

The HuBMAP Integration, Visualization, and Engagement (HIVE) Collaboratory Pre-Application Webinar

August 27th 2021, 2:00 - 3:00PM EDT

To submit questions during the webinar please use the chat.
We will address questions at the end of the presentation.
Following the webinar, questions can be sent to

HuBMAP@mail.nih.gov



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Office of Strategic Coordination - The Common Fund

- Common Fund & HuBMAP Program — 5 mins
- HIVE Components and Structure— 10 mins
- Other Transactions Application and Review— 10 mins
- Other Transactions Financial Management — 3 mins
- Q&A Session — Until we run out of questions or time

What is the NIH Common Fund?



The Common Fund

- Supports a set of **trans-NIH** scientific programs;
- **Spurs subsequent biomedical advances** that otherwise would not be possible without an initial strategic investment;
- Short-term (5-10 year), **goal-driven** programs focused on developing specific deliverables (data, tools, technologies, etc.) to **catalyze research**;
- Managed by the **Office of Strategic Coordination** within the NIH Office of the Director, in partnership with the NIH Institutes and Centers.



Common Fund programs are intended to benefit the entire biomedical research community

Vision: Catalyze the development of a framework for mapping the human body at single cell resolution

By:

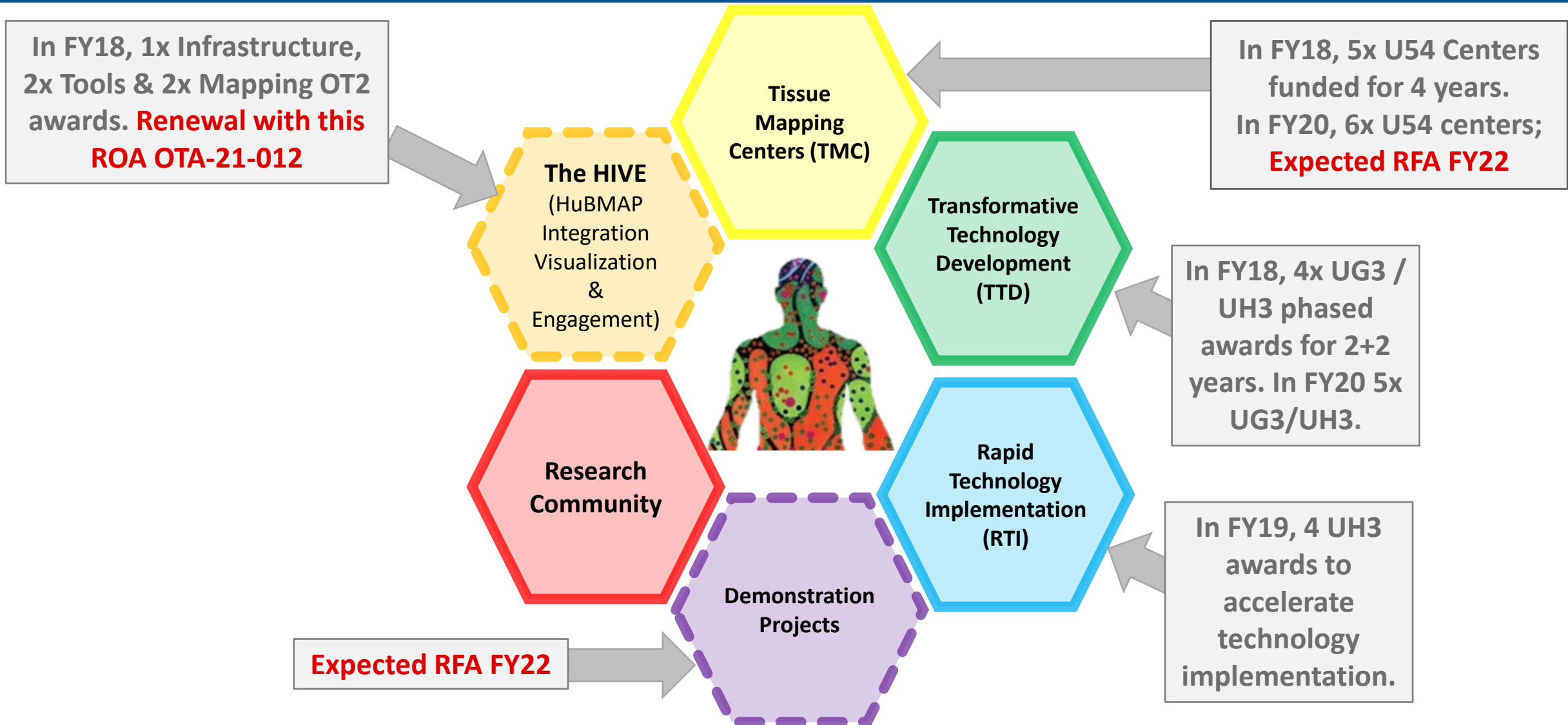
1. Accelerating development of next generation tools and techniques
2. Generating foundational 3D human tissue maps
3. Establishing an open data platform
4. Collaborating with the research community
5. Supporting pilot projects that demonstrate value of HuBMAP resources



