

Biomarker-guided translation of brain imaging into disease pathway models

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Supplementary Table 1. Imaging information extracted from the literature and manually corrected and categorized into disease stages for Alzheimer's disease

Disease stage	Imaging technique	Regions affected (PMIDs)
Severe AD	DTI	Cingulum (23011219, 18219201) Thalamus (20157252, 17444598) Hippocampus (17444598) Temporal lobe (20157252, 19406355)
	fMRI	Cerebral cortex (20656843, 18945600) Hippocampus (22766738, 20656843) Temporal lobe (19747163, 18400793, 20656843)
	MRI	Temporal lobe (23561509, 9341577, 22717328, 18765650, 11511703, 16797786, 17533169, 7480379, 8648331, 8059176, 19228848, 10077306, 15374058) Hippocampus (22414571, 8986328, 2103656, 22717328, 11511703, 8239283, 20656843, 16797786, 8648331, 10662960, 8059176, 11160463, 17178234)
	PET	Posterior cingulate (21971455, 11960900, 10843517, 16407119) Temporal lobe (21853308, 21971455, 9339671, 11511703, 2674513, 3512063, 12812674)
Moderate AD	DTI	-
	fMRI	-
	MRI	Cingulate cortex (20872914)
	PET	Prefrontal cortex (19617327) Posterior cingulate (12593416)
Early (mild) AD/MCI	DTI	Corpus callosum (22545143, 21182970, 22256149, 20368633, 20164572, 20847446) Temporal lobe (20615058, 16801648, 17905894)
	fMRI	Temporal lobe (16842102, 22815064, 22216234, 16997428, 17021177, 20656843, 18928090, 16087905) Precuneus cortex (15954139, 22456451)

	MRI	<p>Temporal lobe/hippocampus (22766164 , 22354229, 23071546, 22986782, 22994551, 22922563, 20443979, 21264200, 18021379, 16321457, 14663029, 12438466, 9920358, 16286546, 16396228, 12397142, 21116054, 21808873, 20938031, 20705437, 9305341, 20847406, 19901171, 12215875, 11511703, 20541374, 18809228, 7477910, 22300935, 21437929, 16511646, 10911878, 9219745, 8648331, 20143386, 19259976, 17399959, 17434756, 15883311, 12849541, 11388566, 10802781, 19280688, 17960142, 11971085, 11930016, 15734360, 15123335, 12094908, 23303849, 22308496, 22759884, 12595205, 22095921, 19835661, 16125145, 11942499, 10563634, 20375138, 17936858, 9442345, 19698521, 8624070, 8108005, 1779721, 8788077, 22078174)</p> <p>Entorhinal cortex (22986782, 21494034, 19073399, 17923632, 7991745, 18809228, 15925102, 22300935, 10911878, 15883311, 12849541, 10802781, 16470518, 11971085, 15123335, 22815064, 9562498)</p>
	PET	<p>Temporal lobe (23179062, 18325543, 17475957, 16300967, 11511703, 15800784, 9219745, 15747152, 3512063, 22592018, 10559570)</p> <p>Precuneus cortex (22926714, 19073399, 12593416, 20430977, 21700583, 19412465, 18021379, 18191617, 23112868, 16709580, 15616176)</p>

Supplementary Table 2. List of potential Alzheimer's biomarkers that were retrieved and extracted from the PubMed abstracts and mapped onto the temporal lobe model

Potential biomarker	Biomarker evidence in the literature	Reference
CFLAR	Decreased expression in AD brains	PMID: 11178964 PMID: 12608703 PMID: 12885274
PSEN1	Decreased expression in AD hippocampus	PMID: 9067452 PMID: 10754226
PSEN2	Reduced expression in AD neurons	PMID: 8918895 PMID: 9067452 PMID: 10891593
FASLG	Increased activity in AD hippocampus	PMID: 12742739 PMID: 12738769 PMID: 11113303
RELA	Significant increase in the immunoreactivities of NF- κ Bp65 in the hippocampus and the temporal and frontal cortices of AD brains	PMID: 8905182 PMID: 9406869 PMID: 22177240 PMID: 9775392 PMID: 21592054
FAS	Increased expression in AD hippocampus; increased serum levels; increased expression in T cells of AD patients	PMID: 9395128 PMID: 16736246 PMID: 12391607 PMID: 11893840 PMID: 15538542
CASP6	Increased expression in AD temporal cortex	PMID: 15277226 PMID: 23020846
CASP8	Significant increase in the enzymatic activity	PMID: 11741396 PMID: 15473998 PMID: 12183349 PMID: 16772874
CASP3	Increase in active caspase-3 expression levels	PMID: 10550301 PMID: 18818379 PMID: 19774677

		PMID: 10079193 PMID: 23546897 PMID: 23181759
PARP1	Enhanced PARP activity in Alzheimer's disease	PMID: 10071053 PMID: 12738769
BCL2	Marked expression in AD hippocampus	PMID: 17967740 PMID: 10406024 PMID: 11311497 PMID: 9560019 PMID: 8730800 PMID: 8593592
DAXX	Increased expression in AD hippocampus	PMID: 12391607 PMID: 15176485