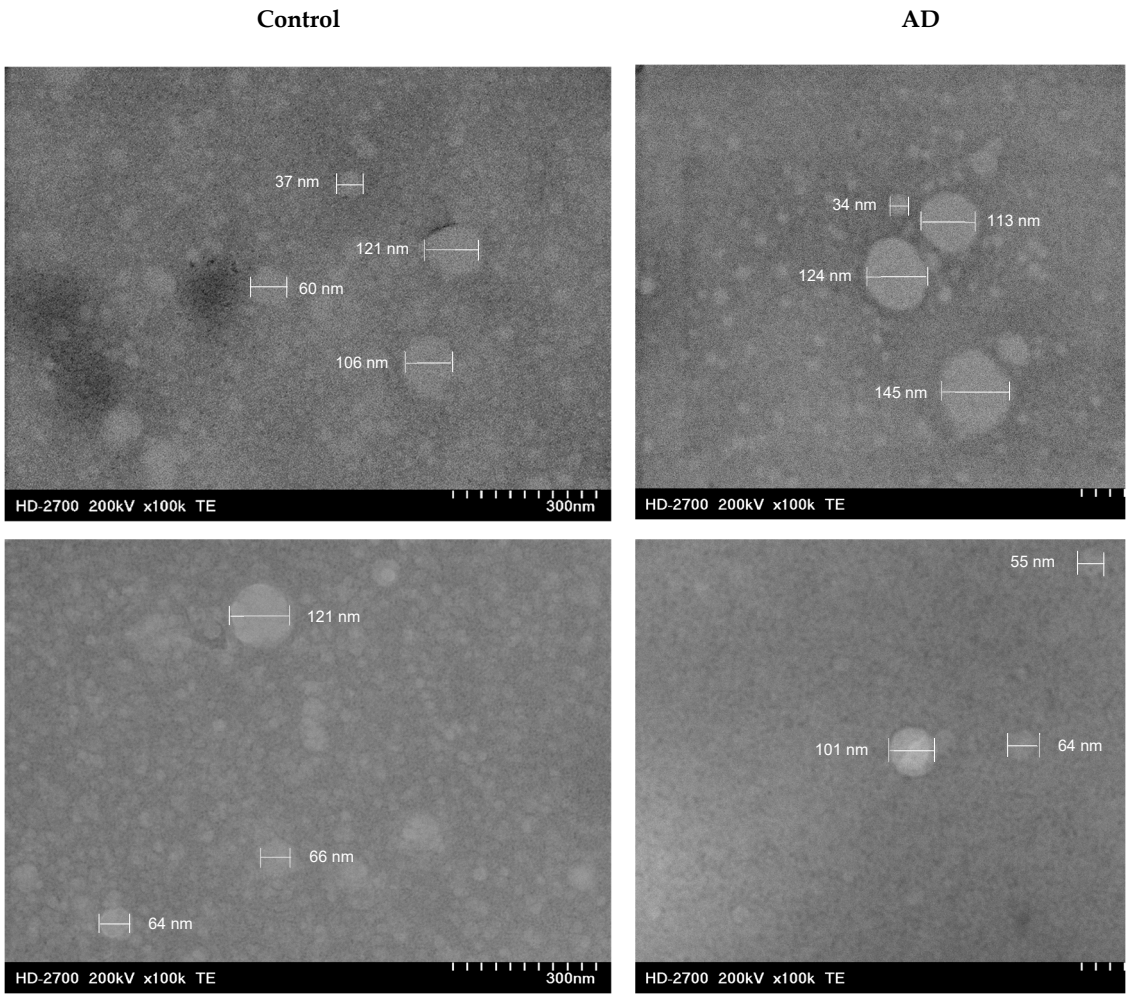
Manuscript: Phosphoproteome Microarray Analysis of Extracellular Particles as a Tool to Explore Novel Biomarker Candidates for Alzheimer's Disease

