Mapping The Human Body At Single Cell Resolution: Developing The Human Reference Atlas

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Background

- Advances in single cell analysis make it possible to capture the spatial location of single cells and to develop a Common Coordinate Framework (CCF) for the healthy human adult body, see **Fig. 1**.
- The Human Reference Atlas (HRA) [1] represents Anatomical Structures, Cell Types, plus Biomarkers (ASCT+B) linked to 3D representations of anatomical structures and 2D illustrations of Functional Tissue Units (FTUs), all of which are mapped to Uberon and Cell ontology IDs, if available, see **Fig. 2**.

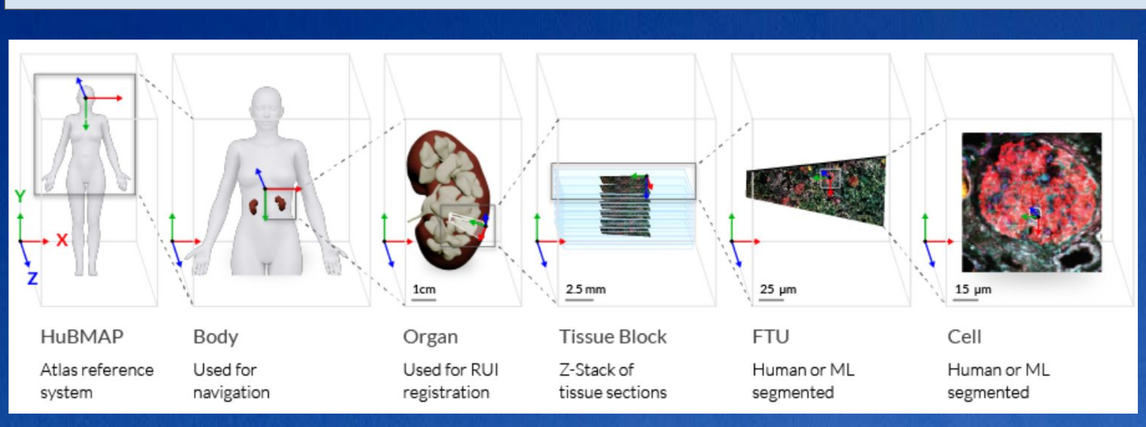


Figure 1: Example of kidney in Common Coordinate Framework (CCF).

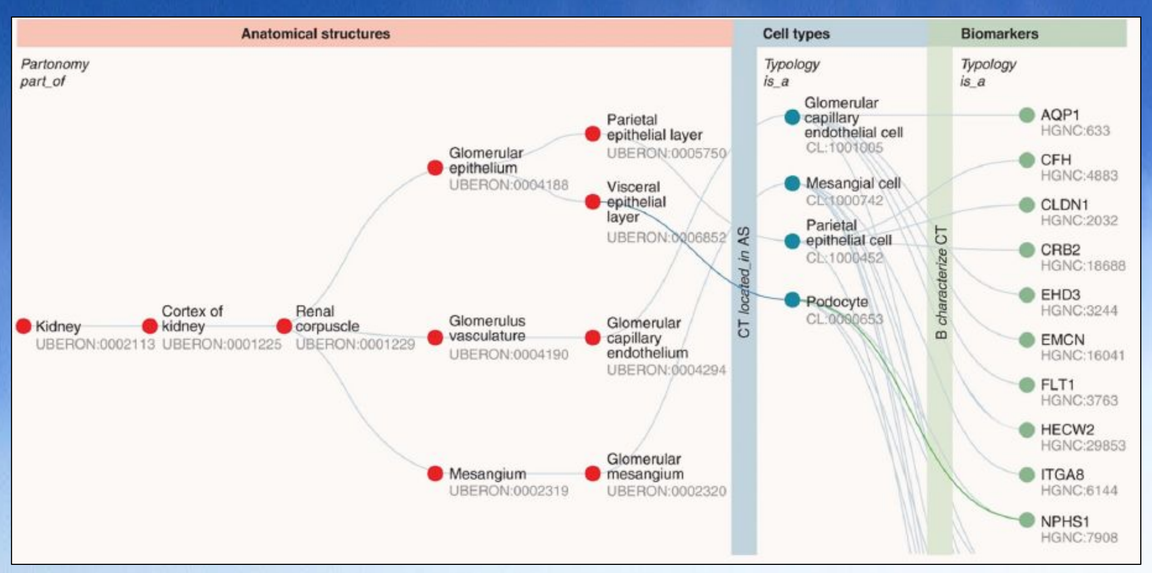
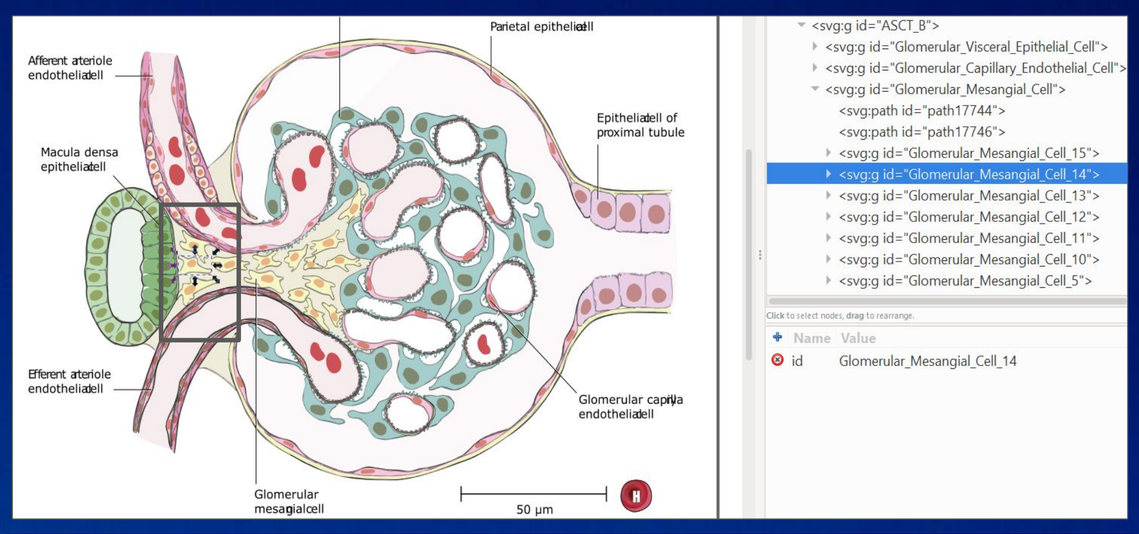


