Supporting Information

Materials and Chemicals.

Graphene, concentrated nitric acid, tetraethyl orthosilicate (TEOS), ethylene glycol, ethanol, sodium hydroxide, concentrated ammonia solution (28 wt%) and sodium dodecylsulphate are of analytical grade and purchased from Shanghai Chemical Corp. 3-(methacryloyloxy)propyltrimethoxysilane and methyl methacrylate,99% was purchased from Alfa Aesar (Tianjin, China). Standard peptide (Angiotensin II: Mw=1046.2; Sequence is Asp-Arg-Val-Tyr-Ile-His-Pro-Phe; Purity>97.77%) was purchased from Sangon Biotech (Shanghai) Co., Ltd.. Bovine Serum Albumin (BSA), Horse heart Myoglobin (MYO) were obtained from Bio Basic Inc. (Toronto, Canada). α-Cyano-4-hydroxy-cinnamic acid (CHCA) was purchased from Sigma (Shanghai, China). Sequencing grade–modified trypsin was purchased from Promega (Madison, WI). Mice were provided by Shanghai Medical College. All of other chemicals are of analytical grade. Milli-Q water prepared using by Milli-Q system (Millipore, Bedford, MA) was used in all experiments.

Preparation of graphene@SiO_2@PMMA material

The synthesis of graphene@SiO_2@PMMA materials involve three steps, showed in scheme 1. Firstly, the pristine graphene flakes were treated in a concentrated nitric acid solution at 60^{o}C for 6h in a three-necked round bottom flask equiped with a mechanical agitation and condenser. Then, the acidizing solution was neutralized by slowly adding NaOH solution until pH 7.0. and collected by centrifugation to obtain the hydrophilic graphene nanosheets, washed with water and dried at 60°C in vacuum. Secondly, the product was obtained by sol-gel process according to previous reports with some modifications [1-3]. Secondly, 50 mg of as-prepared graphene powder was dispersed in 50 ml of deionized water by ultrosonication for 30 min, resulting in a homogeneous dispersion. Additional 400 ml of deionized water and 50ml of 0.01M NaOH solution were added into the dispersion which was further ultrasonicated for 10 minutes and heated at 60°C for 30 minutes under mechanical agitation. Afterwards, 2.5ml of tetraethylorthosilicate (TEOS)/ethanol (v/v: 1/4) solution was added by injection at 60°C for 12 hours. The product was collected by centrifugation and washed with deionized water. Finally, the products were dispersed in 70ml ethanol and 3-(methacryloyloxy)propyltrimethoxysilane was added in the dispersion with a mechanical agitation for 48 hours at 30°C. The sodium dodecylsulphate (5g) and methyl methacrylate(1.0g) were added in the dispersion in sequence and kept the solutions under nitrogen atmosphere and reflux at 70°C for 24 hours. The graphene@SiO_2@PMMA materials were washed repeatedly with deionized water and ethanol dried at 50°C for 12 hours in vacuum for future use.

Characterization

Scanning electron microscopy (SEM) images were recorded on a Philips XL30 electron microscope (Netherlands) operating at 20 kV. A thin gold film was sputtered on the sample before characterization. Transmission electron microscopy (TEM) images were taken with a JEOL 2011 microscope (Japan) operating at 200 kV. Fourier-transform infrared (FT-IR) spectra were collected on a Nicolet Fourier spectrophotometer (USA) using KBr pellets.

Preparation of standard protein digests. Bovine serum albumin (BSA)(2mg) and Horse heart Myoglobin (MYO)(2mg) were dissolved in 25mM NH4HCO3 buffer at pH 8.3 and treated with trypsin (2%, w/w) for 16 h at 37 °C respectively. MALDI-TOF MS analysis. MALDI-TOF MS experiments were performed in positive ion mode on a 5800 Proteomics Analyzer (Applied Biosystems, USA) in the reflector TOF detection modes. The sample was excited using a Nd:YAG laser (383 nm) operated at a repetition rate of 200 Hz and acceleration voltage of 20 kV. The MASCOT server was used to interpret the MALDI-TOF MS data by searching the species of mammals for identification of two standard proteins with peptide fingerprint mass spectra.

