Glioblastoma tumor extracellular vesicle specific peptides inhibit EV-induced neuronal cytotoxicity

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Supplemental Table S1. Summary of subject demographics

Diagnostic	Glioblastoma (GBM), WHO Grade IV	Meningioma (MMA), WHO Grade I	Healthy Controls (HC)*
Subject (n)	40	40	20
Male (n)	28	13	6
Female (n)	12	27	14
Age (years, mean ± SD)	55.4±12.7	55.3±12.2	45.2±12.9

*Additional healthy plasma were purchased from Innovative Research (https://www.innov-research.com/products/pooled-human-plasma-blood-derived): Pooled Human Plasma (Blood Derived).

Supplemental Table S2. Pathology of GBM patients, sex, and age

ID	Pathology	Sex	Age
J5-1	Glioblastoma: WHO grade 4 IDH wildtype negative for MGMT promoter methylation positive for point mutation in TERT promoter region positive for EGFR amplification negative for loss of PTEN	Female	67
J6-7	Diffuse astrocytoma: WHO grade 2 IDH1 mutant by IHC negative for 1p36 deletion negative for 19q13 deletion polysomy and agin of 19q12 observed negative for EGFR amplification negative for loss of PTEN	Male	32
J8-1	Glioblastoma: WHO grade 4, with high cell density IDH wildtype negative for IDH1 R132H by IHC positive for high level EGFR amplification negative for whole chromosome 7 gain positive for loss of PTEN, consistent with whole chromosome 10 loss positive for point mutation in TERT promoter region (c.1-124C>T) positive for MGMT promoter methylation	Female	65

J9-6	Glioblastoma: WHO grade 4 IDH-wildtype negative for IDH1 R132H by IHC positive for high level EGFR amplification negative for whole chromosome 7 gain positive for loss of PTEN, consistent with whole chromosome 10 loss positive for MGMT promoter methylation positive for point mutation in TERT promoter region (c.1-146C >T) negative for mutation in IDH1, IDH2, and BRAF positive for mutation in EGFR, anticipated single amino acid substitution (p.A289V)	Female	56
J5-5	Glioblastoma: WHO grade 4, clinically recurrent IDH-wildtype positive for EGFR amplification positive for loss of PTEN indeterminate for MGMT	Male	79
J10-3	Glioblastoma: WHO grade 4, with sarcomatous areas (gliosarcoma) IDH-wildtype negative for IDH1 R132H by IHC positive for high level EGFR amplification negative for whole chromosome 7 gain positive for loss of PTEN, consistent with whole chromosome 10 loss negative for mutation in BRAF negative for mutation in IDH1 and IDH2 negative for mutation in H3F3A positive for point mutation in TERT promoter region (c.1-124C>T) negative for deletion of CDKN2A (p16) sequences positive for the presence of a KIAA1549-BRAF fusion product positive for MGMT promoter methylation	Male	62

I21-6	Glioblastoma: WHO grade 4 IDH-wildtype negative for IDH1 R132H by IHC rare cells with amplification of EGFR sequences trisomy for 7p/7cen sequences, consistent with whole chromosome 7 gain positive for loss of PTEN, consistent with whole chromosome 10 loss positive for MGMT promoter methylation positive for point mutation in TERT promoter region	Female	58
I24-6	Glioblastoma: WHO grade 4, with extensive necrosis IDH-wildtype history of clinically residual glioblastoma, IDH-wildtype, WHO grade 4 previous sample was positive for amplification of EGFR sequences positive for loss of PTEN, consistent with monosomy 10	Female	64
I17-6	Glioblastoma: WHO grade 4, with primitive neuronal component IDH mutant; positive for IDH1 R132H by IHC negative for deletion of 1p36 sequences positive for deletion of 19q13 sequences negative for amplification of EGFR trisomy and tetrasomy for 7p/7cen sequences, consistent with whole chromosome gain of 7 negative for loss of PTEN sequences and whole chromosome loss of 10; trisomy and tetrasomy for PTE, consistent with whole chromosome gain of 10 positive for amplification of MYCN sequences positive for amplification of CMYC sequences MGMT promoter methylation not detected TERT promotor mutation not detected	Female	28