HuBMAP Structure



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HIVE Components and Structure



Ajay Pillai (NHGRI)

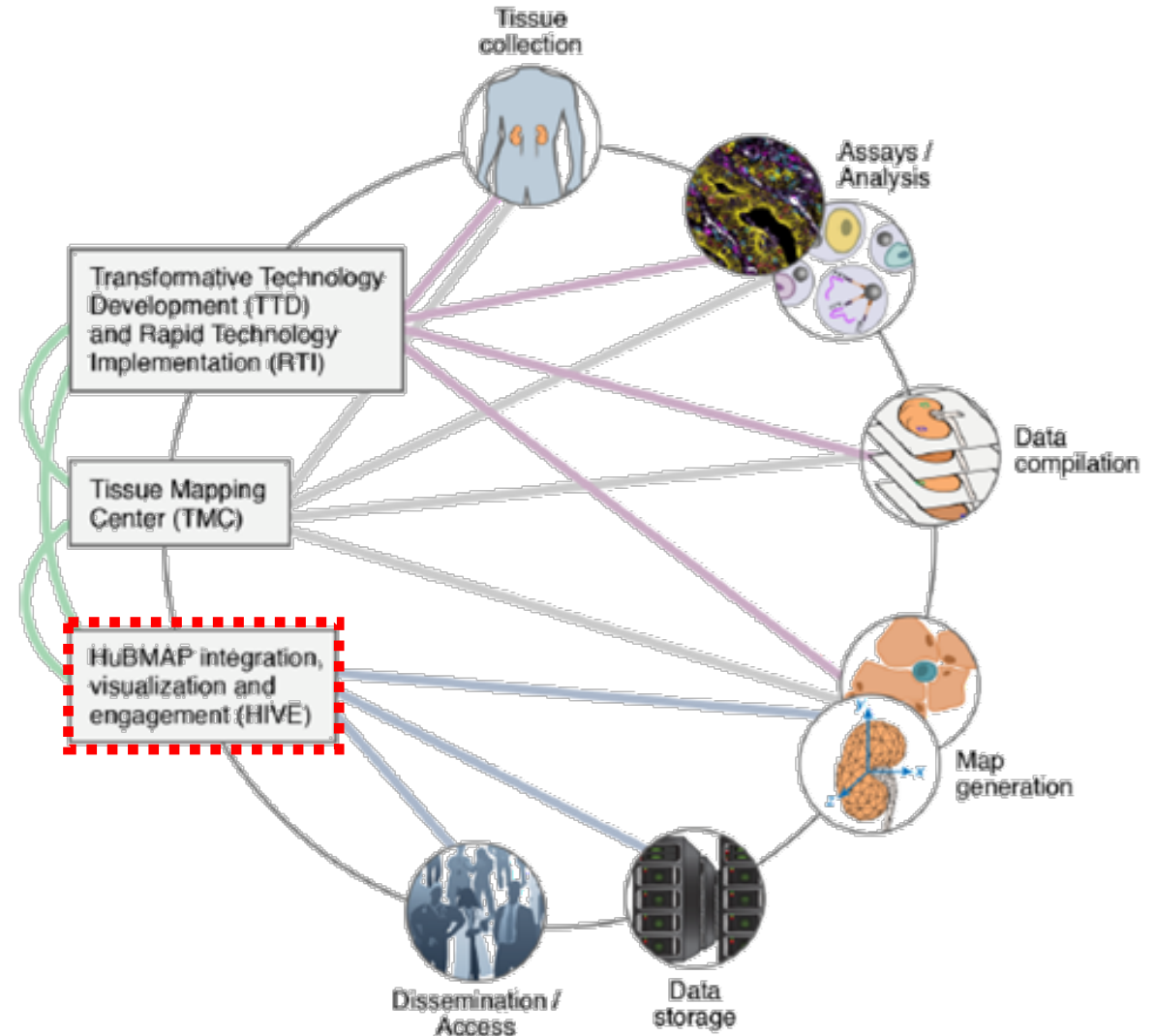


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Role of the HIVE in HuBMAP

The HuBMAP Integration, Visualization & Engagement (HIVE) Collaboratory:

1. Manages the data generated by the HuBMAP Consortium,
2. Coordinates internal and external Consortium activities,
3. Develops novel tools for visualizing, searching and modelling data, and
4. Building an atlas of tissue maps.



