Anatomical Structures, Cell Types and Biomarkers (ASCT+B) Tables: Design & Usage

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HTAN All-hands Meeting, Cross-Consortium Presentation

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Fig. 3 | Map generation and assembly across cellular and spatial scales. HuBMAP aims to produce an atlas in which users can refer to a histological slide from a specific part of an organ and, in any given cell, understand its contents on multiple 'omic levels—genomic, epigenomic, transcriptomic, proteomic, and/or metabolomic. To achieve these ends, centres will apply a combination of imaging, 'omics and mass spectrometry techniques to specimens collected in a reproducible manner from specific sites in the body. These data will be then be integrated to arrive at a high-resolution, high-content three-dimensional map for any given tissue. To ensure inter-individual differences will not be confounded with collection heterogeneity, a robust CCF will be developed.
What is a CCF?

The Common Coordinate System (CCF) consists of ontologies and reference object libraries, computer software (e.g., user interfaces), and training materials that

- enable biomedical experts to semantically annotate tissue samples and to precisely describe their locations in the human body ("registration"),
- align multi-modal tissue data extracted from different individuals to a reference coordinate system ("mapping") and,
- provide tools for searching and browsing HuBMAP data at multiple levels, from the whole body down to single cells ("exploration").

See [CCF Portal](http://example.com/ccfportal) and [SciTech Webinar from Oct 12, 2020](http://example.com/webinar).
## ASCT+B Tables

Anatomical Structures, Cell Types, and Biomarkers (ASCT+B) tables aim to capture the partonomy of anatomical structures, cell types, and major biomarkers (e.g., gene, protein, lipid or metabolic markers).

<table>
<thead>
<tr>
<th>Structure/Region</th>
<th>Substructure/Subregion</th>
<th>Cell Type</th>
<th>Subset of Marker Genes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Corpuscle</td>
<td>Bowman’s Capsule</td>
<td>Parietal epithelial cell</td>
<td><em>CRB2</em>, <em>CLDN1</em></td>
</tr>
<tr>
<td></td>
<td>Glomerulus</td>
<td>Podocyte</td>
<td><em>NPHS2</em>, <em>PODXL</em>, <em>NPHS1</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Capillary Endothelial Cell</td>
<td><em>EHD3</em>, <em>EMCN</em>, <em>HECW2</em>,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>FLT1</em>, <em>AQP1</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mesangial Cell</td>
<td><em>POSTN</em>, <em>PIEZ02</em>, <em>ROBO1</em>,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><em>ITGAB</em></td>
</tr>
</tbody>
</table>

Partial ASCT Table from
ASCT+B Table Usage

ASCT+B tables guide CCF Ontology and 3D Reference Object Library design that semantically name and spatially place tissue data from different donors into one CCF (i.e., mapping).

<table>
<thead>
<tr>
<th>ASCT Table</th>
<th>Ontology</th>
<th>3D Reference Object Library</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structure/Region</td>
<td>Sub structure/Sub region</td>
<td>Cell Type</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Corpuscle</td>
<td>Tissue blocks are registered into the CCF using the Registration User Interface (RUI), and they can be explored via the Exploration User Interface (EUI).</td>
<td></td>
</tr>
<tr>
<td>Proximal Tubule</td>
<td>Proximal Tubule Epithelial Cell (general)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Proximal Convoluted Tubule Epithelial Cell Segment 1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Proximal Tubule Epithelial Cell Segment 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Proximal Tubule Epithelial Cell Segment 2</td>
<td></td>
</tr>
<tr>
<td>Loop of Henle, Proximal &amp;</td>
<td>Descending Thin Limb Cell (general)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ascending Thin Limb Cell (general)</td>
<td></td>
</tr>
<tr>
<td>Loop of Henle, Distal &amp;</td>
<td>Thin &amp; Ascending Limb Cell (general)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cortical TAL Cell</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Medullary TAL Cell</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TAL Macula Densa Cell</td>
<td></td>
</tr>
<tr>
<td>Loop of Henle, Distal &amp;</td>
<td>Distal Convoluted Tubule Cell (general)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DCT Type 1 Cell</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DCT Type 2 Cell</td>
<td></td>
</tr>
<tr>
<td>Loop of Henle, Collecting</td>
<td>Collecting Tubule Cell (general)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cortical Principal Cell</td>
<td></td>
</tr>
</tbody>
</table>
AS terms linked to Uberon

CT terms linked to CL

https://hubmapconsortium.github.io/ccf-asct-reporter
CCF Registration User Interface (RUI) v1.0.0

New Features:

- Organ carousel with 4 reference organs
- Support for tissue extraction sites
- Expanded ontology
- Semantic annotation via collision detection & manual annotation
- Support for non-HuBMAP usage

