ASCT+B Tables and SenNet Biomarkers

Katy Börner & Ellen M. Quardokus
(CODCC, Indiana University)

June 1, 2022
Why construct a Human Reference Atlas (HRA)?

Data Generation, Harmonization and Integration

Human Reference Atlas (HRA)

Advance Research
Improve Human Health
The Human Reference Atlas (HRA)

1. defines the 3D space and shape of anatomical structures and cell types that are of biomedical relevance plus the biomarkers used to characterize them. Anatomical structures, cell types and biomarkers are validated and represented in/added to ontologies (Uberon/FMA, CL, HGNC).

2. defines how new datasets can be mapped to the HRA, e.g., spatially using the Visible Human CCF or Vasculature CCF (or both, see next slide), via ASCT+B ontology terms/IDs, or via gene expression data as in Azimuth.

3. it is
   - authoritative (there exists expert agreement and it was validated by data),
   - computable (supports API queries, UIs),
   - published as LOD (connected to gene, disease, and other ontologies and data),
   - open (anyone can use the HRA data and code), and
   - continuously evolving (e.g., as new technologies become available).

https://www.nature.com/articles/s41556-021-00788-6
Constructing the Human Reference Atlas – Together!
VHP F Spleen

White pulp of spleen

Partonomy Tree

- part_of
  - Red Pulp
  - Venous Sinuses
  - Arterial Capillaries
  - Sinuses
  - Vessels
  - Stroma
  - Splenic Cortex
  - Secondary Follicles
  - Germinal Centers
  - Marrow Zone
  - Primary & Secondary Folli...
  - Superficial (Marginal) Zone
  - Central Arteriole (in follicles)
  - PALS and Follicles
  - PALS
  - Perifollicular Zone
  - Splenic Artery

Cell Types (CT)

- is_a
  - Adventitial stromal cell
  - B cell
  - Dendritic cell
  - Endothelial
  - Endothelial cell
  - Erythrocytes
  - Fibroblast
  - Fibroblastic reticular cell
  - Follicular Dendritic cell
  - Granulocytes
  - Lymphocytes
  - Lymphocyte
  - Monocytes
  - Myeloblast
  - Neutrophils
  - NK cell
  - Plasma cell
  - Plasma blasts
  - Platelets

Bimodal network describing which CT are located in what AS

Bimodal network describing which CT characterize what CT

Biomarkers (B)

- BG - Genes
  - CD10
  - CD11b
  - CD11c
  - CD133
  - CD14
  - CD141
  - CD15
  - CD163
  - CD19
  - CD20
  - CD21
  - CD22
  - CD23
  - CD35a
  - CD27
  - CD27-9
  - CD271
  - CD3-5
  - CD31
  - CD34
  - CD4
  - CD4 (helper)
  - CD41
HRA Validation/Expansion

New ATLAS publications

Azimuth Maps
Validated Antibodies

BF – Proteoforms
BL – Lipids
BM – Metabolites

2D/3D Maps & Ontology Crosswalks

New ATLAS datasets

Partonomy Tree

Typology Tree

HRA Validation/Expansion

New ATLAS publications

Azimuth Maps
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2D/3D Maps & Ontology Crosswalks

New ATLAS datasets

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
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</thead>
<tbody>
<tr>
<td>Which senescent cell types will your team work on?</td>
<td>Your answer</td>
</tr>
<tr>
<td>Which senescent markers will your team use?</td>
<td>Your answer</td>
</tr>
<tr>
<td>Who on your team should be invited to CCF and Human Reference Atlas meetings?</td>
<td>Your answer</td>
</tr>
<tr>
<td>Who on your team is working on 2D or 3D representations of organs?</td>
<td>Your answer</td>
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SenNetMarkers_To_HGNC-UniProt_shared was shared to SenNet Biomarkers working group: https://docs.google.com/spreadsheets/d/1VHqmY1mDo7XeVXWqiWXXp2O0Dbyy6rnTKbvlgzoX8Gl/edit?usp=sharing
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<th>Description</th>
<th>Function</th>
<th>Comment</th>
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<td>COL</td>
<td>C-C motif chemokine ligand 2</td>
<td>This is a measurement of a cell not a gene</td>
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<td>7q21</td>
<td>cyclin A2</td>
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<tr>
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<td>5q31</td>
<td>cyclin G2</td>
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<td>collagen</td>
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<td>C</td>
<td>D</td>
<td>E</td>
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<td>SenNet CCF Survey, Nov '21</td>
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<tr>
<td>DDR</td>
<td>DDR</td>
<td>DNA damage response</td>
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<td>H2AX</td>
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<td>high mobility group box 2</td>
<td>HGNC:5000</td>
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<td>interleukin 1 alpha</td>
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<td>P01583</td>
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<tr>
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<td>interleukin 1 beta</td>
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<td>interleukin 6</td>
<td>HGNC:6018</td>
<td>P05231</td>
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<td>IL8</td>
<td>IL8</td>
<td>C-X-C motif chemokine ligand 8</td>
<td>HGNC:6025</td>
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SenNet
MONTHLY SCIENCE TALK
APRIL 27, 2022
2:30 PM EST

