

Supplementary File 1:

	DOI	Code/Model
Lewis2010 (iNL403)	DOI: 10.1038/nbt.1711	Model: Supplementary Model 1
Sertbaş2014 (iMS570)	DOI: 10.1016/j.fob.2014.05.006	Model: http://www.systemsbioinformatics.info.tr/downloads/iMS570_cobra_with_constraints.xml
Özcan2016	DOI: 10.3389/fnins.2016.00156	Model: Supplementary MateriaDataSheet2.ZIP (iMS570g_growth_implemented.xml)
MartínJiménez2017	DOI: 10.3389/fnagi.2017.00023	Model: https://www.ebi.ac.uk/biomodels/MODEL1608180000
Thiele2020	DOI: 10.15252/msb.20198982	Model: https://github.com/opencobra/COBRA.papers/tree/master/2020_WholeBodyModelling/SuppliedResults , OrganAtlas_Harvey.mat, OrganAtlas_Harvetta.mat
Baloni2020	DOI: 10.1016/j.xcrm.2020.100138	Model and code: https://github.com/PriceLab/Bile_acid_AD
EcheverriPeña2021 (Neuro-Glia_GEM)	DOI: 10.1016/j.heliyon.2021.e07671	Model: https://github.com/dasalazarb/Neuro-Glia_GEM/blob/main/Neuron_Glia_GEM.xml Code: https://github.com/dasalazarb/Neuro-Glia_GEM
Lam2021	DOI: 10.3390/biomedicines9101310	Models: https://github.com/SimonLammmm/ad-pd-retinoid/tree/main/supplementary-files/SuppFile2_iADPD Code: https://github.com/SimonLammmm/ad-pd-retinoid
Larsson2020	DOI: 10.3389/fgene.2020.00381	Patient-derived models: https://www.ebi.ac.uk/biomodels/MODEL1707110000 Code: https://github.com/idalarsson/GEM-for-GBM

Table S1: Public availability of brain genome-scale metabolic models

Model	Transcriptomic	Proteomic	Metabolomic	Other data used for manual curation/ validation
Lewis2010 (iNL403)	-Microarray data of AD (GSE5281, n=161)	-Human Protein Reference Database -HINV -HUPO brain proteome project		-Literature information for transport reactions for each compartment - Constraints for neuron cell types.
Sertbaş2014 (iMS570)	-Microarray data of six NDD (GSE26927, n=118)			-Literature-derived constraints for a healthy brain

Özcan2016	-Microarray data of three GBM cell lines (GSE13041-GPL570, n=54; GSE13041-GPL96, n=191; GSE13276, n=15)			-Curated growth objective function -Literature-derived constraints for 26 reactions for GBM
MartínJiménez2017	-Microarray data of foetal cortical astrocytes (GSE53404, n=3)			-Literature-derived constraints for healthy astrocyte exchange reactions
Thiele2020		-Human Proteome Map - HPA	- Human Metabolome Database and other resources.	- Organ-specific reactions from literature
Baloni2020	- RNA-Seq data for brain regions from post-mortem of normal and AD patients (https://www.synapse.org/#!Synapse:syn2580853/).	- HPA	- Metabolomics of primary and secondary bile acids from the post-mortem brain samples (https://www.synapse.org/#!Synapse:syn10235594 , n=111)	- BBB reactions from Thiele2020 - Constraints from Lewis2010
EcheverriPeña2021 (<i>Neuro-Glia_GEM</i>)				- Reactions of the sulfatide degradation from the myelin band
Lam2021	- RNA-Seq of healthy brain from HPA & GTEx - CAGE expression of healthy brain samples from FANTOM5 - RNA-Seq of AD and PD brain samples from Rajkumar dataset and Zhang/Zheng dataset - Single-cell RNA-Seq of AD and PD brain samples from ROSMAP			- Constraints from Baloni2020
Larsson2020	- RNAseq of TCGA-GBM (n=166)			- CRISPR-Cas9 data for GBM - Healthy brain GEM from HMA

Table S2: Detailed type of OMICs for the data used in the brain metabolic models and the number of samples.

