an important role as part of an international ecosystem of synergistic programs, each focused on studying tissues utilizing techniques relevant to their goals. The HuBMAP Integration, Visualization, and Engagement (HIVE) plays a pivotal role in building the strong connections HuBMAP has developed with other programs including the Human Cell Atlas Initiative (HCA), the Human Tumor Atlas Network (HTAN) and the Kidney Precision Medicine Program (KPMP). For example, after hosting the NIH-HCA Joint Meeting in Spring 2020, the HIVE has taken the lead in establishing 3 open working groups to coordinate: 1) affinity reagent validation, 2) data curation, and 3) developing a common coordinate framework for the human body. Through these partnerships, we expect that these efforts will result in interoperable datasets and enable new discoveries about normal interindividual variability and phenotypes, as well as provide more comprehensive and coordinate resources for the research community.

PROGRESS DURING SCALE-UP PHASE (YEARS 1-4)

The Consortium has made significant progress in a number of key areas over the past 2 ½ years during the scale-up phase. The enthusiasm and shared vision of the participating groups was captured very early in the program by the Marker paper [Snyder et al. *Nature*. 2019; 574(7777)] and a strong collaborative spirit has resulted in more than 35 internal collaborative projects among the funded groups. The program has grown significantly since it began in October 2018, growing from 15 to 29 awards, a budget of $6.5M to $27.5M and from studying 5 organs to studying 11 organs and systems. The first Consortium data release was in Summer 2020, with the second data release and first publication package planned this summer. To date, the consortium has published more than 57 peer reviewed papers, including 6 highly cited (100+ citations) papers and is committed to making information and resources available rapidly through sources such as BioRxiv, Protocols.io and GitHub.

The 5 awards comprising the HIVE have played a central role in facilitating HuBMAP coordination and collaborations, including outside HuBMAP. The PIs combined experience working on other programs, has enabled the HIVE to rapidly set up a data management system utilizing schemas, packages, standards, benchmarks, and workflows developed by other programs to enhance interoperability and sustainability. In addition, the teams have developed several new packages for annotating data and integrating different data types, as well as providing multiple routes for accessing the data, including through the portal, BRIDGES, and APIs. Finally, the HIVE has established tools and procedures for registering the spatial location of tissue samples, visualizing different types of maps, and for utilizing the reference datasets being generated.

PRODUCTION PHASE (YEARS 5-8)

To refine the priorities for the production phase of the program (FY22-25), the NIH Working Group organized 4 focus groups meetings in Winter 2020 with different groups of stakeholders. Several common themes emerged, including focusing on generating high quality data using proven assays on tissues already being studied by the consortium, developing additional tools to integrate across spatial scales and molecular classes to avoid data types becoming siloed, and to have a balance between clear use cases driving data collection by the consortium and modular tools and curated datasets that enable other researchers to build their own maps.

The NIH Working Group has incorporated this feedback into the scope of the production phase initiatives for which Council support is sought:

1. Reissuing the HIVE RFA is critical to continuing the work of the consortium and build on the progress made during the scale-up phase. The goals of this open funding opportunity would include building richer reference datasets, extending the Common Coordinate Framework to all of the organ systems studied by HuBMAP, and demonstrating a deeper interoperability with related consortia. This work would strengthen the HIVE's role in the single-cell ecosystem as a global leader in 3D tissue mapping, integrated analysis, and as a responsive knowledgebase for the research community.

2. Issuing a Demonstration Projects RFA is critical for highlighting the utility of HuBMAP resources, and to provide important use cases and feedback to the consortium. This initiative will fund teams that will test biological hypotheses by working closely with HuBMAP to develop new models, tools and datasets that show the utility of the Common Coordinate Framework, methods and data generated by HuBMAP alongside other available resources. The knowledge from these studies is expected to include new insights into tissue organizing principles, inter-individual variance, interactions between solid tissues and the inflammatory system, or molecular biomarkers associated with transition to acute or chronic diseases.