DR. ANDREAS BUECKLE
&
ELLEN M. QUARDOKUS

Cellular Senescence Network (SenNet) Consortium Organization and Data Coordinating Center (CODCC)
Onboarding TMCs – CCF Registration User Interface (RUI) and CCF Exploration User Interface (EUI)

**Presenter:** Dr. Andreas Bueckle, Research Scientist, Cyberinfrastructure for Network Science Center, Department of Intelligent Systems Engineering, Luddy School of Informatics, Computing, and Engineering, Indiana University;

**Abstract:** Constructing the Human Reference Atlas (HRA) requires spatial annotations for registered human tissue across all organs. In this demo, we will introduce the CCF Registration User Interface (RUI) and CCF Exploration User Interface (EUI) which allow users to spatially register and semantically annotate tissue blocks and to spatially/semantically explore them across 50+ adult human reference organs via a web browser.

**Learning Objective:** Learn how to 3D register tissue and explore tissue blocks spatially and semantically.
Onboarding TMCs - Authoring and Using Anatomical structures, Cell types and Biomarker tables (ASCT+B), design of 3D organ reference library models

Presenter: Ellen M. Quardokus, Senior Research Analyst Biologist, Cyberinfrastructure for Network Science Center, Department of Intelligent Systems Engineering, Luddy School of Informatics, Computing, and Engineering, Indiana University;

Abstract: Constructing the Human Reference Atlas (HRA) requires spatial and semantic annotations for registered human tissue across all organs. ASCT+B tables capture into structured tables the nomenclature for each organ on three scales: anatomy, cell types located in the anatomy, and the biomarkers that characterize the cell types. The information is used to annotate 3D models, which are used in the Tissue Registration User Interface (RUI), Exploration User Interface (EUI) and data search. 3D organ models are designed with expert user input to capture the gross anatomical level needed to virtually register tissue blocks.

Learning Objective: Learn how to author and use ASCT+B tables and 3D reference organs efficiently.
Recordings

Recordings are at
Andi: https://youtu.be/FrblrWjeLRs
Ellen: https://youtu.be/QDP58N8JYRk

Visible Human Massive Open Online Course (VHMOOC):
https://expand.iu.edu/browse/sice/cns/courses/hub/map-visible-human-mooc
Relevant Papers


Standardized Tissue Registration

Learn how to 3D register tissue and explore tissue blocks spatially and semantically.
CCF Registration User Interface (RUI)

https://hubmapconsortium.github.io/ccf-ui/rui/
CCF Exploration User Interface (EUI)

https://portal.hubmapconsortium.org/ccf-eui
Note: The screenshot above shows HuBMAP data
Exclusive Preview: Spatial Search

https://andreasbueckle.github.io/rui-3d-interactions/
Relevant SOPs and Videos

- SOP: Using the CCF Registration User Interface: https://doi.org/10.5281/zenodo.5575776
- RUI 3.0.0 Tutorial: https://youtu.be/gY3_-LloKaU
- How to Double-check a RUI Registration with the Exploration User Interface: https://youtu.be/UloDIg0S64w
- SOP: Assigning the Same RUI Location to Multiple Tissue Blocks: https://doi.org/10.5281/zenodo.5746143
Onboarding TMCs - Authoring and Using Anatomical structures, Cell types and Biomarker tables (ASCT+B), and design of 3D organ reference library models

Presenting:
Ellen M. Quardokus (CODCC, Indiana University)

April 27, 2022
Learning Objective

Learning Objective: Learn how to author and use ASCT+B tables and 3D reference organs efficiently
Background—Structuring knowledge

What does an ASCT+B table do?