I23-2	Glioblastoma: WHO grade 4, possibly arising in a ganglioglioma IDH-wildtype negative for IDH1 R132H by IHC negative for amplification of EGFR trisomy for 7p/7cen sequences, consistent with gain of whole chromosome 7 positive for loss of PTEN consistent with whole chromosome 10 loss negative for MGMT promoter methylation negative for BRAF mutation positive for point mutation in TERT promoter region (c.1-124C>T) positive for EGFR mutation (p.T263P)	Male	43
J12-4	Glioblastoma: WHO grade IV; history of a left temporal anaplastic astrocytoma IDH mutant MGMT methylation indeterminate very rare cells with EGFR amplification	Female	56
J12-2	Glioblastoma: WHO grade 4 IDH-wildtype negative for IDH1 R132H by IHC negative for amplification of MYCN positive for trisomy and tetrasomy for chromosome 2 negative for amplification of EGFR positive for multiple copies of 7p/7cen, consistent with whole chromosome 7 gain borderline for loss of PTEN and 10 centromere (monosomy 10) negative for MGMT promoter methylation positive for point mutation in TERT promoter region	Male	60

J6-3	Glioblastoma: WHO grade 4 (clinically recurrent) IDH-wildtype negative for IDH1 IHC negative for amplification of EGFR positive for monosomy 10 indeterminate MGMT methylation positive for TERT promotor mutations	Male	42
J3-6	Glioblastoma: WHO grade 4; clinically recurrent history of right parietal glioblastoma, IDH-wildtype, WHO grade 4 positive for MGMT methylation high level amplification of EGFR sequences loss of PTEN, consistent with monosomy 10	Male	58
J3-1	Glioblastoma: WHO grade 4 IDH-wildtype negative for IDH1 R132H by IHC negative for amplification of EGFR polysomy for 7p/7cen sequences, consistent with whole chromosome 7 gain negative for deletion of 19q13 sequences negative for loss of PTEN sequences or whole chromosome 10 loss negative for deletion of 1p36 sequences negative for MGMT promoter methylation positive for point mutation in TERT promoter region (c.1-124C>T)	Male	80
J1-6	Glioblastoma: WHO grade 4 + IDH-wildtype positive for EGFR amplification negative for whole chromosome 7 gain positive for monosomy 10	Male	58
I24-4	Glioblastoma: WHO grade 4 (clinically recurrent) IDH wildtype	Male	56

I24-3	Glioblastoma: WHO grade 4 IDH-wildtype negative for IDH1/2 mutation negative for IDH1 R132H by IHC positive for mutation in H3F3A (p.G35R) negative for H3K27M by IHC strong diffuse p53 immunostaining loss of nuclear ATRX positive for amplification of EGFR sequences polysomy for 7p12 (EGFR) and 7cen sequences, consistent with whole chromosome 7 gain borderline for loss of PTEN and 10 centromere sequences negative for amplification of MYCN (2p24.1) sequences loss of MYCN (2p24.1) sequences negative for amplification of C-MYC sequences polysomy for 8q24 (C-MYC) and 8cen sequences negative for MGMT promoter methylation negative for point mutation in evaluated TERT promoter region	Male	33
I21-1	Glioblastoma: WHO grade 4 IDH-wildtype negative for 1p/19q deletion borderline for loss of 1p36 sequences negative for deletion of 19q13 sequences negative for amplification of EGFR trisomy and tetrasomy for 7p/7cen sequences, consistent with gain of whole chromosome 7 positive for two populations with loss of PTEN sequences	Male	61