Figure 2: Example of kidney ASCT+B Table in Reporter Tool.

Functional Tissue Units

- Functional Tissue Units (FTUs) are defined as the smallest level of tissue organization that performs the organ's major physiological function, see **Fig. 3** for examples
- FTU illustrations are created by professional illustrators in close collaboration with organ experts and inspired by parallel efforts such as the Kidney Tissue Atlas [3].

HuBMAP CCF Portal:
Number of ASCT+B tables: 26
Total number of 3D organ models: 53
Total number of 2D FTUs: 8
https://hubmapconsortium.github.io/ccf



anatomical_structure_of	source_spatial_entity	node_name	label	OntologyID	representation_of	svg file of single 2DFTU	exist_asctb	type	REF/1	RI
#FTURenalCorpuscle	#2DRefObjects	Glomerular_Mesangial	glomerular mesang	CL:1000742	http://purl.obolibrary.o	renal_corpuscle_kidney	1	CT		
#FTURenalCorpuscle	#2DRefObjects	Glomerular_Mesangial	glomerular mesang	CL:1000742	http://purl.obolibrary.o	renal_corpuscle_kidney	1	CT		
#FTURenalCorpuscle	#2DRefObjects	Glomerular_Mesangial	glomerular mesang	CL:1000742	http://purl.obolibrary.o	renal_corpuscle_kidney	1	CT		

Figure 3: Example of kidney FTU Illustration (top left), SVG file (top right), and crosswalk to kidney ASCT+B Table (bottom).
All FTU illustrations are available at https://hubmapconsortium.github.io/ccf/pages/ccf-2d-reference-library.hml.

2D Cell Segmentation

- Manual segmentation of FTU illustrations uses Adobe Illustrator.
- Algorithmic cell segmentation uses the Watershed machine learning algorithm [4], see **Fig. 4.**

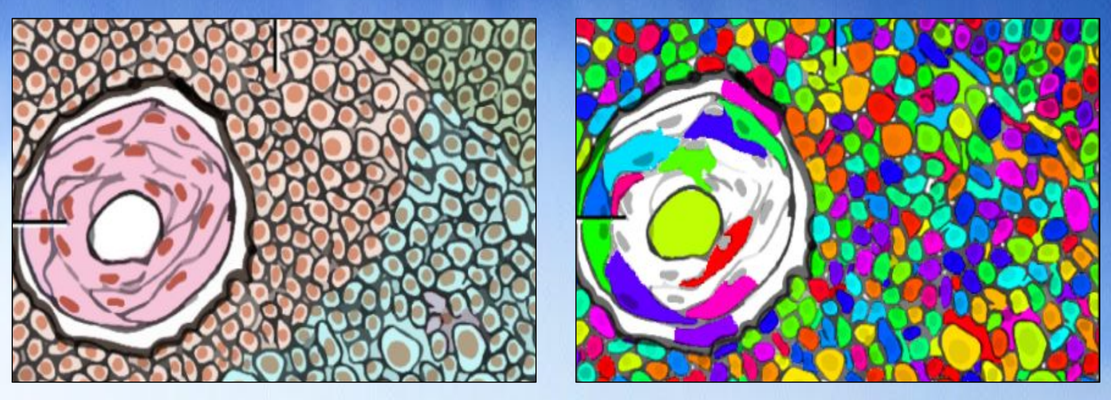


Figure 4: FTU illustration by human expert of cells in white pulp of spleen. Algorithm input of nucleus/cytoplasm positions and diameters is shown on left and algorithm output of segmentation mask is given on right.

Discussion

- 20 FTUs for the 4th HRA release will become available in December 2022.
- Blood Vasculature will be added to FTUs and linked to ASCT+B tables at single-cell level.
- 2D-cell segmentation will be automatized using machine learning.
- FTU SVGs will be linked to experimental data analogous to the KPMP Kidney Tissue Atlas Explorer [3].

References

1. Börner, K., Teichmann, S.A., Quardokus, E.M. et al. Anatomical structures, cell types and biomarkers of the Human Reference Atlas. *Nat Cell Biol* 23, 1117–1128 (2021). https://doi.org/10.1038/s41556-021-00788-6.
2. Anatomical Structure, Cell Types, and Biomarkers Reporter. CCF Portal. (https://hubmapconsortium.github.io/ccf-asct-reporter.)
3. The Kidney Tissue Atlas Explorer (https://atlas.kpmp.org/explorer).
4. Stringer, C., Wang, T., Michaelos, M. et al. Cellpose: A generalist algorithm for cellular segmentation. *Nat Methods* 18, 100–106 (2021).

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