Nomenclature versioning in MTG and DLPFC

During our analysis, the SEA-AD team has worked to improve the accuracy of cell supertype classifications by aligning them more closely with established brain cell types. As a result, we've updated the names of five supertypes between initial data release and publication of Gabitto, Travaglini, et al 2024. While these changes have been incorporated into some of our tools and resources, others may still reflect the older names. The table below provides a mapping between the old and new names for these five supertypes. All other supertypes have consistent names across all public files.

SEA-AD official name Version 2024-02-13	Initial name Version 2023-05-05
Pericyte_1	VLMC_2
SMC-SEAAD	VLMC_2_1-SEAAD
Pericyte_2-SEAAD	VLMC_2_2-SEAAD
Lymphocyte	Micro-PVM_2_2-SEAAD
Monocyte	Micro-PVM_1_1-SEAAD

More specifically, the Comparative Viewer and CELLxGENE resource include the initial name, while all other tools (ABC Atlas, Gene Expression Trajectory Viewer, MapMyCells, and Annotation Comparison Explorer) and our manuscript use the official name.

Extension of the taxonomy to additional brain regions

The MTG/PFC taxonomy described above was subsequently extended to additional brain regions as part of the SEA-AD multi-region study (Travaglini, Gabitto, Ding, et al 2026). That release encompasses ten neo- and allocortical regions spanning the cortical arc of AD neuropathological staging: the previously released middle temporal gyrus (MTG) and prefrontal cortex (PFC/A9), plus hippocampus (HIP), medial entorhinal cortex (MEC), lateral entorhinal cortex (LEC), inferior temporal gyrus (ITG), superior temporal gyrus (STG), frontal insula (FI), angular gyrus (AnG), and primary visual cortex (V1C). All 84 donors from the previous MTG release had their MTG, DFC, and MEC profiled, while the remaining regions were profiled in a subset of 43 donors without severe comorbidities (the "AD Spectrum" donors).

Rather than building a separate taxonomy for each region, nuclei from every region were mapped to the existing SEA-AD MTG/PFC taxonomy to hierarchically assign a major cell "Class", a "Subclass" beneath it, and a fine-grained "Supertype" below that, using the same deep-learning mapping approach used to build the MTG taxonomy. The taxonomy was then expanded to incorporate types that were not present in the previous MTG/PFC taxonomy, principally region-specific excitatory populations in regions such as HIP, MEC, and V1C. In total, the taxonomy was expanded with five new subclasses corresponding to regionally restricted populations (EC-IT, Sub-CA1, CA2–4, DG, and Ependymal) and 70 new molecularly distinct cell types, so that every nucleus maps to one of 207 finely resolved cell types organized into 28 subclasses and 3 higher-level classes.

Cell type labels that are common across regions are retained, so a label such as Sst_25 still refers to the same kind of cell type in the updated taxonomy, preserving consistent nomenclature across SEA-AD dataset releases (including the five renamed supertypes described above). As part of the re-mapping, a very small number of MTG and DFC nuclei were assigned a new cell type annotation, the supertype color palette was updated to account for the new types, and a small number of additional nuclei that had not been flagged by the initial quality control cutoffs were flagged and removed. The latent space and UMAP projection released with the multi-region data are computed from the entire multi-region dataset rather than from a single region, and are now (or will soon be) included in the ABC Atlas.

Derivation of the caudate nucleus taxonomy

The SEA-AD caudate nucleus (Ca) study (Kana et al 2026) uses a taxonomy derived from two sources rather than a single MTG-based reference. Because the caudate is a basal ganglia structure whose neuronal composition differs substantially from cortex, its cell types were assigned using a combined reference that pairs the SEA-AD MTG taxonomy with the BRAIN Initiative Cell Atlas Network's (BICAN) Human and Mammalian Brain Cell Atlas (HMBA) cross-species consensus taxonomy of the basal ganglia (Johansen, Fu, et al. 2025).

In practice, the two taxonomies contribute to different parts of the caudate. Neuronal populations specific to the basal ganglia – principally the lateral ganglionic eminence (LGE)-derived medium spiny neurons that have no cortical counterpart – are labeled using the HMBA basal ganglia taxonomy, while non-neuronal populations, which are largely shared with cortex, are labeled using the existing SEA-AD MTG taxonomy. A subset of inhibitory interneuron populations (SST+ CHODL+ and a subset of VIP+) are shared across both taxonomies. To build the combined reference, the SEA-AD MTG taxonomy and the human caudate (head and body) portion of the HMBA basal ganglia taxonomy were integrated, the overlap between the two atlases was quantified per cluster, and HMBA cells that fell in well-mixed clusters were relabeled with their corresponding SEA-AD labels while the remaining basal-ganglia-specific clusters retained their HMBA labels. This combined SEA-AD MTG/HMBA reference was then used to annotate the caudate nuclei. Consequently, the caudate taxonomy inherits cortical (MTG-derived) labels for its shared non-neuronal and select interneuron types and basal-ganglia (BICAN/HMBA-derived) labels for its specialized neuronal types.