I20-2	Glioblastoma: WHO grade 4, epithelioid IDH-wildtype negative for IDH1 R132H by IHC positive for amplification of EGFR sequences no evidence for gain of whole chromosome 7 positive for loss of PTEN, consistent with loss of whole chromosome 10 positive for point mutation in promoter region of TERT no BRAF mutation detected	Male	59
I18-1	Glioblastoma: WHO grade 4, clinically recurrent IDH-wildtype negative for IDH1 R132H by IHC positive for amplification of EGFR sequences negative for whole chromosome 7 gain positive for loss of PTEN, consistent with a loss of whole chromosome 10	Male	56
J3-3	Glioblastoma: WHO grade 4, recurrent; on clinical trial IDH wildtype	Male	56
I17-2	Glioblastoma: WHO grade 4 IDH-wildtype negative for IDH1 R132H by IHC positive for amplification of EGFR sequences; no evidence of whole chromosome 7 gain positive for loss of PTEN, consistent with whole chromosome loss of 10 postivie for TERT promoter variant, c.1-124C>T MGMT promoter methylation not detected	Male	46
E17-5	GBM, according to Pathology	Male	57
E19-6	Glioblastoma: WHO Grade IV, with oligodendroglial component, and acute hemorrhage IDH1 positive by IHC negative for 1;36 deletion negative for 19q13 deletion negative for EGFR amplification positive for loss of PTEN, consistent with monosomy 10	Female	32

E11-5	Glioblastoma: WHO grade 4 negative for MGMT promoter methylation	Male	64
E17-2	GBM, according to Pathology	Female	49
E17-3	GBM, according to Pathology	Male	70
E19-6	GBM, according to Pathology	Female	32
E12-2	Glioblastoma: WHO grade 4 IDH wildtype IDH-1 negative by IHC positive for high level of EGFR amplificaiton loss of PTEN, consistent with monosomy 10 negative for MGMT methylation	Male	60
I18-4	Glioblastoma: Grade 4 point mutation in TERT promoter region	Male	64
I17-7	Glioblastoma: WHO grade 4 IDH-wildtype negative for IDH1 R132H by IHC positive for amplification of EGFR sequences negative for whole chromosome 7 gain positive for loss of PTEN, consistent with whole chromosome loss of 10 TERT Promoter variant c.1-124C>T MGMT promoter methylation detected	Male	65
I17-5	Glioblastoma: WHO grade 4 (clinically recurrent) IDH-wildtype prior resection specimen negative for MGMT methylation positive for TERT promoter mutation positive for EGFR amplification	Female	58
E17-4	GBM, according to Pathology	Female	66
E13-7	Glioblastoma: WHO grade 4, with epithelioid features negative for MGMT methylation negative for EGFR amplification borderline positive for PTEN loss, consistent with monosomy 10	Male	36

E13-1	Glioblastoma: WHO grade 4 IDH wildtype IDH1 negative by IHC IDH1 negative for mutation strong nuclear p53 IHC strong EGFR expression positive for amplification of EGFR sequences negative for loss of PTEN sequences MGMT methylation detected	Male	56
E11-1	Glioblastoma: WHO grade 4 IDH wildtype IDH1 negative by IHC positive for EGFR amplification negative for PTEN loss MGMT methylation not detected	Male	74
J13-6	Glioblastoma: WHO grade 4, clinically recurrent right temporal glioblastoma IDH-wildtype negative for IDH1 R132H by IHC positive for amplification of EGFR sequences positive for loss of PTEN, consistent with monosomy 10 MGMT promoter methylation not detected no fusion or potentially oncogenic transcripts identified in ALK, ROS1 or MET EGFR-SEPT14 fusion transcript identified [EGFR exon 24 to SEPT14 exon 10] TERT promoter variant identified (c.1-124C>T).	Male	51
J13-3	Glioblastoma: WHO grade 4 positive for EGFR amplification positive for loss of PTEN consistent with whole chromosome 10 loss	Male	56

E20-7	Anaplastic astrocytoma: WHO grade 3, clinically gliomatosis cerebri by history IDH wildtype IDH1 IHC negative IDH1, exon 4: no mutation detected IDH2, exon 4: no mutation detected EGFR protein expression negative ATRX retained	Male	50