Snyder et al. [Nature](https://doi.org/10.1038/s41586-019-1000-4). 2019; 574(7777)

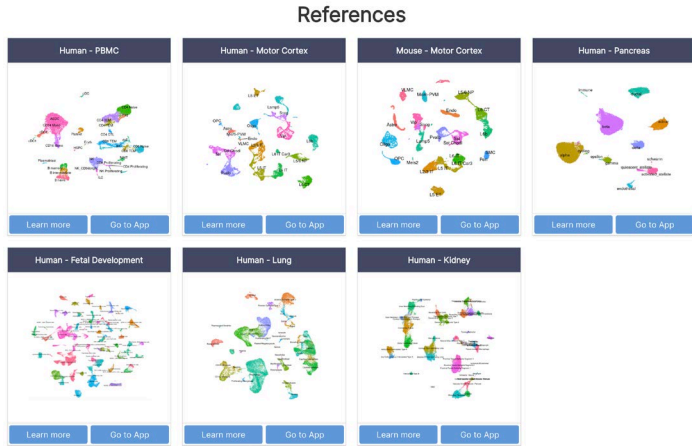
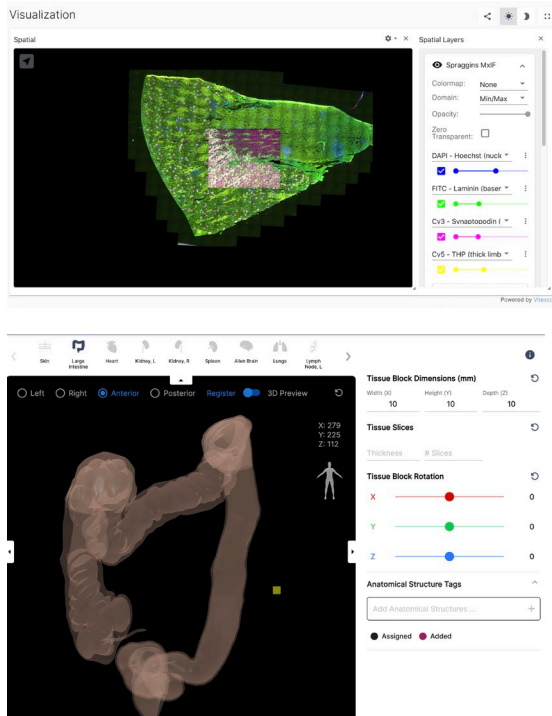
- Heart
- Lung
- Liver
- Pancreas
- Kidney
- Spleen
- Thymus
- Lymph node
- Large intestine
- Small intestine

Assay Format
snRNA-seq, scRNA-seq, BulkRNA-seq
sciATAC-seq snATAC-seq scATAC-seq Bulk ATAC-seq
CODEX Imaging Mass Cytometry
Untargeted LC-MS TMT LC-MS Targeted shotgun LC-MS
MALDI IMS
seqFISH
H&E, PAS,

Standard Pipelines

- RNASeq
- ATACSeq
- CODEX

<https://portal.hubmapconsortium.org/>



Pending

- Vasculature
- Bone & Bone Marrow
- Tonsil
- Skin
- Uterus
- Fallopian Tubes
- Ovary
- Placenta
- Breast

Pending

- MxIF
- cellDIVE
- nanoPOTS
- MIBI
- Slide-seq, Visium, GeoMx, ...
- Micro-CT, MRI

- **Portal: On the way to a resource ...**
 - Data Ingest, Uniform Pipelines (for some assays), Visualization engine/frameworks, References for scRNA-seq, Spatially locating samples, etc
- **Many open challenges and questions remain towards a roadmap of a true community resource**
 - What are the most useful maps? 3D?
 - Integrating multiple modalities—are they consistent/contradictory?
 - Integrating in ontologies.
 - Focus on standards: data sharing, APIs, Machine learning
 - Deeper integration of prior knowledge of cell types and related questions.
- ROA open to new ideas, new perspectives on solving these outstanding questions.
 - Open competition for the ROA.

The HuBMAP Integration, Visualization & Engagement (HIVE) Initiative



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- **Goal:** Catalyze the creation and use of cellular-resolution molecular maps of non-diseased human tissues as references for the research community.
- **Objectives:**
 - Build and expand HuBMAP-based reference maps as new data is produced and adapt as the technology improves;
 - Undertake data integration to create more comprehensive, well-annotated maps;
 - Actively accept and manage single-cell and related data from the community;
 - Play a crucial role in coordinating HuBMAP efforts with the worldwide ecosystem of single cell resources;
 - Develop novel tools to enhance the community's access, capability to assess quality, to query data, and help the resource developed by HuBMAP to **become THE single cell reference for normal human tissue.**