AS terms from ASCT+B

https://hubmap-ccf-ui.netlify.app/rui/
Azimuth
App for reference-based single-cell analysis

https://satijalab.org/azimuth

CT terms from ASCT+B
linked to Cell Ontology
CCF Exploration User Interface (EUI)

https://portal.hubmapconsortium.org/ccf-eui

AS terms from ASCT+B
Human Reference CCF Atlas: Checklist

Common Coordinate Framework (CCF) Design:
1. Make sure the Anatomical Structures, Cell Types, and Biomarkers (ASCT+B) that you use/submit are listed in the **ASCT+B tables**. The tables are authored and reviewed by an international team of anatomists, pathologists, physicians, and other experts, see this [SOP](#).
2. Spatially register all tissue samples using the CCF Registration User Interface (RUI) in the Ingest Portal. End of October 2020, kidney, spleen, heart, colon registration are supported. For other organs, see [SOP](#).
3. After submitting data, review data in the **CCF Exploration User Interface** and make sure spatial, semantic, and other metadata are correct.
4. For functional tissue unit (FTU) segmentation, submit a list of FTUs for your organ(s) and make sure FTU names and all relevant cell types (CT) are captured in the ASCT+B table. Use assays/biomarkers (B) that make it possible to identify FTUs—initially manually, later automatically. Submit tissue with 1000 FTUs manually identified FTUs.
5. In support of the **Vasculature-based CCF**, provide cell segmentation data for blood vessels and different cell types.

For questions, email [infoccf@indiana.edu](mailto:infoccf@indiana.edu).
ASCT+B Table Working Group

Meetings take place monthly to review and approve tables, formalize and unify table design language, discuss and expand table usage, see [WG Charter](#).

Next meetings: Dec 3, 1:30p EST. In 2021: Jan 6, Feb 3, March 3, 11a-noon ET. Please [register](#) to receive invites and updates.
Public private partnership panel with NIH, Google, Broad, Lilly and potentially Roche.

Hacking the Kidney Hackathon

PARTICIPATION OPENS NOV 5TH, 10:00 AM EST

TOTAL PRIZE MONEY $60,000 TO BE AWARDED TO THE WINNING TEAMS!

OUR SPONSORS

Google, Deloitte, CAS, Roche, Pistoia Alliance, Maven Wave, DEERFIELD

https://innovationdigi.com/hubmap-hackathon
HuBMAP: Hacking the Kidney
Identify glomeruli in human kidney tissue images

Our best estimates show there are over 7 billion people on the planet and 300 billion stars in the Milky Way. By comparison, the adult human body contains 37 trillion cells. To determine the function and relationship among these cells is a monumental undertaking. Many areas of human health would be impacted if we better understand cellular activity. A problem with this much data is a great match for the Kaggle community.

Just as the Human Genome Project mapped the entirety of human DNA, the Human BioMolecular Atlas Program (HuBMAP) is a major endeavor. Sponsored by the National Institutes of Health (NIH), HuBMAP is working to catalyze the development of a framework for mapping the human body at a level of glomeruli functional tissue units for the first time in history. Hoping to become one of the world’s largest collaborative biological projects, HuBMAP aims to be an open map of the human body at the cellular level.

This competition, "Hacking the Kidney," starts by mapping the human kidney at single cell resolution.

Your challenge is to detect functional tissue units (FTUs) across different tissue preparation pipelines. An FTU is defined as a “three-dimensional block of cells centered around a capillary, such that each cell in this block is within diffusion distance from any other cell in the same block” (de Bono, 2013). The goal of this competition is the implementation of a successful and robust glomeruli FTU detector.

You will also have the opportunity to present your findings to a panel of judges for additional consideration. Successful submissions will construct the tools, resources, and cell atlases needed to determine how the relationships between cells can affect the health of an individual.

Advancements in HuBMAP will accelerate the world’s understanding of the relationships between cell and tissue organization and function and human health. These datasets and insights can be used by researchers in cell and tissue anatomy, pharmaceutical companies to develop therapies, or even parents to show their children the magnitude of the human body.
PAS stained tissue sections provided by TMC-VU. Cortex segmentation (left) and glomeruli segmentations (right)
**Small Intestine**
Provided by Jeanne Shen, TMC-Stanford

Red brown: Small intestinal villus epithelium  
**Green: Small intestinal crypt**  
Brown: Small intestinal Brunner's gland

**Kidney**
Provided by Heath Patterson, TMC-VU

Black: Glomeruli

Used in HuBMAP Kaggle Competition
Thanks go to all the patients that agreed to volunteer healthy tissue and open use of their data.
Q&A