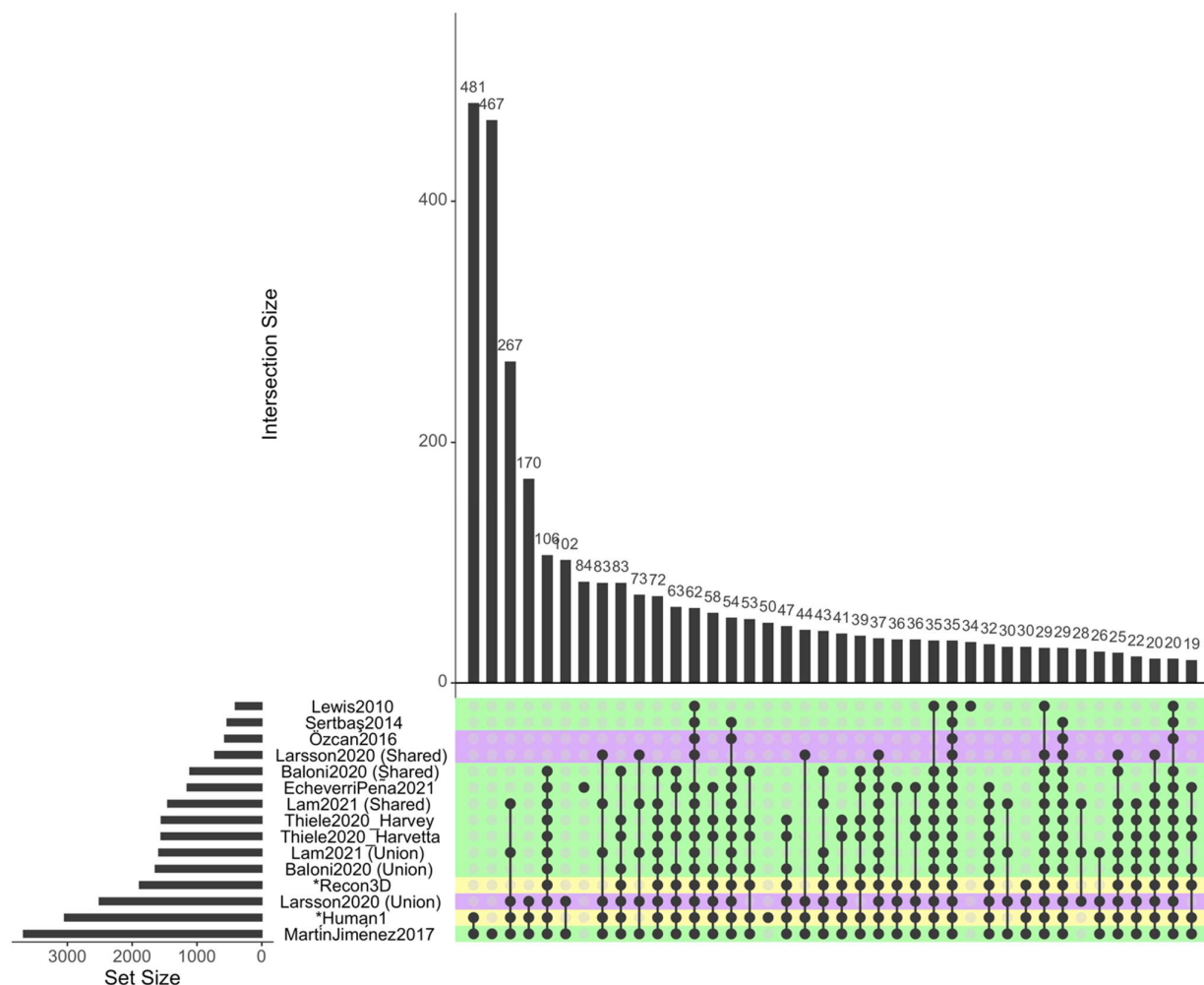


Figure S1: Low overlap between the genes included in the brain genome-scale metabolic models:

To evaluate the overlap between the genes of the brain models, the intersection of these genes was counted in an UpSet plot. Brain models were retrieved as explained in **Supplementary 1, Table S1** in addition to two consistent generic models (Human1 and Recon3D). For studies that have more than two models (**Baloni2020**, **Larsson2020** and **Lam2021**), the intersection and the union of all the model's genes were appended into two gene lists. The y-axis represents the number of intersected genes between different sets on the x-axis, and the "Set Size" represents the total number of genes in that set.