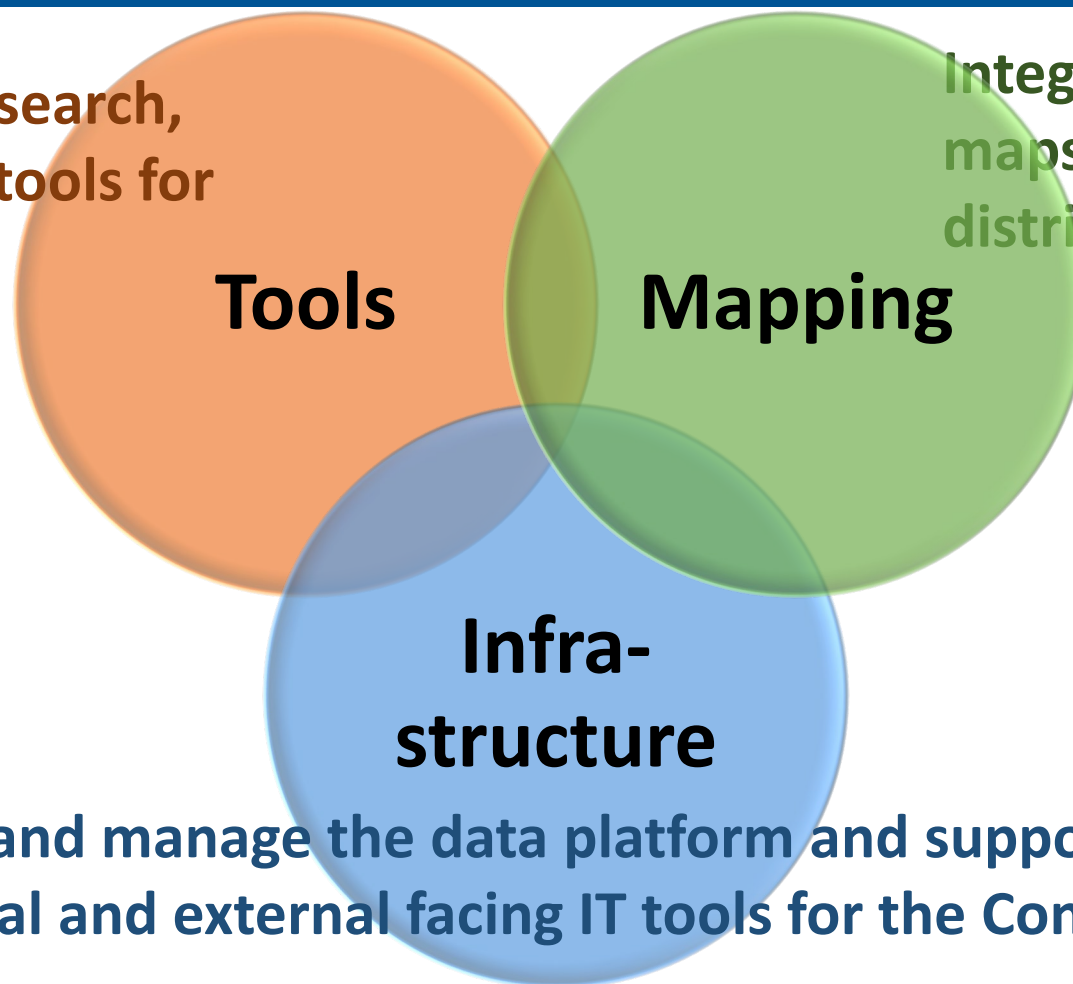


The 3 HIVE Components



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Build and manage suite of search, analysis, and visualization tools for HuBMAP data



Integrate data to build spatial maps of biomolecular distribution for the human body

Build and manage the data platform and support the internal and external facing IT tools for the Consortium

NOTE: Each application may propose only one Component. However, a coordinated set of separate applications, each describing a separate Component but with a common vision, can be proposed

Key Points for the HIVE Initiative



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Other Transactions

- Actively managed awards with much more NIH input – be prepared with project manager & award management

Seamless Integration

- 3 components must work seamlessly together – be prepared for intense interactions

Flexibility

- Consortium, data and technologies will evolve – be prepared to work with NIH staff to adjust, add, delete activities and partners

Practical Deliverables

- Building a resource that needs to be usable – be prepared to regularly demonstrate progress, use off-the-shelf / modular solutions & harmonize with others

Joint Responsibilities for all HIVE Components



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All HIVE teams share the responsibility to:

- Ensure **FAIR-ness** of HuBMAP resources
- Ensure HuBMAP resources are **well-curated and documented**
- **Obtain buy-in** from the consortium for best –fit solutions and rapidly developing and implementing them
- Include **human centered design** and user experience thinking
- Enhance the usability, utility, and usage of HuBMAP resources
- Ensure **on-time delivery of milestones** so as to minimize adverse impact on other Components of the HIVE and other HuBMAP awardees
- Ensure that a **federated ecosystem of single-cell resources** is supported around the community
- **Engage the community** to identify and meet the overall goals of the program



Plan for Coordination, Collaboration and Engagement (CCE) Activities



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- Plan for CCE is **required** for all applications
- Applications should demonstrate a **cohesive vision:** and should address within HIVE, within HuBMAP and within the larger single-cell community.
- CCE activities may include:
 - organizing HuBMAP **workshops** and **meetings**
 - facilitating **collaborative projects**, both within HuBMAP and with other consortia
 - managing **communication** channels **within the consortium** that will enable the HuBMAP consortium to work effectively and productively
 - managing **communication** with the **wider research community**
 - providing **technical training** on how to implement and use HuBMAP resources