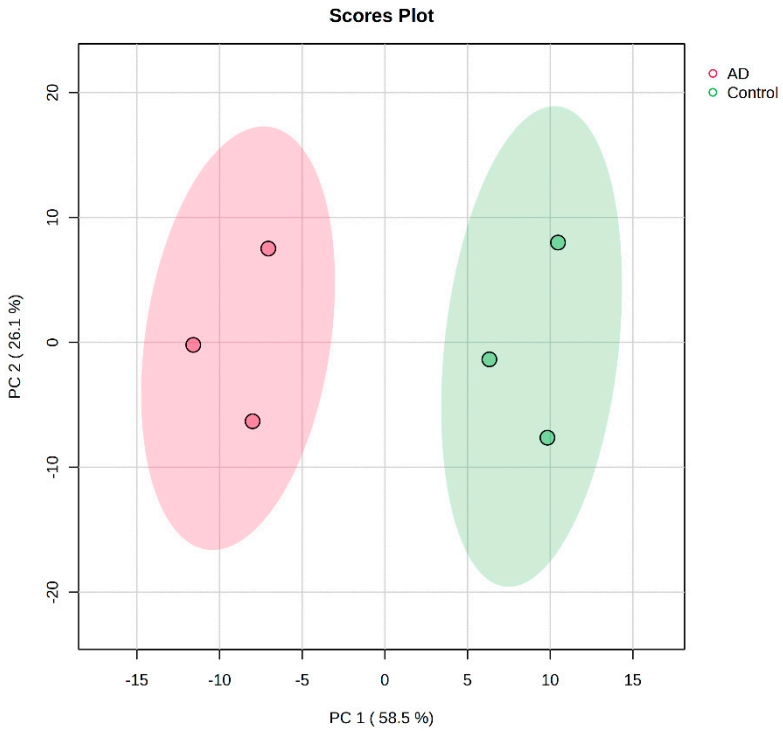
Supplementary Materials

Supplementary Figure S1



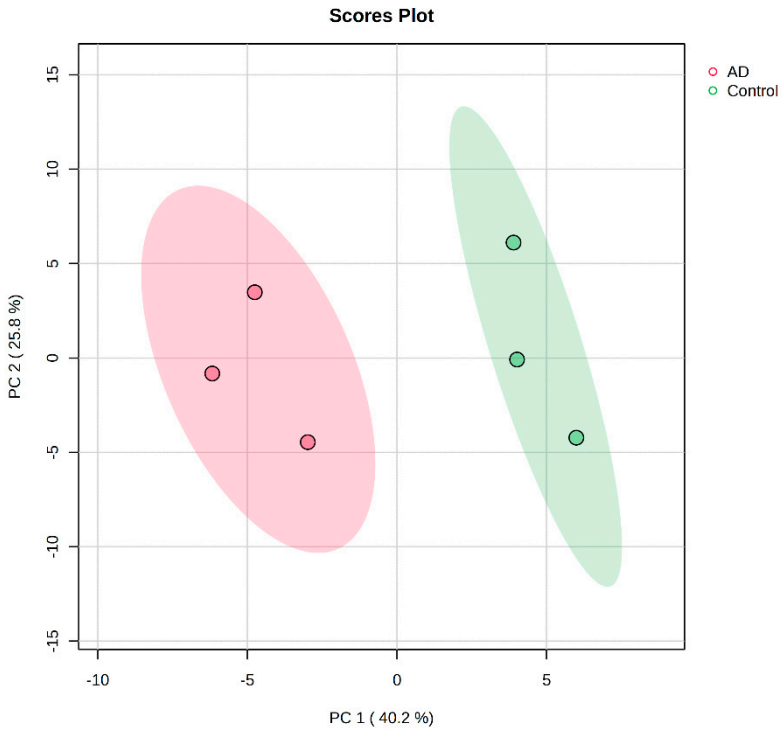
Supplementary Figure S1. TEM image frames for Controls and AD cases. Large size entire TEM frames depicted in the manuscript Figure 1 for Controls (**A**) or AD cases (**B**).

Supplementary Figure S2



Supplementary Figure S2. PCA of bdEPs proteome significantly different in AD cases. A PCA score plot was performed to assess the discrimination between Controls (C1-C3 batches) and AD cases (AD1-AD3 batches). In score plot, the green and pink areas represent the 95% confidence region.

Supplementary Figure S3



Supplementary Figure S3. PCA of bdEPs phosphoproteins that significantly changed in AD cases. A PCA score plot was performed to assess the discrimination between Controls (C1-C3 batches) and AD cases (AD1-AD3 batches). In score plot, the green and pink areas represent the 95% confidence region.

Supplementary Tables

Supplementary Table S1

Supplementary Table S1. Demographics and clinical data of Controls and AD cases. Data distribution was assessed by Shapiro–Wilk and age; cognitive tests and CSF biomarker concentrations were compared using the non-parametric Kruskal–Wallis test.

	Controls			**AD cases**			**Controls vs AD cases**
	Batch C1	**Batch C2**	**Batch C3**	**Batch AD1**	**Batch AD2**	**Batch AD3**	**P-value**
Age (mean±SD)	64.40±10.33	66.00±5.57	66.40±12.88	65.60±10.48	67.80±11.54	67.60±9.53	0.994
CDT (points) (mean±SD)	1.00±0.00	1.67±1.16	1.80±0.84	2.40±1.34	3.25±0.50	3.40±1.14	0.040*
MMSE scores (mean±SD)	23.75±3.30	29.00±1.73	28.5±1.73	22.40±4.62	21.60±4.62	24.00±2.92	0.031**
CSF Aβ1-42 (ng/mL) (mean±SD)	1198.0±136.8	1388±638.2	1437.0±593.0	602.8±100.7	606.8±134.5	618.8±135.9	0.002
CSF Aβ1-40 (ng/mL) (mean±SD)	8879±2395	10216±2387	11219±3559	13034±2610	12676±5932	13183±5481	0.354
CSF Aβ1-42/1-40 (mean±SD)	1.40±0.24	1.35±0.58	1.31±0.34	0.47±0.11	0.54±0.33	0.50±0.11	0.001
CSF P-tau 181 (pg/mL) (mean±SD)	42.40±7.50	42.60±14.64	52.00±16.93	100.60±39.83	100.6±34.63	74.80±25.12	0.003
CSF T-tau (pg/mL) (mean±SD)	221.20±44.03	242.80±90.26	193.00±82.40	985.00±598.30	838.80±359.00	472.60±170.40	<0.001

Abbreviations: AD, Alzheimer's disease cases; C, Controls; CDT, Clock-Drawing Test; CSF, Cerebrospinal fluid; MMSE, Mini-Mental State Examination; SD, Standard deviation. * Data available for n=11 Controls and n=15 ADs. ** Data available for n=11 Controls and n=14 ADs.