Supplemental Table S3. MMA patient ID, pathology, sex and age

ID	Pathology	Sex	Age
J11-2	Meningioma: WHO grade 1	Female	58
J11-7	Meningioma: WHO grade 1	Male	59
J10-7	Meningioma: WHO grade 1	Male	48
J10-6	Meningioma: WHO grade 1; point mutation in TERT promoter region	Male	55
J8-6	Meningioma: WHO grade 1	Female	43
J9-3	Meningioma: WHO grade 1	Female	70
J4-7	Meningioma: WHO grade 1	Female	36
J7-5	Meningioma: WHO grade 1	Female	46
J7-6	Meningioma: WHO grade 1	Female	58
J6-2	Meningioma: WHO grade 1	Female	57
E6-4	Meningoma; recurrent	Female	75
E6-1	Meningioma: WHO grade 1	Female	36
E8-3	Meningioma: WHO grade 1; angiomatous variant with focal atypical features	Male	63
E5-3	Meningioma: WHO grade 1	Female	64
I22-6	Meningioma: WHO grade 1	Female	48
I19-2	Meningioma: WHO grade 1	Female	53
J4-7	Meningioma: WHO grade 1	Female	36
J4-1	Meningioma: WHO grade 1	Female	64
I20-7	Meningioma: WHO grade 1	Male	74
J1-4	Meningioma: WHO grade 1; extensive transdural and dural sinus involvement	Female	39
E4-6	Meningioma: WHO grade 1	Female	62
E8-1	Meningioma: WHO grade 1	Female	53
E8-2	Meningioma: WHO grade 2 (atypical)	Male	41

J3-2	Meningioma: WHO grade 1; clinically radiation-induced	Male	74
J2-2	Meningioma: WHO grade 1	Female	65
I18-5	Meningioma: WHO grade 1	Female	37
J4-4	Meningioma: WHO grade 1	Male	67
J11-6	Meningioma: WHO grade 1	Female	57
I15-5	Meningioma: WHO grade 1	Female	43
I20-4	Meningioma: WHO grade 1	Male	66
E4-5	Meningioma: WHO grade 1	Male	74
E15-6	Meningioma: WHO grade 1	Female	43
E6-2	Meningioma: WHO grade 1; psammomatous type	Male	37
I18-2	Meningioma: WHO grade 1	Female	55
I24-2	Meningioma, WHO grade I	Female	75
J5-7	Meningioma: WHO grade 1; no TERT mutation found	Female	51
J4-2	Meningioma: WHO grade 1	Female	49
J10-2	Meningioma: WHO grade 1	Male	64
I19-3	Meningioma: WHO grade 1	Female	53
I21-4	Meningioma: WHO grade 1; psammomatous subtype	Female	63

Supplemental Table S4. Healthy Control ID, sex and age

Healthy Control ID	Sex	Age
ACP-HC1	F	51
ACP-HC2	F	54
ACP-HC3	F	29
ACP-HC4	F	43
ACP-HC5	F	24
ACP-HC6	F	23
ACP-HC7	F	44
ACP-HC8	F	61
ACP-HC9	F	30
ACP-HC10	F	57
ACP-HC11	F	55
ACP-HC12	F	54
ACP-HC13	F	49
ACP-HC14	F	43
ACP-HC15	M	61
ACP-HC16	M	57
ACP-HC17	M	40