Plan for Enhancing Diverse Perspectives (PEDP)



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- PEDP is **required** for all applications
- Applicants are strongly encouraged to read the ROA instructions carefully and view the available PEDP guidance material:
<https://commonfund.nih.gov/HuBMAP/generalfaq>
- Examples that **enhance inclusivity** include:
 - Inclusion of personnel (MPIs, PIs, Co-Is ...) from groups historically underrepresented.
 - Appropriate training at different career stages.
 - Outreach to community groups and other stakeholders.
 - Use research infrastructure for opportunities to undertake research
 - Suitable evaluation criteria for progress?



Other Transactions, Application and Review



Tyler Best (OSC)

“...OTs are not contracts, grants, or cooperative agreements...”



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Other Transactions (OT) Overview



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Other Transactions (OT)

- **Not a grant, cooperative agreement, nor a contract**
- OTs allow the **nimble addition or subtraction** of expertise, tools, technologies, and partnerships
- OTs facilitate **engagement of nontraditional partners** as well as flexible cost-sharing and ownership
- Many [Public Policies](#) apply to OT, though not FAR or NIH Grants Policy
- HuBMAP has its own [OT Policy Guide](#)
- **Institutional requirements** for application are similar to a grant application (e.g. DUNS, SAM, eRA Commons registration...)
- Award **funding is different** (e.g. variable segment lengths, no future commitment, can be terminated or extended by NIH...)
- Changes in project and budget are different (e.g. **NIH can propose changes**, threshold for prior approval...)
- **Reporting requirements are similar** (e.g. financial, invention, lobbying, audits) though different in places (e.g. frequency based on segment length)

<https://commonfund.nih.gov/HuBMAP/OtherTransactions>

Application Process



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Discuss

- *Optional*, but applicants are strongly encouraged to discuss with the HuBMAP team: HuBMAP@mail.nih.gov

Letter of Intent (Required)

- Email letter of intent by **October 1, 2021**
- Must propose to address one of the three HIVE Components

Invitation to Submit

- Within ~2 weeks, a subset of LOI applicants will be invited to submit a full OT2 application

OT2 Application

- Full OT2 applications are due by **Dec 3, 2021**
- These applications are by invitation only

Invitation to Interview

- In Feb 2022, a subset of meritorious OT2 applicants will be invited to present their applications and address questions in an interactive review

Interview

- March 7-8, 2022 teams with meritorious applications will be invited for a video / in-person interview to clarify questions about proposal

Negotiate

- In Apr-May 2021 HuBMAP will negotiate budget, benchmarks, and deliverables with selected applicants

Award

- June 2022 NIH will award an Other Transaction Award (OT2) after successful negotiation

Required Letter of Intent (LOI)



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Email LOI to HUBMAP@mail.nih.gov by October 1st, 2021 11:59pm ET

Letter of Intent (5 pages Maximum):

- Cover Page (1 page):
- Overview and Strategy (3 pages maximum)
- Personnel Qualifications (1 page)
- Up to 3 letters of support, as appropriate (do not count toward page limits)
- See funding announcement for full instructions
- A separate LOI will be required for each component (denote "[M of N]" (e.g., 1 of 3) in the cover page)
- A subset of LOI applicants will be invited to submit a full OT2 application

Follow OT Instructions to submit via ASSIST found here: <https://era.nih.gov/files/OTA-Submissions.docx>

- Items 1-7 of instructions are online forms completed in ASSIST.
- Item 8: upload a Cover Letter (same as from LOI)
- Item 9: Attachments—PDF files, this is where the majority of the application is submitted and includes:
 - Research Plan (20 pg max): Include sub-sections as described in the ROA
 - Vision and Overview (3 pages max)
 - Scientific, Technical and Management Strategy (12 pages max)
 - Key Personnel Experience and Staffing Plan (3 pages max)
 - Previous Experience (2 pages max)
 - Other Documents (do not count toward 20-page max of research plan)
 - Budget documents accessed here: <https://commonfund.nih.gov/OTforms>
 - Biosketches of Key Personnel
 - Resource Sharing Plan (5 pages max)
 - Plan for Enhancing Diverse Perspectives (PEDP; 1 page max)
 - Plan for Coordination, Collaboration and Engagement (2 pages max)
 - Invitation to Submit full proposal (after LOI)
 - Appropriate Letters of Support



Objective Review – **not a typical NIH Grant review**

- Reviewers selected from academia, government, industry
- **Not a consensus** review, NIH Program staff take reviewer comments into consideration for funding recommendations
- Appeals of the Objective Review will **not be accepted**

Review Criteria (scored 1-9 by reviewers; 1=high score, 9 = low score)

- Merit of Scientific, Technical and Management Strategy:
 - Vision, Approach, Management, PEDP, CCE plan, Resource Stewardship plan,
- Personnel Qualifications
- Institutional Commitment

- Selected meritorious applications invited to **interactive interview March 7-8, 2022** to clarify reviewer and NIH staff questions. 1-hour interviews will be either in-person or via videocast. NIH will not support travel for these interviews.
- A written summary of review will be provided upon request.