Supplementary Table S2. Total proteome significantly changed between Controls and AD cases. Proteins detected with pan- and/or phosphosite-specific antibodies were included. Average signal intensity and standard deviation were calculated for the 3 batches of Controls (C1-C3) or the 3 batches of AD cases (AD1-AD3). A total of 150 proteins were found to be significantly altered in AD. The changes in signal intensity between Controls and AD cases are presented as the percentage change from Controls (%CFC). The protein signal decrease in AD cases is represented in blue, and the signal increase is represented in light pink. Signal intensities obtained for each target between 3 batches of age-matched Controls and 3 batches of AD cases were compared using a paired t-test.

					Controls			AD				
Target Name	**Antibody P-Site**	**Cat No.**	**UniProt ID**	**Gene name**	**Mean**	**S.D.**	**S.D. %**	**Mean**	**S.D.**	**S.D. %**	**%CFC**	**p-Value**
MFN2 (Marf; CPRP1)	Pan	NN290-1	O95140	MFN2	2410	315	13	1032	226	22	-57	0.009
ATF2 (CRE-BP1)	Pan	9222	P15336	ATF2	317	65	20	141	42	30	-56	0.020
GRIN1 (NMDAR1; GPRIN1)	Pan	NN264-1	Q7Z2K8	GPRIN1	1467	88	6	770	143	19	-48	0.020
HSP40 (DNAJB1; DNAJ1; HDJ1; HSPF1)	Pan	NN057-2	P25685	DNAJB1	1660	242	15	935	172	18	-44	0.005
Arrestin b	Pan	610551	P49407	ARRB1	2216	403	18	1318	116	9	-40	0.049
PAK3 (PAKb)	Pan	sc-1871	O75914	PAK3	478	47	10	313	7	2	-34	0.048
RPS6	S235+ S236	PN685	P62753	RPS6	3221	994	31	2116	650	31	-34	0.049
Tubulin-alpha (TUBA1B)	Pan	NN380-1	P68363	TUBA1B	248	13	5	168	8	5	-32	0.009
NPAS4 (BHLHE79; NXF; PASD10)	Pan	NN299-1	Q8IUM7	NPAS4	2046	114	6	1415	189	13	-31	0.008
mTOR (FRAP)	Pan	NK116-4	P42345	MTOR	15776	353	2	11148	1119	10	-29	0.024
TARDBP	S409+ S410	PN674	Q13148	TARDBP	1994	259	13	1424	160	11	-29	0.030
S100A9	Pan	NN459-3	P06702	S100A9	3462	573	17	2497	402	16	-28	0.019
Fer (TYK3)	Pan	AP7704b	P16591	FER	159	13	8	116	5	4	-27	0.039
MERTK (MER)	Y753	PK704	Q12866	MERTK	1919	141	7	1400	84	6	-27	0.028
TrkA (NGFR; NTRK1)	T496	sc-8058	P04629	NTRK1	35	5	14	26	3	12	-27	0.024
HGS (Hrs)	Y216	PN519	O14964	HGS	3876	260	7	2893	66	2	-25	0.049
EphB2	Y780	PK610	P29323	EPHB2	3076	403	13	2298	330	14	-25	0.015
STRAD (STLK5)	Pan	sc-515635	Q7RTN6	STRADA	85	30	36	63	25	39	-25	0.037
I1PP2A (ANP32A/B; PHAPI)	Pan	B13007	P39687	ANP32A	3182	232	7	2390	213	9	-25	0.026