Standardize how information is captured, formatted, labeled

Knowledge about organs, anatomical structures, cell types, biomarker sets that uniquely define cell types

Ontologies like the multi-species Uber Anatomy (Uberon) and Cell Ontology (CL) capture nomenclature, synonyms, descriptions, relationships between entities, provenance for knowledge, assigns unique ID for this unit of knowledge

Structured knowledge unifies nomenclature that describe datasets so we are all speaking in the same language

Unstructured Knowledge sources

~80% of biomedical knowledge
ASCT+B Working Group Meetings

- **WG Charter**: https://docs.google.com/document/d/1KxcZfKiDtSYx0BrCr9NucFaixPTdMixvlohZe6BkzY/edit
- **WG Expert Registration**: https://iu.co1.qualtrics.com/jfe/form/SV_bpaBhIr8XfdiNRH
- **WG Listserv**: https://lists.hubmapconsortium.org/g/ASCT-B
- **WG Slack**: https://asct-b.slack.com
- **2022 Meetings**: First Wednesdays, 11-noon ET: June 1, July 6, ...
What are ASCT+B tables?

ASCT+B tables capture:
- organ name,
- anatomical structures,
- cell types,
- biomarker sets that uniquely define cell types (differentially expressed genes, proteins, proteoforms, lipids, metabolites)
- Citations providing evidence for relationships

Ontologies like multi-species Uber Anatomy (Uberon) and Cell Ontology (CL) capture:
- nomenclature,
- synonyms,
- relationships between entities,
- Descriptions of the entities
- provenance for knowledge,
- assigns unique ID for this unit of knowledge to unite information

Ontologies do NOT have everything we need yet to map every AS+CT+B sets:
The ASCT+B WG facilitates bringing SMEs together with ontology experts to capture new knowledge. This knowledge is directly used in our Tissue Registration and our Data Exploration user interfaces.
ASCT+B Reporter Vis of ASCT+B tables

https://hubmapconsortium.github.io/ccf-asct-reporter
Metrics for ASCT+B tables can be found using the downloadable reports feature.

We are adding report types that researchers may find helpful for different applications.

This information has been useful for another working group for developing organ mapping antibody panels (OMAPs).
3D reference models

- Custom built by our medical illustrator (current Heidi Schlehlein; former: Kristen Brown, NIAID) using Visible Human Project Male and Female data based on Subject Matter Expert input
- Support the Tissue Registration (RUI) and Exploration User Interfaces
- Anatomical structures are labeled with ontology IDs which are used by the RUI during collision detection that brings the ontology labels with the registered block coordinates when tissue blocks are registered
- 3D reference models and ontology labels are also used for Dataset exploration in EUI.

NEW: 2D functional tissue unit (FTU) illustrations

- Custom built by our medical illustrator Rachel Bajema based on Subject Matter Expert input through ASCT+B table knowledge capture.
- Support Dataset exploration in EUI at microanatomical levels.
- These will have clickable cell types and structures for cell type exploration.
Workflow: CCF Registration to CCF Exploration

Partonomy
- kidney
  - kidney capsule
  - cortex of kidney
  - outer cortex of kidney
  - renal medulla
  - inner medulla
  - renal column
  - renal pyramid

Knowledge Graph
- UBERON
- FMA
- CL
- KTAO

Exploration User Interface (EUI)

CCF Info Portal
- Anatomical Structures and Cell Types (ASCT)

TMC Data

IEC Data Store

Semantic Annotation via 3D Object Collision
- Cortex
- Medullary Pyramids
- Calyces

Registration User Interface (RUI)

Clickable FTU illustrations for exploring microanatomy and cell types

3D Object Library
- Cortex
- Medullary Pyramids
- Calyces
Where do I start? Relevant SOPs and Videos

- SOP: Authoring ASCT+B Tables (Updated: February 1, 2022)
  https://zenodo.org/record/5944386#.YfnrsPnMJaq
- ASCT+B Reporter Visualization Tool
  https://hubmapconsortium.github.io/ccf-asct-reporter/
- SOP: 3D Reference Object Approval (Updated: February 1, 2022)
  https://zenodo.org/record/5944197#.YfntS_lKhaQ
- SOP: Construction of Organ Mapping Antibody Panels for Multiplexed Antibody-Based Imaging of Human Tissues
  https://doi.org/10.5281/zenodo.5749883 (with Affinity Reagents WG)
- Visible Human Massive Open Online Course (VHMOOC):
  https://expand.iu.edu/browse/sice/cns/courses/hubmap-visible-human-mooc
Ways you can help

Use your cell phone camera or a QR code reader to go directly to these website urls
Questions: email infoccf@indiana.edu

Scan me to register
As an Expert

VHMOOC Scan Me
Learn more about HuBMAP

CCF Portal Scan Me

EUI Scan Me
Explore HuBMAP data

RUI Scan Me
Register Tissue Blocks