Other Transaction Financial Management



Heather Weiss (NIMH)

“...OTs are not contracts, grants, or cooperative agreements...”



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Financial Award Management



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- Incremental award segments based on negotiated milestones
 - Award “segments” can vary in length up to 12 months of funding
 - No obligation for future funding
 - Each segment requires frequent reporting / demonstration of milestones met
 - Future support is contingent on satisfactory progress, programmatic priorities, the availability of funds, and the continued best interests of the Federal government
 - When milestones are ahead of schedule, additional funds and milestones may be negotiated
 - Both parties (applicant organization and NIH) must agree to terms and conditions of the award
- NIH may extend or terminate an award for convenience
- Segments may be extended, milestones re-negotiated or budgets adjusted

Wrap-up

Tyler Best (OSC)



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Important Dates



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- **Letter of Intent Due Date:**
October 1, 2021
- **Application Receipt Date:**
December 3, 2021
- **OT Objective Review Date:**
February 2022
- **Earliest Start Date:**
June 2022



<https://commonfund.nih.gov/sites/default/files/HuBMAP-HIVE-OTA-21-012-v2-508.pdf>



Connect with us:

- General mailbox: HUBMAP@mail.nih.gov
- Website: <https://commonfund.nih.gov/HuBMAP>
- Existing Awards: <https://commonfund.nih.gov/hubmap/fundedresearch>
- Consortium website: <https://hubmapconsortium.org/>
- Mailing list: [https://list.nih.gov/cgi-bin/wa.exe?SUBED1=hubmap news and information&A=1](https://list.nih.gov/cgi-bin/wa.exe?SUBED1=hubmap_news_and_information&A=1)
- HuBMAP Portal: <https://portal.hubmapconsortium.org/>

Frequently Asked Questions:

<https://commonfund.nih.gov/HuBMAP/generalfaq>

Interested in applying:

We strongly recommend you discuss any application with us in advance.



Questions?

To submit questions please use the Chat box.

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Supplemental Slides



Consortium Webpage:

<https://hubmapconsortium.org>

- [Consortium Publications](#), [BioRxiv channel](#), and [marker paper](#)
- [Open Working Groups](#): Cell Atlas Curation, Affinity Reagent Imaging and Validation, ASCT+B Working Group
- [Consortium Policies](#)
- [Image of the Week](#)
- [Protocols on Protocols.io](#)

HuBMAP Data Portal:

<https://portal.hubmapconsortium.org>

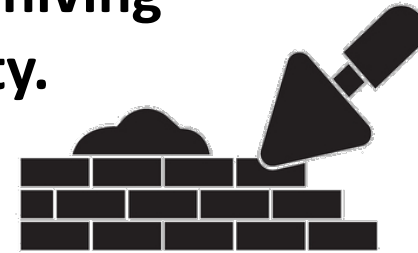
- [Anatomical Structures, Cell Types and Biomakers Reporter](#)
- [CCF Registration User Interface](#)
- [CCF Exploration User Interface](#)
- [Data Analysis Pipelines](#)
- [GitHub](#) - code repository
- [Vitessce](#) - visualization platform
- [Azimuth](#) – reference labelling for RNA-seq data

Infrastructure Component (IC)



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Goal: Establish, optimize, and scale a reliable, accessible infrastructure for archiving and analysis of data generated by HuBMAP and the wider research community.



Example Responsibilities:

- Provide infrastructure for storage, computational needs, the pipelines for ingesting, archiving, and exposing the data in a controlled, monitored fashion;
- Support the internal and external facing informatics tools and Application Programming Interface(s) (APIs) for the Consortium;
- Provide infrastructure to test, deploy, and support the tools and services developed by HuBMAP consortium members;
- Enable efficient use of workflows & pipelines at scale. Automating and containerizing workflows & pipelines as needed;
- Host the HuBMAP web (data) portal and track usage of the portal;

Goal: Create and/or use community standard methods for data analysis, processing, interpretation, and visualization of HuBMAP data

Example Responsibilities:

- Build and optimize search, analysis, and visualization tools for data;
- Scale-up the data ingestion, management, and curation tools to support an increasing amount of data;
- Develop tools to enable biologists and computational scientists to identify and use relevant data for scientific inquiry;
- Enable query framework that accounts for technical variation to better understand and identify biologically relevant data;
- Establish machine learning models to address questions in single cell biology while enabling the larger community to build such models;



Mapping Component (MC)