EphA8	Pan	AP7613a	P29322	EPHA8	1102	110	10	831	24	3	-25	0.050
VIM (Vimentin)	S34	KAM-CC246	P08670	VIM	388	30	8	294	41	14	-24	0.019
Huntingtin (HTT)	S421	PN829	P42858	HTT	3191	378	12	2413	355	15	-24	0.009
MuSK	Pan	sc-6010	O15146	MUSK	1914	73	4	1452	54	4	-24	0.021
WNK1	Pan+ S382	PK855	Q9H4A3	WNK1	583	60	10	443	20	5	-24	0.044
PTPN6 (PTP1C; SH-PTP1)	Pan	sc-7289	P29350	PTPN6	109	19	17	83	22	27	-24	0.029
14-3-3 (KCIP-1)	Pan	NN441-2	P31946	YWHAB	3359	90	3	2564	174	7	-24	0.006
ERK1 (MAPK3; ERT2)	Pan	NK055-1	P27361	MAPK3	24963	1145	5	19112	623	3	-23	0.031
ERF	T526	PN584	P50548	ERF	7199	526	7	5558	391	7	-23	0.011
DUSP2 (PAC1)	Pan	NP008-4	Q05923	DUSP2	11746	411	3	9107	835	9	-22	0.048
eIF4E	Pan	610270	P06730	EIF4E	3389	87	3	2628	53	2	-22	0.011
TAO1 (TAOK1)	Y309	PK827	Q7L7X3	TAOK1	2974	522	18	2307	363	16	-22	0.031
FGFR4	Pan	NK239-1	P22455	FGFR4	1899	166	9	1479	191	13	-22	0.012
CDK8	Pan	sc-1521	P49336	CDK8	1331	48	4	1041	111	11	-22	0.035
LEF1	Pan+ T155	PN616	Q9UJU2	LEF1	1602	116	7	1256	77	6	-22	0.035
PTPN6 (PTP1C; SH-PTP1)	Pan	P17320 610126	P29350	PTPN6	606	86	14	476	46	10	-21	0.045
IRF3	T135	PN610	Q14653	IRF3	3146	84	3	2476	178	7	-21	0.043
Jun (c-Jun)	Pan	sc-74543	P05412	JUN	34	8	25	27	8	32	-21	0.021
ErbB3 (HER3)	Pan	NK231-2	P21860	ERBB3	6350	445	7	5046	610	12	-21	0.012
PTPN11 (PTP1D; PTP2C; SHP2; SHPTP2; Syp)	Pan	P54420 610622	Q06124	PTPN11	995	114	12	792	73	9	-20	0.039
DUSP6	Pan	NP040-3	Q16828	DUSP6	5591	454	8	4461	284	6	-20	0.012
Raf1 (c-Raf; RafC)	Pan	NK156-5	P04049	RAF1	4479	731	16	3621	566	16	-19	0.026
TRPV4	Pan	NN464-2	Q9HBA0	TRPV4	915	90	10	741	60	8	-19	0.016
MEKK2 (MAP3K2)	Pan	NK108-5	Q9Y2U5	MAP3K2	24101	303	1	19506	362	2	-19	0.010
STAT1	Pan+ S727	PN667	P42224	STAT1	11021	382	3	8946	321	4	-19	0.017
HRAS (H-Ras)	Y157	PN755	P01112	HRAS	6258	166	3	5086	273	5	-19	0.009
Met (HGF receptor)	Pan	NK110-2	P08581	MET	19637	743	4	15992	337	2	-19	0.027
ATG2A	Pan	NN209-1	Q2TAZ0	ATG2A	1806	179	10	1471	145	10	-19	0.028
FOXO1A (FKHR; FKHRL1)	S256	11115	Q12778	FOXO1	725	97	13	592	58	10	-18	0.040
PRKAR2A (PRKAR2; PKR2)	Pan	sc-137220	P13861	PRKAR2A	20	3	16	17	4	24	-18	0.038
TRIM28 (TIF1B)	S473	PK833	Q13263	TRIM28	838	169	20	693	152	22	-17	0.015
KCNQ2	Pan	NN275-1	O43526	KCNQ2	514	61	12	425	52	12	-17	0.022

14-3-3 (KCIP-1)	Pan	sc-1657	P31946	YWHAB	968	82	8	808	61	7	-17	0.029
Plk1 (PLK)	Pan	NK145-2	P53350	PLK1	28422	514	2	23786	866	4	-16	0.012
CDC34	Pan	C25820 610250	P49427	CDC34	5955	427	7	4989	274	6	-16	0.016
HRAS (H-Ras)	Pan	NN281-3	P01112	HRAS	6418	586	9	5410	509	9	-16	0.045
ATM	Pan	NK230-1	Q13315	ATM	15436	902	6	13015	987	8	-16	0.002
CDK15 (PFTAIRE2; ALS2CR7)	Pan	NK004-2	Q96Q40	CDK15	8166	171	2	6892	174	3	-16	0.006
ADRA2C (ADRA2L2; ADRA2RL2)	Pan	NN190-2	P18825	ADRA2C	212	107	50	180	99	55	-15	0.034
DLG4 (PSD95)	Pan	NN142	P78352	DLG4	9953	1528	15	8471	1219	14	-15	0.042
NRP1	Pan	NN604-2	O14786	NRP1	20438	1125	6	17403	643	4	-15	0.013
Hsc70 (HSPA8; Hsc70; HSP73; HSPA10)	Pan	NN060-12	P11142	HSPA8	1769	71	4	1511	110	7	-15	0.034
MEKK1 (MAP3K1)	Pan	KAP-SA001	Q13233	MAP3K1	2784	383	14	2382	454	19	-14	0.033
PML	Pan+ S518	PN641	P29590	PML	12768	110	1	10932	287	3	-14	0.015
RIOK2	S332+ S335+ S337	PK890	Q9BVS4	RIOK2	11389	756	7	9766	439	4	-14	0.019
IKZF1	Y413	PN707	Q13422	IKZF1	642	59	9	556	42	8	-13	0.027
Met (HGF receptor)	Pan	NK110-4	P08581	MET	10649	265	2	9226	543	6	-13	0.025
CAMK2d	Pan	NK019-3	Q13557	CAMK2D	13916	237	2	12127	298	2	-13	0.016
RSK1 (RPS6KA1; p90RSK)	S221	PK804	Q15418	RPS6KA1	2242	251	11	1954	321	16	-13	0.050
PPP3CC (Calcinerin Ag)	Pan+ S463	PP506	P48454	PPP3CC	4161	784	19	3629	678	19	-13	0.024
ERK1 (MAPK3; ERT2)	S283	PK879	P27361	MAPK3	18022	354	2	15718	949	6	-13	0.044
SRPK1	S222	PK819	Q96SB4	SRPK1	392	49	13	342	47	14	-13	0.001
Huntingtin (HTT)	Pan+ S417+ S419	PN828	P42858	HTT	4394	146	3	3842	38	1	-13	0.040
CDK15 (PFTAIRE2; ALS2CR7)	Pan	NK004-3	Q96Q40	CDK15	6910	406	6	6080	249	4	-12	0.035
Tyro3	Y685+ Y686	PK848	Q06418	TYRO3	609	56	9	536	42	8	-12	0.025
CD63	Pan	ab68418	P08962	CD63	9594	494	5	8494	702	8	-11	0.018
MEKK6 (MAP3K6; ASK2)	Pan	NK225-2	O95382	MAP3K6	5787	372	6	5137	457	9	-11	0.049
ATR	Pan	NK237-1	Q13535	ATR	8122	220	3	7240	183	3	-11	0.012
MLK4 (MAP3K21)	Pan	NK280-1	Q5TCX8	MAP3K21	11348	136	1	10170	196	2	-10	0.018