1D nano-ESI-LC/MS/MS analysis. Nano Aquity UPLC system (Waters Corporation, Milford,USA) connected to an LTQ Orbitrap XL mass spectrometer (Thermo Electron Corp., Bremen, Germany) equipped with an online nanoelectrospray ion source (Michrom Bioresources, Auburn, USA). The separation of the peptides was performed in a Symmetry®C18, 5μm, 180μm id×2cm trap-column and a BEH300 C18，1.7μm, 75μm id×15cm reverse phase column (Waters Corporation, Milford, USA).

References

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2 W. R. Zhao, J. L. Gu, L. X. Zhang, H. R. Chen, J. L. Shi, *J. Am. Chem. Soc.* 2005, **127**, 8916-8917.

3 Y. H. Deng, D. W. Qi, C. H. Deng, X. M. Zhang, D. Y. Zhao, *J. Am. Chem. Soc.* 2008, **130**, 28–29.

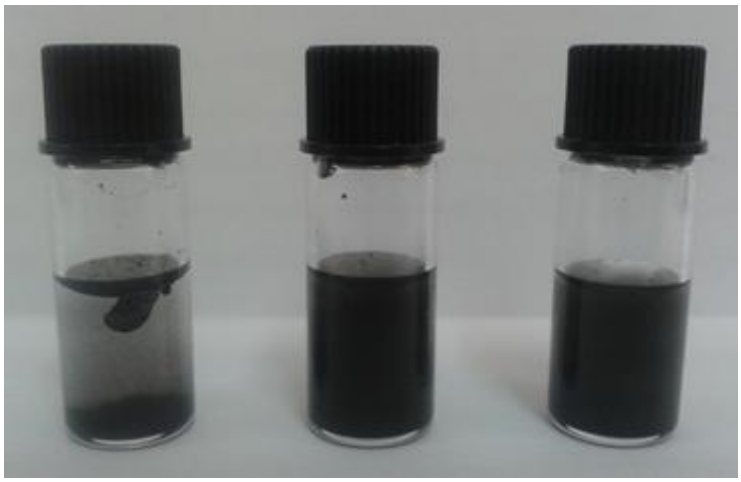

Fig. S1 The photographs of the aquous dispersion of pristine graphene sheets (left), graphene@SiO_2 (middle) and graphene@SiO_2@PMMA(right)

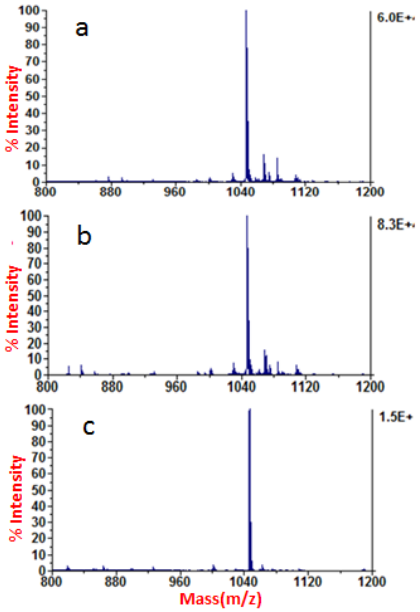

Fig. S2 The mass spectra of 10 nM standard peptides (Angiotensin II: Molecular Weight = 1046.2) enriched by graphene@SiO_2@PMMA and eluted by different eluents a) 0.4M, b) 1M ammonia water, c) mixture containing 50% acetonitrile and 0.1% trifluoroacetic acid.