Supplemental Table S5. Phage peptides identified by brain tumor EVs

EV ID	Phage ID	Peptide	EV ID	Phage ID	Peptide
GBM pooled plasma EVs	JC1a/C2	SKADWNMAEAYF	MMA pooled plasma EVs	JC1a/D2	FETTVLMDLYRY
	JC1a/C3	NHAHYLGALLST		JC1a/D11	YLDAHFYSEGAK
	JC1a/C5	MLPIKQEYHFPI		JC1a/D7	SNTWTWISSAYG
	JC1a/C6	TILKPAAQGFAD		JC1a/D9	FAKPDMRSNLGW
	JC1a/C7	AEAXTGFSASGV		JC1a/D10	VNASDFDFSRKK
	JC1a/C8	AEAWTGFSASGV	MMA plasma EVs	JC1a/E2	SIVKTHTQIDIF
	JC1a/C9	AEAWTGFSASGV		JC1a/E3	YSPVLIW
	JC1a/C12	AEAWTGFSASGV		JC1a/E4	QQMHEWYFQSLP
GBM plasma EVs	JC1a/F1	GWNEAVNLMDSM		JC1a/E6	DHAMHQNQNISN
	JC1a/F3	SHYQGNHVDNKL		JC1a/F7	SHWGSDHQSVMT
	JC1a/F4	LMPVTPK		JC1a/F12	SHYQGNHVDNKL
	JC1a/F5	NHAHYLGALLST		JC1a/F9	QMYGLNIGGSWT
	JC1a/F6	TMVLAYDKTADI		JC1a/F10	NHAHYLGALLST
	JC1a/E9	TILKPAAQGFAD		JC1a/F11	DVSAILYRSGFP
	JC1a/E7	TILKPAAQGFAD	MMA cell line EVs	E9-2MF1.G10	VHWDFRQWWQPS
	JC1a/E8	NDIITSEQFKQG		E9-2MF2.C8	VHWDFRQWWQPS
	JC1a/E10	ISYDRGSFEAQS		E9-2MF1.A9	VHWDFRQWWQPS
	JC1a/E11	WAGLVSWMPNFS		E9-2MF2.B9	IGRMVTLEPGVM
	JC1a/E12	TPSSDNYLRTHN		E9-2MF2.B10	FEVNGTDHLPIH
GBM cell line EVs	F3-8 JC1a	HQMMLQAQPVKN		E9-2MF2.C9	IRNHVETINAGI
	F3-8 SF1	HLYALMT		E9-2MF2.H9	SFDDNVGQPPSP
	F3-8 JC1a	WIPRFTD		E9-2MF2.H10	HFVPLVNLGVLS

Supplemental Table S6. For EVs derived from similar sources, EV-binding peptides reveal conserved sequences (https://www.ebi.ac.uk/Tools/msa/clustalo/)

GBM pooled plasma EVs	
JC1a/C7	AEAXTGFSASGV
JC1a/C8	AEAWTGFSASGV
JC1a/C9	AEAWTGFSASGV
JC1a/C12	AEAWTGFSASGV
	*** ********
GBM plasma EVs	
JC1a/F6	-TMV---LAYDKTADI
JC1a/E9	-TILK--PAAQGFAD-
JC1a/E7	-TILK--PAAQGFAD-
JC1a/E8	NDIITSEQFKQG----
	:: :
MMA pooled plasma EVs	
JC1a/D9	FAKPDMRSNLGW------
JC1a/D7	------SNTWTWISSAYG
JC1a/D2	FETTVLMDLYRY------
JC1a/D11	-----YLDAHFYSEGAK-
JC1a/D10	------VNASDFDFSRKK
	. :
MMA plasma EVs	
JC1a/E6	DHAMHQNQNISN--
JC1a/F7	--SHWGSDHQSVMT
JC1a/F12	--SHYQGNHVDNKL
JC1a/F9	--QMYGLNIGGSWT
	: .

Supplemental Table S7. BLAST searches of peptide sequences showing homologies to known proteins