p70S6K (S6Ka; RPS6KB1)	Pan	NK223-4	P23443	RPS6KB1	10262	812	8	9208	630	7	-10	0.027
CDK1 (CDC2)	T161	11134	P06493	CDK1	5966	344	6	5425	212	4	-9	0.042
UT-A1 (Slc14a2; HUT2; UT2)	Pan	NN355-1	Q15849	SLC14A2	342	3	1	311	9	3	-9	0.028
DNAPK (PRKDC)	Pan	NK048-6	P78527	PRKDC	27666	1476	5	25164	988	4	-9	0.040
CDK5	Y15	PK570	Q00535	CDK5	8322	240	3	7582	243	3	-9	0.023
Cas-L	Pan+ Y166	PN505	Q14511	NEDD9	9706	525	5	8867	611	7	-9	0.006
CDK1 (CDC2)	Pan	sc-954	P06493	CDK1	11465	227	2	10489	329	3	-9	0.037
CDK6	Pan	C150M	Q00534	CDK6	9012	375	4	8284	530	6	-8	0.025
ILK1 (ILK)	Pan	KAP-ST203	Q13418	ILK	225	8	4	207	4	2	-8	0.031
NFKB1	S903	PN634	P19838	NFKB1	18069	559	3	16636	160	1	-8	0.042
ERK1 (MAPK3; ERT2)	Pan	NK055-2	P27361	MAPK3	6499	246	4	5984	393	7	-8	0.046
MKK3 (MAP2K3; MEK3)	Pan	NK101-6	P46734	MAP2K3	18500	73	0	17095	45	0	-8	0.001
Raf1 (c-Raf; RafC)	Pan	NK155-5	P04049	RAF1	8251	743	9	7653	678	9	-7	0.035
CDK7 (MO15)	Pan	NK030-1	P50613	CDK7	6901	470	7	6413	573	9	-7	0.024
ErbB2 (Neu; HER2)	Y1248	PK613	P04626	ERBB2	9188	417	5	8540	303	4	-7	0.020
AMPKa2 (PRKAA2)	S377	PK522	P54646	PRKAA2	6756	188	3	6291	198	3	-7	0.028
PRMT5	T634	PN549	O14744	PRMT5	21174	422	2	20052	738	4	-5	0.041
DNMT3A	S105	PN746	Q9Y6K1	DNMT3A	16328	276	2	15547	58	0	-5	0.041
GTF2I	S412	PN602	P78347	GTF2I	10249	459	4	9917	420	4	-3	0.047
TP53 (p53)	S6+S9	PN637	P04637	TP53	19420	566	3	18849	623	3	-3	0.032
CDK1 (CDC2)	T161	PK561	P06493	CDK1	5565	425	8	5408	395	7	-3	0.018
CDC25B	Pan	NP002-4	P30305	CDC25B	11204	158	1	10926	130	1	-2	0.006
Fyn	Pan	NK065-2	P06241	FYN	6521	112	2	6401	92	1	-2	0.017
MRLC1	T19+S20	PN836	P24844	MYL9	15972	386	2	16236	349	2	2	0.020
IRS1	Y612	44-816G	P35568	IRS1	423	31	7	433	34	8	2	0.050
NOS3 (eNOS)	T1175+ S1177	PN712	P29474	NOS3	19919	540	3	20431	453	2	3	0.030
FOXO3 (FKHRL1)	S253	PN821	O43524	FOXO3	11084	150	1	11504	199	2	4	0.032
GABBR1 (GABA B Receptor 1; GPRC3A)	T873	PN796	Q9UBS5	GABBR1	8232	166	2	8556	120	1	4	0.029
PTPRK (PTP-kappa)	Y916	PP524	Q15262	PTPRK	15708	348	2	16527	510	3	5	0.029
GCN2 (EIF2AK4)	Pan	AP8062a	Q9P2K8	EIF2AK4	85	8	9	89	8	9	5	0.023