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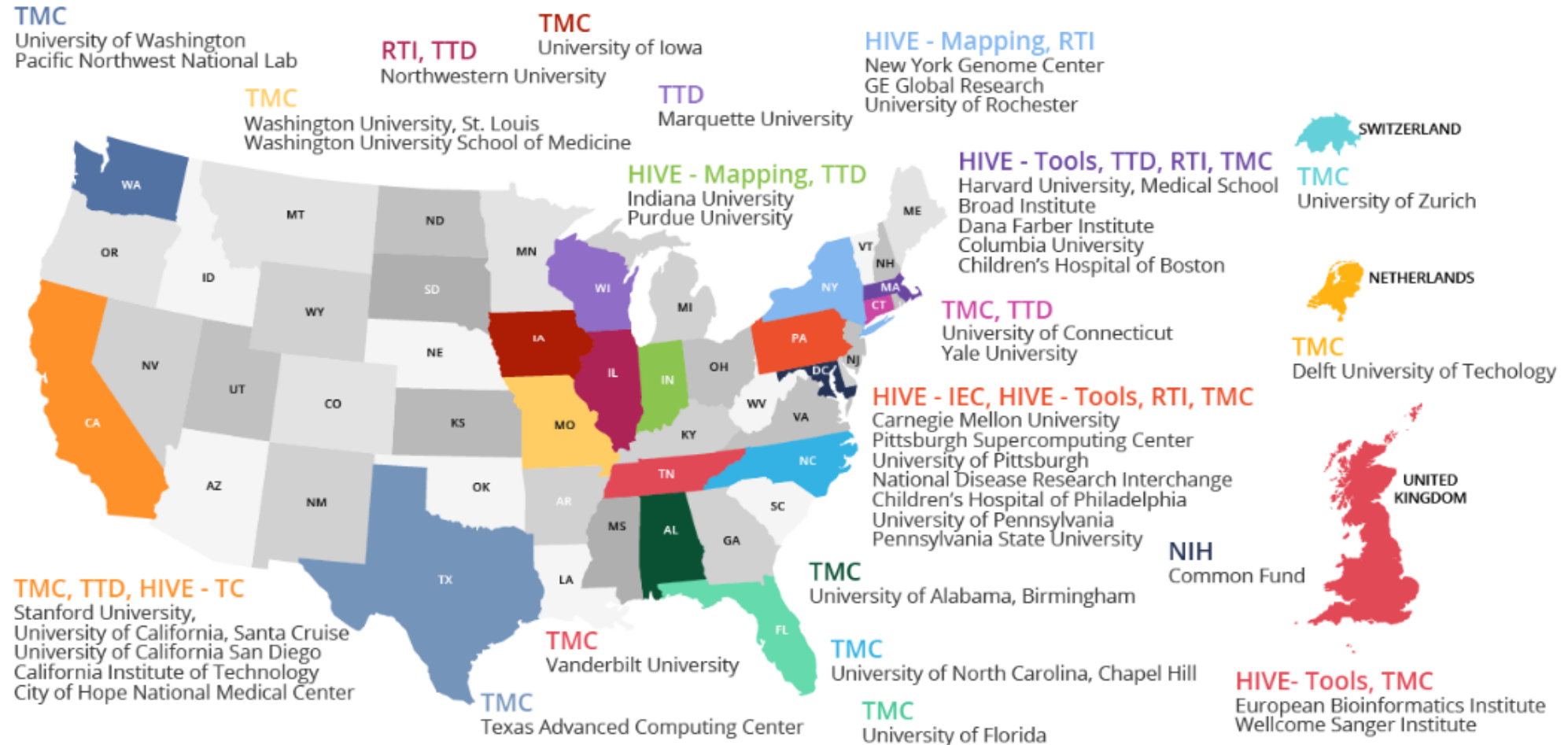
Goal: Develop the framework for spatially mapping the data in the context of the human body, organ(s), and regions.



Example Responsibilities:

- Build and optimize the framework for integrating tissue maps that can stitch together multi-modal data in the context of the human body;
- Establish pipelines that construct spatially integrative maps from HuBMAP and non-HuBMAP data;
- Define appropriate formats for querying, integrating, and sharing such maps;
- Provide maps and mapping tools to biologists and computational scientists for scientific inquiry;
- Enable biological use-case driven approaches to maps construction, storage, and sharing for computational modeling and machine learning methods.