Peptide ID	Peptide sequence	Protein name	Identity	Protein name	Identity
GBM cell line XO-1	HLYALMT	focal adhesion kinase 1 isoform X1	5/6(83%)	phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit delta isoform isoform X1	5/6(83%)
GBM cell line XO-2	HTWLHAVQPRFA	immunoglobulin heavy chain junction region	7/9(78%)	autism susceptibility gene 2 protein isoform X1	6/9(67%)
GBM cell line XO-4	HQMMLQAQPVKN	atrophin-1 related protein	7/9(78%)	arginine-glutamic acid dipeptide (RE) repeats, isoform CRA_b	7/9(78%)
GBM cell line XO-5	WIPRFTD	immunoglobulin heavy chain variable region, partial	5/5(100%)	deleted in malignant brain tumors 1 protein isoform e precursor	6/7(86%)
GBM Pl-2	VHWDFRQWWQPS	immunoglobulin heavy chain junction region	5/7(71%)	anti-HIV-1 immunoglobulin heavy chain variable region, partial	5/6(83%)
GBM PXO	GPRPSDLTMATR	serine/threonine-protein phosphatase 4 regulatory subunit 1 isoform X1	9/14(64%)	immunoglobulin heavy chain junction region	7/9(78%)
GBM PPXO	SKADWNMAEAYF	immunoglobulin heavy chain junction region	7/8(88%)	sodium/hydrogen exchanger 10 isoform 1	6/7(86%)
GBM PPXO JC1a/C3	NHAHYLGALLST	probable E3 ubiquitin-protein ligase HERC1 isoform X1	7/8(88%)	teneurin-4 isoform X1	6/6(100%)
GBM PPXO JC1a/C5	MLPIKQEYHFPI	leucine-rich repeat transmembrane protein FLRT1	10/20(50%)	immunoglobulin light chain junction region	5/7(71%)
GBM PPXO JC1a/C6	TILKPAAQGFAD	TPA_inf: olfactory receptor OR17-8	8/10(80%)	immunoglobulin heavy chain junction region	7/8(88%)

GBM PPXO JC1a/C7	AEAXTGFSASGV	immunoglobulin heavy chain junction region [Homo sapiens]	7/10(70%)	ATPase WRNIP1 isoform 1 [Homo sapiens]	8/11(73%)
GBM PXO	SIVKTHTQIDIF	MHC class I antigen, partial	7/8(88%)	oxysterol-binding protein-related protein 10 isoform X4	8/11(73%)
GBM PXO JC1a/E10	ISYDRGSFEAQS	immunoglobulin heavy chain junction region	7/9(78%)	GTP-binding protein REM 1 isoform X1	7/9(78%)
GBM PXO JC1a/E11	WAGLVSWMPNFS	arachidonate 12-lipoxygenase, 12R-type	5/5(100%)	immunoglobulin heavy chain junction region	5/6(83%)
GBM PXO JC1a/E12	TPSSDNYLRTHN	immunoglobulin heavy chain junction region	7/9(78%)	dmX-like protein 1 isoform X1	6/6(100%)
GBM PXO JC1a/E3	YSPVLIW	protein transport protein Sec16A isoform X1	6/6(100%)	immunoglobulin heavy chain junction region	6/7(86%)
GBM PXO JC1a/E4	QQMHEWYFQSLP	mitogen-activated protein kinase kinase kinase 15	6/7(86%)	immunoglobulin heavy chain junction region	5/6(83%)
GBM PXO JC1a/E6	DHAMHQNQNISN	alternative protein DIRAS2 [Homo sapiens]	6/11(55%)	chromodomain-helicase-DNA-binding protein 9 isoform X1	5/6(83%)
GBM PXO JC1a/E8	NDIITSEQFKQG	PDS5, regulator of cohesion maintenance, homolog A	6/8(75%)	BAH and coiled-coil domain-containing protein 1 isoform 1	6/6(100%)
MMA cell line XO-2	SFDDNVGQPPSP	aprataxin and PNK-like factor	6/7(86%)	Structure of CHD4 double chromodomains depicts cooperative folding for DNA binding	6/6(100%)
MMA cell line XO-3	FEVNGTDHLPIH	serine/threonine-protein phosphatase 6 regulatory ankyrin repeat subunit C	6/7(86%)	immunoglobulin heavy chain junction region	6/8(75%)
MMA cell line XO-4	IRNHVETINAGI	very-long-chain (3R)-3-hydroxyacyl-CoA dehydratase 3	7/8(88%)	dynein, axonemal, heavy polypeptide 7, isoform CRA_b	8/11(73%)