ERK5 (MAPK7; BMK)	Pan	sc-398015	Q13164	MAPK7	9154	493	5	9678	373	4	6	0.026
Met (HGF receptor)	Pan	NK110-3	P08581	MET	2163	112	5	2327	154	7	8	0.034
PPP5C (PP5C; PP5; PPT)	Y119	PP507	P53041	PPP5C	13138	1194	9	14258	1204	8	9	0.016
EGFR (ErbB1)	Y1172	XBP-4085	P00533	EGFR	2840	50	2	3090	103	3	9	0.022
HMGCR	S872	PN705	P04035	HMGCR	9269	500	5	10108	371	4	9	0.019
PTPN1 (PTP1B)	Y46	PP533	P18031	PTPN1	14053	341	2	15347	674	4	9	0.040
IKKb (IkBKB; IKKB)	Pan	KAP-TF118	O14920	IKBKB	3043	68	2	3324	96	3	9	0.016
CDK11B (PITSLRE; p58/GTA; CLK-1)	Pan	sc-928	P21127	CDK11B	2497	169	7	2736	163	6	10	0.044
ZAP70	Pan	Z24820 610240	P43403	ZAP70	122	7	5	134	3	2	10	0.042
MEK5 (MAP2K5; MKK5)	S311	PK699	Q13163	MAP2K5	14896	619	4	16430	586	4	10	0.002
Mos	Pan	NK112	P00540	MOS	5186	219	4	5722	72	1	10	0.049
GIT1	Y545	PN517	Q9Y2X7	GIT1	2208	165	7	2436	187	8	10	0.039
p73 (TP73)	Y99	PN861	O15350	TP73	5285	130	2	5849	94	2	11	0.035
PU.1	S146	PN647	P17947	SPI1	1781	106	6	1976	161	8	11	0.038
FAK (PTK2)	S722	sc-16662-R	Q05397	PTK2	3661	419	11	4064	482	12	11	0.035
GLUT2 (SLC2A2)	Pan	NN262-1	P11168	SLC2A2	2520	155	6	2800	198	7	11	0.017
PPP2R4 (PP2A subunit B'; PTPA)	Y223	PP550	Q15257	PTPA	10131	96	1	11281	357	3	11	0.042
PPPM1B (PP2Cb; PPM1B)	Y367	PP540	O75688	PPM1B	4732	402	9	5271	559	11	11	0.046
ACTB (beta-actin)	Y53	PN501	P60709	ACTB	3865	212	5	4357	89	2	13	0.036
RSK1 (RPS6KA1; p90RSK)	S380	PK805	Q15418	RPS6KA1	1520	176	12	1714	145	8	13	0.013
PCTK2 (PCTAIRE2; CDK17))	S180	PK756	Q00537	CDK17	5889	803	14	6646	825	12	13	0.016
CLK3	Pan	AP7531a	P49761	CLK3	36	11	29	41	9	23	13	0.039
Tec	Y519	PK829	P42680	TEC	847	38	5	960	61	6	13	0.041
PAK2 (PAKg)	Pan	sc-1872	Q13177	PAK2	2865	153	5	3255	119	4	14	0.030
TERF1	T371	PN675	P54274	TERF1	1211	169	14	1380	131	10	14	0.025
Nek2	Pan	71-3700	P51955	NEK2	375	18	5	428	31	7	14	0.036
Gab1	Y406	PN516	Q13480	GAB1	1956	344	18	2238	430	19	14	0.043
ATR	S435+ S436	PK528	Q13535	ATR	14817	1393	9	16973	1108	7	15	0.024
Nek2	S171	PK732	P51955	NEK2	13503	703	5	15538	1042	7	15	0.017

UGDH	Y352	PN782	O60701	UGDH	2910	238	8	3348	139	4	15	0.031
SGK1	Pan	NK294-1	O00141	SGK1	752	67	9	876	81	9	16	0.008
Met (HGF receptor)	S1236	PK705	P08581	MET	3216	86	3	3761	164	4	17	0.049
MAFG	Pan+ S124	PN617	O15525	MAFG	3341	153	5	3931	216	5	18	0.012
FLT3 (STK1; CD135)	Pan	NK240-2	P36888	FLT3	5109	60	1	6012	156	3	18	0.006
IkBa (MAD3; IkBa)	Pan	DB075	P25963	NFKBIA	1290	40	3	1527	54	4	18	0.036
KRS2	Pan	33-3000	Q13043	STK4	3980	286	7	4715	381	8	18	0.021
MOR1 (mu opiod receptor)	T372+ S377+ T378	PN802	P35372	OPRM1	4856	252	5	5786	88	2	19	0.020
HIPK2	Pan	NK272-1	Q9H2X6	HIPK2	2872	229	8	3427	318	9	19	0.045
ARID1A	S363	PN740	O14497	ARID1A	9211	866	9	11025	546	5	20	0.026
BLNK	Y84	44-220	Q8WV28	BLNK	4451	749	17	5334	485	9	20	0.043
ERK1 (MAPK3; ERT2)	Pan	NK055-4	P27361	MAPK3	2085	71	3	2524	63	2	21	0.002
PKN1 (PRK1)	T774	PK781	Q16512	PKN1	3972	629	16	4813	407	8	21	0.034
p38a MAPK (MAPK14; CSBP; MXI2; SAPK2a)	Pan	NK120-4	Q16539	MAPK14	1021	134	13	1259	185	15	23	0.031
GSK3b	Pan	KAP-ST002	P49841	GSK3B	2105	182	9	2602	196	8	24	0.000
NMDAR2A NMDA (GRIN2A; Glutamate [NMDA] receptor subunit epsilon-1)	Pan	NN297-1	Q12879	GRIN2A	673	90	13	835	87	10	24	0.001
VACAMKL	Y245	PK892	Q8NCB2	CAMKV	541	45	8	671	71	11	24	0.020
SMARCA4	S610+ S613	PN726	P51532	SMARCA4	1067	146	14	1327	96	7	24	0.019
GATA3	S369	PN702	P23771	GATA3	1914	141	7	2416	213	9	26	0.012
PTPN12 (PTP-PEST; PTPG1)	Pan	P105M	Q05209	PTPN12	158	39	24	201	39	19	27	0.015
Nur77	Pan+ S351	PN636	P22736	NR4A1	2995	71	2	3835	195	5	28	0.033
VEGFR2 (KDR)	Y1059	11531	P35968	KDR	186	20	11	242	33	13	30	0.030
TrkB (NTRK2)	Y706+ Y707	PK917	Q16620	NTRK2	1708	65	4	2247	100	4	32	0.039
AMPKa1 (PRKAA1)	T183+ S184	PK521	Q13131	PRKAA1	4926	499	10	6566	564	9	33	0.039
HGK (MAP4K4; NIK; ZC1)	Pan	NK300-1	O95819	MAP4K4	295	16	5	393	34	9	34	0.019
MEK5 (MAP2K5; MKK5)	Pan	sc-1287	Q13163	MAP2K5	2772	339	12	3752	156	4	35	0.031