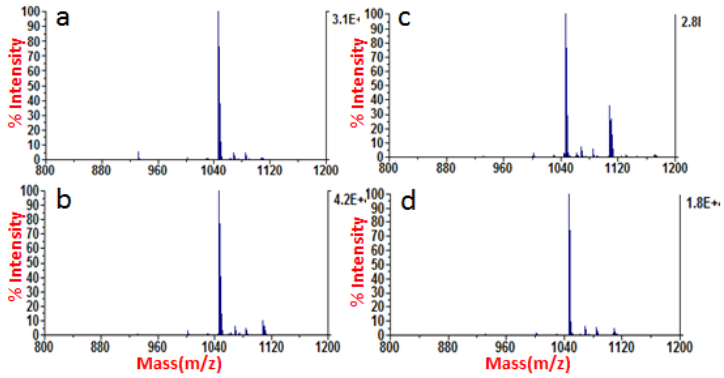

Fig. S3 The Mass spectra of 10 nM standard peptides (Angiotensin II: Molecular Weight = 1046.2) enriched by different amount of materials a)5 μL, b) 10 μL, c) 15 μL, d) 20μL, 10mg/ml in water.

Table S1 Peptides of myoglobin digest enriched by graphene@SiO_2@PMMA materials and identified by MALDI-TOF MASS

Start-End	Observed	Mr(expt)	Mr(calc)	Delta	Miss	Sequence
18-32	1606.782	1605.775	1605.848	-0.0725	0	K.VEADIAGHGQEVLIR.L
33-43	1271.601	1270.594	1270.656	-0.0619	0	R.LFTGHPETLEK.F
81-97	1853.865	1852.857	1852.954	-0.0969	0	K.GHHEAELKPLAQSHATK.H
120-134	1502.585	1501.578	1501.662	-0.0841	0	K.HPGDFGADAQGAMTK.A
135-146	1361.68	1360.673	1359.751	0.9216	1	K.ALELFRNDIAAK.Y
147-154	941.4443	940.4371	940.4654	-0.0284	1	K.YKELGFQG.-

Table S2 Peptides of albumin bovine serum digest enriched by graphene@SiO_2@PMMA materials and identified by MALDI-TOF MASS

Start-End	Observed	Mr(expt)	Mr(calc)	Delta	Miss	Sequence
37-44	974.5095	973.5022	973.4505	0.0517	0	K.DLGEEHFK.G
66-75	1163.647	1162.64	1162.623	0.0163	0	K.LVNELTEFAK.T
161-167	927.549	926.5417	926.4861	0.0556	0	K.YLYEIAR.R
402-412	1305.733	1304.726	1304.709	0.0172	0	K.HLVDEPQNLIK.Q
421-433	1479.829	1478.822	1478.788	0.0335	0	K.LGEYGFQNALIVR.Y
437-451	1639.974	1638.967	1638.931	0.0364	1	R.KVPQVSTPTLVEVSR.S
438-451	1511.874	1510.867	1510.836	0.0316	0	K.VPQVSTPTLVEVSR.S
508-523	1823.95	1822.942	1822.892	0.05	0	R.RPCFSALTPDETYVPK.A
588-597	1050.491	1049.483	1049.485	-0.0017	0	K.EACFAVEGPK.L

Table S3 the peptides and small molecular proteins of mouse brain enriched by graphene@SiO_2@PMMA and identified by 1D nano-ESI-LC/MS/MS.