MMA cell line XO-5	HFVPLVNLGVLS	tumor necrosis factor alpha-induced protein 3	7/8(88%)	Peripherin 2 (retinal degeneration, slow)	9/14(64%)
MMA cell line XO-6	IGRMVTLEPGVM	immunoglobulin heavy chain junction region	7/8(88%)	zinc finger protein 469	7/10(70%)
MMA PPXO	FETTVLMDLYRY	methylcytosine dioxygenase TET2 isoform a	6/6(100%)	fetal liver non-specific cross-reactive antigen-3 precursor protein [Homo sapiens]	6/7(86%)
MMA PPXO JC1a/D10	VNASDFDFSRKK	immunoglobulin heavy chain junction region	7/8(88%)	inaD-like protein isoform X1	6/7(86%)
MMA PPXO JC1a/D11	YLDAHFYSEGAK	immunoglobulin heavy chain junction region	6/6(100%)	autophagy-related protein 2 homolog A isoform X1	7/9(78%)
MMA PPXO JC1a/D7	SNTWTWISSAYG	immunoglobulin heavy chain variable region, partial	7/9(78%)	IG c804_heavy_IGHV4-39_IGHD6-13_IGHJ4, partial	6/7(86%)
MMA PPXO JC1a/D9	FAKPDMRSNLGW	protein AHNAK2 isoform 1 [Homo sapiens]	7/8(88%)	immunoglobulin light chain junction region [Homo sapiens]	6/6(100%)
MMA PXO	GWNEAVNLMDSM	histone H2B type F-M isoform X1 [Homo sapiens]	7/9(78%)	PRKC, apoptosis, WT1, regulator, isoform CRA_a	7/8(88%)
MMA PXO JC1a/F11	DVSAILYRSGFP	Rh-associated glycoprotein [Homo sapiens]	7/9(78%)	50 kDa erythrocyte plasma membrane glycoprotein [Homo sapiens]	7/9(78%)
MMA PXO JC1a/F3	SHYQGNHVDNKL	immunoglobulin heavy chain junction region	8/11(73%)	cytochrome P450 27C1 isoform 2	6/6(100%)
MMA PXO JC1a/F4	LMPVTPK	serine/threonine-protein kinase D3	6/6(100%)	PRKD3 protein	6/6(100%)
MMA PXO JC1a/F6	TMVLAYDKTADI	E3 ubiquitin-protein ligase MARCHF9 precursor	8/10(80%)	membrane-associated ring finger (C3HC4) 9, isoform CRA_b	8/10(80%)
MMA PXO JC1a/F9	QMYGLNIGGSWT	immunoglobulin heavy chain junction region	7/10(70%)	armadillo repeat containing, X-linked 4, isoform CRA_a	6/6(100%)

Notes:

ppXO: Pooled plasma EVs

pXO: Individual plasma EVs

Pl: Plasma

Supplemental Table S8. List of synthetic peptides with high affinity to corresponding EVs

Pep ID	Sequence (N--C)	Molecular Weight	Water Solubility	Notes
GBM PPXO C2	SKADWNMAEAYF	1772	Poor	EVs from GBM pooled plasma
GBM PPXO E5	GPRPSDLTMATR	1641	Poor	EVs from GBM pooled plasma
MMA-D2	FETTVLMDLYRY	1550	Poor	EVs from meningioma pooled plasma
MMA JC1A/D11	YLDAHFYSEGAK	1440	Good	EVs from patient plasma
F3-8 JC1A/B4	WIPRFTD	934	Good	Surface pan. EVs from GBM cell line
F3-8 (SF1)F5	HLYALMT	1073	Poor	Surface pan. EVs from GBM cell line
HC-XO G1	LVVPHRSLSEVR	1391	Good	EVs from commercial HC plasma
HC-XO G4	FSGLSLTRMFYK	1449	Poor	EVs from commercial HC plasma