JAK1	Pan	sc-277	P23458	JAK1	259	13	5	356	11	3	37	0.028
NLK	Pan	sc-8211	Q9UBE8	NLK	317	45	14	447	30	7	41	0.013
Ankyrin (ANK1; Ankyrin-R)	Pan	NN195-1	P16157	ANK1	482	59	12	683	94	14	42	0.043
WNK4 (PRKWNK4)	Pan	NK255-1	Q96J92	WNK4	1563	241	15	2373	362	15	52	0.034
TAO1 (TAOK1)	S181	PK826	Q7L7X3	TAOK1	262	17	6	419	50	12	60	0.023
GRK1 (Rhodopsin kinase)	Pan	sc-8004	Q15835	GRK1	288	20	7	615	49	8	114	0.017

Supplementary Table S3. Phosphoproteins that significantly changed between Controls and AD cases. Only proteins detected with phosphosite-specific antibodies were included. Average signal intensity and standard deviation were calculated for the 3 batches of Controls (C1-C3) or the 3 batches of AD cases (AD1-AD3). The changes in signal intensity between Controls and AD cases are presented as the percentage change from Controls (%CFC). Signal decrease in AD cases is represented in blue, and the signal increase is represented in light pink. Signal intensities obtained for each target between 3 batches of age-matched Controls and 3 batches of AD cases were compared using a paired t-test.

					Controls			AD				
Target Name	**Antibody P-Site**	**Cat No.**	**UniProt ID**	**Gene name**	**Mean**	**SD**	**SD %**	**Mean**	**SD**	**SD %**	**%CFC**	**p-Value**
RPS6	S235+S236	PN685	P62753	RPS6	3221	994	31	2116	650	31	-34	0.049
TARDBP	S409+S410	PN674	Q13148	TARDBP	1994	259	13	1424	160	11	-29	0.030
MERTK (MER)	Y753	PK704	Q12866	MERTK	1919	141	7	1400	84	6	-27	0.028
TrkA (NGFR; NTRK1)	T496	sc-8058	P04629	NTRK1	35	5	14	26	3	12	-27	0.024
HGS (Hrs)	Y216	PN519	O14964	HGS	3876	260	7	2893	66	2	-25	0.049
EphB2	Y780	PK610	P29323	EPHB2	3076	403	13	2298	330	14	-25	0.015
VIM (Vimentin)	S34	KAM-CC246	P08670	VIM	388	30	8	294	41	14	-24	0.019
Huntingtin (HTT)	S421	PN829	P42858	HTT	3191	378	12	2413	355	15	-24	0.009
ERF	T526	PN584	P50548	ERF	7199	526	7	5558	391	7	-23	0.011
TAO1 (TAOK1)	Y309	PK827	Q7L7X3	TAOK1	2974	522	18	2307	363	16	-22	0.031
IRF3	T135	PN610	Q14653	IRF3	3146	84	3	2476	178	7	-21	0.043
HRAS (H-Ras)	Y157	PN755	P01112	HRAS	6258	166	3	5086	273	5	-19	0.009
FOXO1A (FKHR; FKHRL1)	S256	11115	Q12778	FOXO1	725	97	13	592	58	10	-18	0.040
TRIM28 (TIF1B)	S473	PK833	Q13263	TRIM28	838	169	20	693	152	22	-17	0.015
RIOK2	S332+S335+S337	PK890	Q9BVS4	RIOK2	11389	756	7	9766	439	4	-14	0.019
IKZF1	Y413	PN707	Q13422	IKZF1	642	59	9	556	42	8	-13	0.027
RSK1 (RPS6KA1; p90RSK)	S221	PK804	Q15418	RPS6KA1	2242	251	11	1954	321	16	-13	0.050
ERK1 (MAPK3; ERT2)	S283	PK879	P27361	MAPK3	18022	354	2	15718	949	6	-13	0.044
SRPK1	S222	PK819	Q96SB4	SRPK1	392	49	13	342	47	14	-13	0.001
Tyro3	Y685+Y686	PK848	Q06418	TYRO3	609	56	9	536	42	8	-12	0.025