HuBMAP Contributing Sites



IMAGING

DNA/RNA

DART-FISH
seqFISH
smFISH
MERFISH
Slide-seq
SABER-FISH
GeoMx

Lipids/Metabolites

MALDI Imaging MS
SIMS Imaging
DESI Imaging MS
NanoDESI Imaging MS

Proteins

Multiplexed IF
IHC
Lightsheet
CODEX
Cell DIVE
DART-FISH
CyTOF Imaging
MALDI Imaging MS
nanoPOTS
MIBI
Immuno-SABER

Other

MR Imaging
CT Imaging
Autofluorescence
Stained Microscopy

SEQUENCING

snDropseq
scRNAseq
snRNA-seq
snATAC-seq
sciRNAseq
sciATACseq
scTHSseq
SNAREseq
scATACseq

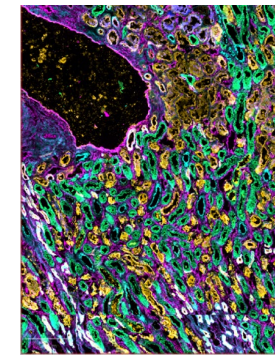
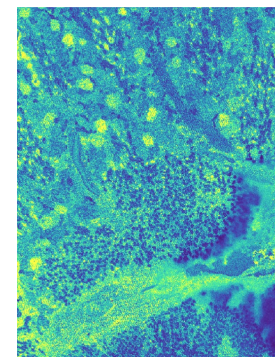
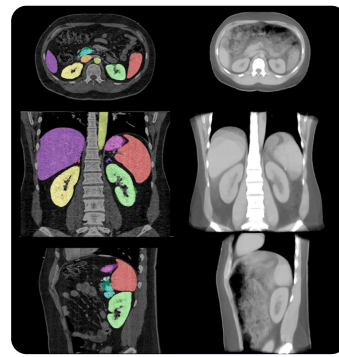
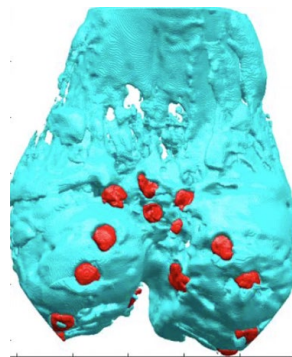
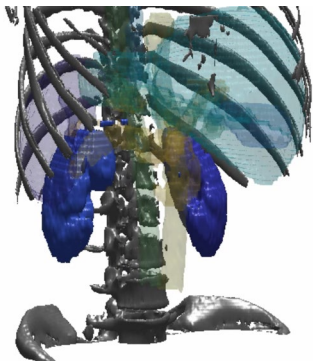
BULK OMICS

Lipids/Metabolites

LC-MS/MS

Proteins

Bottom-up LC-MS/MS
Top-down LC-MS/MS
TMT LC-MS/MS



Data on HuBMAP Portal



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Heart	Lung	Liver	Pancreas	Kidney	Spleen	Thymus	Lymph node	Large intestine	Small intestine
sciATAC-seq	sciATAC-seq	sciATAC-seq	sciATAC-seq	Autofluorescence Microscopy	CODEX	CODEX	CODEX	Bulk ATAC-seq	Bulk ATAC-seq
sciATAC-seq [SnapATAC]	sciATAC-seq [SnapATAC]	sciATAC-seq [SnapATAC]	sciATAC-seq [SnapATAC]	MALDI IMS negative	CODEX [Cytokit + SPRM]	CODEX [Cytokit + SPRM]	CODEX [Cytokit + SPRM]	Bulk ATAC-seq [BWA + MACS2]	Bulk ATAC-seq [BWA + MACS2]
seqFISH	snRNA-seq			MALDI IMS positive	Imaging Mass Cytometry	Imaging Mass Cytometry	Imaging Mass Cytometry	Bulk RNA-seq	Bulk RNA-seq
seqFISH [Lab Processed]	snRNA-seq [Salmon]			PAS Stained Microscopy	Lightsheet Microscopy	Lightsheet Microscopy	Lightsheet Microscopy	Bulk RNA-seq [Salmon]	Bulk RNA-seq [Salmon]
				scATAC-seq (SNARE-seq) [Lab Processed]	scRNA-seq (10x Genomics)	scRNA-seq (10x Genomics)	scRNA-seq (10x Genomics)	CODEX	CODEX
				SNARE-seq	scRNA-seq (10x Genomics) [Salmon]	scRNA-seq (10x Genomics) [Salmon]	scRNA-seq (10x Genomics) [Salmon]	CODEX [Cytokit + SPRM]	CODEX [Cytokit + SPRM]
				snRNA-seq				snATAC-seq	sciATAC-seq
				snRNA-seq (SNARE-seq) [Lab Processed]				snATAC-seq [Snap-ATAC]	sciATAC-seq [SnapATAC]
				snRNA-seq [Salmon]				snRNA-seq	seqFISH
				Untargeted LC-MS				snRNA-seq [Salmon]	seqFISH
								Targeted Shotgun / Flow-injection LC-MS	seqFISH [Lab Processed]
								TMT LC-MS	seqFISH [Lab Processed]
								Untargeted LC-MS	Targeted Shotgun / Flow-injection LC-MS
								Whole Genome Sequencing	TMT LC-MS
									Untargeted LC-MS
									Whole Genome Sequencing

- Pending**
- Vasculature
 - Bone & Bone Marrow
 - Tonsil
 - Skin
 - Uterus
 - Fallopian Tubes
 - Ovary
 - Placenta
 - Breast

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