CDK1 (CDC2)	T161	11134	P06493	CDK1	5966	344	6	5425	212	4	-9	0.042
CDK5	Y15	PK570	Q00535	CDK5	8322	240	3	7582	243	3	-9	0.023
NFKB1	S903	PN634	P19838	NFKB1	18069	559	3	16636	160	1	-8	0.042
ErbB2 (Neu; HER2)	Y1248	PK613	P04626	ERBB2	9188	417	5	8540	303	4	-7	0.020
AMPKa2 (PRKAA2)	S377	PK522	P54646	PRKAA2	6756	188	3	6291	198	3	-7	0.028
PRMT5	T634	PN549	O14744	PRMT5	21174	422	2	20052	738	4	-5	0.041
DNMT3A	S105	PN746	Q9Y6K1	DNMT3A	16328	276	2	15547	58	0	-5	0.041
GTF2I	S412	PN602	P78347	GTF2I	10249	459	4	9917	420	4	-3	0.047
TP53 (p53)	S6+S9	PN637	P04637	TP53	19420	566	3	18849	623	3	-3	0.032
CDK1 (CDC2)	T161	PK561	P06493	CDK1	5565	425	8	5408	395	7	-3	0.018
MRLC1	T19+S20	PN836	P24844	MYL9	15972	386	2	16236	349	2	2	0.020
IRS1	Y612	44-816G	P35568	IRS1	423	31	7	433	34	8	2	0.050
NOS3 (eNOS)	T1175+ S1177	PN712	P29474	NOS3	19919	540	3	20431	453	2	3	0.030
FOXO3 (FKHRL1)	S253	PN821	O43524	FOXO3	11084	150	1	11504	199	2	4	0.032
GABBR1 (GABA B Receptor 1; GPRC3A)	T873	PN796	Q9UBS5	GABBR1	8232	166	2	8556	120	1	4	0.029
PTPRK (PTP-kappa)	Y916	PP524	Q15262	PTPRK	15708	348	2	16527	510	3	5	0.029
PPP5C (PP5C; PP5; PPT)	Y119	PP507	P53041	PPP5C	13138	1194	9	14258	1204	8	9	0.016
EGFR (ErbB1)	Y1172	XBP-4085	P00533	EGFR	2840	50	2	3090	103	3	9	0.022
HMGCR	S872	PN705	P04035	HMGCR	9269	500	5	10108	371	4	9	0.019
PTPN1 (PTP1B)	Y46	PP533	P18031	PTPN1	14053	341	2	15347	674	4	9	0.040
MEK5 (MAP2K5; MKK5)	S311	PK699	Q13163	MAP2K5	14896	619	4	16430	586	4	10	0.002
GIT1	Y545	PN517	Q9Y2X7	GIT1	2208	165	7	2436	187	8	10	0.039
p73 (TP73)	Y99	PN861	O15350	TP73	5285	130	2	5849	94	2	11	0.035
PU.1	S146	PN647	P17947	SPI1	1781	106	6	1976	161	8	11	0.038
FAK (PTK2)	S722	sc-16662-R	Q05397	PTK2	3661	419	11	4064	482	12	11	0.035
PPP2R4 (PP2A	Y223	PP550	Q15257	PTPA	10131	96	1	11281	357	3	11	0.042

subunit B'; PTPA)												
PPPM1B (PP2Cb; PPM1B)	Y367	PP540	O75688	PPM1B	4732	402	9	5271	559	11	11	0.046
ACTB (beta-actin)	Y53	PN501	P60709	ACTB	3865	212	5	4357	89	2	13	0.036
RSK1 (RPS6KA1; p90RSK)	S380	PK805	Q15418	RPS6KA1	1520	176	12	1714	145	8	13	0.013
PCTK2 (PCTAIRE 2; CDK17))	S180	PK756	Q00537	CDK17	5889	803	14	6646	825	12	13	0.016
Tec	Y519	PK829	P42680	TEC	847	38	5	960	61	6	13	0.041
TERF1	T371	PN675	P54274	TERF1	1211	169	14	1380	131	10	14	0.025
Gab1	Y406	PN516	Q13480	GAB1	1956	344	18	2238	430	19	14	0.043
ATR	S435+S436	PK528	Q13535	ATR	14817	1393	9	16973	1108	7	15	0.024
Nek2	S171	PK732	P51955	NEK2	13503	703	5	15538	1042	7	15	0.017
UGDH	Y352	PN782	O60701	UGDH	2910	238	8	3348	139	4	15	0.031
Met (HGF receptor)	S1236	PK705	P08581	MET	3216	86	3	3761	164	4	17	0.049
MOR1 (mu opiod receptor)	T372+S377+ T378	PN802	P35372	OPRM1	4856	252	5	5786	88	2	19	0.020
ARID1A	S363	PN740	O14497	ARID1A	9211	866	9	11025	546	5	20	0.026
BLNK	Y84	44-220	Q8WV28	BLNK	4451	749	17	5334	485	9	20	0.043
PKN1 (PRK1)	T774	PK781	Q16512	PKN1	3972	629	16	4813	407	8	21	0.034
VACAMKL	Y245	PK892	Q8NCB2	CAMKV	541	45	8	671	71	11	24	0.020
SMARCA4	S610+S613	PN726	P51532	SMARCA4	1067	146	14	1327	96	7	24	0.019
GATA3	S369	PN702	P23771	GATA3	1914	141	7	2416	213	9	26	0.012
VEGFR2 (KDR)	Y1059	11531	P35968	KDR	186	20	11	242	33	13	30	0.030
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AMPKa1 (PRKAA1)	T183+S184	PK521	Q13131	PRKAA1	4926	499	10	6566	564	9	33	0.039
TAO1 (TAOK1)	S181	PK826	Q7L7X3	TAOK1	262	17	6	419	50	12	60	0.023