MH+	z	Peptide	XC
1383.74130	2	C.GVCNGATAKISHLL.S	2.099
2070.01451	3	P.ERPGPPQRAQQM*TGTKSQG.P	2.630
2490.33510	3	M.LLGSLAFLGADTAGPDTPSQFRKK.W	2.524
1479.79544	2	K.LGEYGFQNAILVR.Y	2.676
1479.79544	2	K.LGEYGFQNAILVR.Y	3.184
1133.57382	2	Y.WPHQPIENL.-	2.338
1196.52119	2	S.SDSMDTGAGSIR.E	2.411
1196.52119	2	S.SDSMDTGAGSIR.E	2.850
2069.96689	3	S.SDSMDTGAGSIREAGGAFGKR.E	3.149
2156.99892	3	D.SSDSMDTGAGSIREAGGAFGKR.E	2.705
2914.44287	2	Y.SVAVPAFSQGLDDYGARSVSSGSGTLVSTV.-	2.587
1632.84524	3	R.SGSAKVAFSAIRSTNH.E	2.637
1632.84524	2	R.SGSAKVAFSAIRSTNH.E	2.865
1632.84524	2	R.SGSAKVAFSAIRSTNH.E	2.899
1459.83011	2	R.SVLMSLKQTPLSR.-	2.115
1718.77689	2	F.HNPHVNPLPTGYEDE.-	2.225
1718.77689	2	F.HNPHVNPLPTGYEDE.-	2.364
1438.80125	2	R.IVAPPGGRSNITSLG.-	2.359
1422.80634	2	R.IVAPPGGRANITSLG.-	2.398
1468.81182	2	R.IVAPPGGRSNITSLS.-	2.222
1734.89086	2	G.GPDEPITVAHIVVEATS.L	2.048
1712.04288	2	A.VGVIKAVDKKAAGAGKVT.K	2.846
1712.04288	2	A.VGVIKAVDKKAAGAGKVT.K	2.506
1799.90617	2	R.LVDNIFPEDPEDGLVK.T	2.204
1375.74274	2	K.SSLVTSKLAGGQVE.-	3.019
1375.74274	2	K.SSLVTSKLAGGQVE.-	3.096
1288.71071	2	S.SLVTSKLAGGQVE.-	2.361
3648.88276	4	R.TKQVEKNDEDQKIEQDGVKPEDKAHKAATKIQ.A	3.299
3648.88276	5	R.TKQVEKNDEDQKIEQDGVKPEDKAHKAATKIQ.A	3.082
3876.02098	5	R.RTKQVEKNDEDQKIEQDGVKPEDKAHKAATKIQA.S	3.202
3876.02098	5	R.RTKQVEKNDEDQKIEQDGVKPEDKAHKAATKIQA.S	3.701
3876.02098	5	R.RTKQVEKNDEDQKIEQDGVKPEDKAHKAATKIQA.S	3.446
3719.91987	4	R.TKQVEKNDEDQKIEQDGVKPEDKAHKAATKIQA.S	4.004
3490.77723	4	K.QVEKNDEDQKIEQDGVKPEDKAHKAATKIQA.S	3.684
1250.56477	2	R.KQNDVFGEADQ.-	2.138
3179.66818	5	L.NPDLSVAVVTIVDNDDLTGAAVSVPVTAGTVAV.D	3.069
2134.11724	2	H.KDIAVSLVAASDGATVCVTTRG.D	2.327
1551.75840	3	R.SKYLATASTMDHAR.H	3.230
1201.64632	2	L.LFPLLENIDQ.V	2.161

1028.55236	2	R.PKLKWDNQ.K	2.262
1239.68443	2	C.HVITWERIVS.H	2.105
1383.74782	2	S.RSELDVPVEILN.I	2.016
3194.67389	5	S.KANNLSSLSKKYRQDAKYLNM*RSTYAK.L	3.569
1734.86255	2	S.RVMEQSRKNVVEME.R	2.182
4961.56904	5	Q.TVRYKYGHNAGEATHNAVDSAINVGLTAYNIDNIGIKAM*VKKTAKQ.T	3.272
2581.42089	4	S.QNQKQGPFRRLEDALKALDVAAL.Q	3.018
3413.78456	4	S.ASFLNQKQEVEKLLEKQDRLQCPNAQVKE.K	3.258
1281.67322	2	-.MREIVHIQAGQ.C	2.899
1281.67322	2	-.MREIVHIQAGQ.C	2.965
1702.88979	2	F.SVVPSPKVSDTVVEPY.N	2.026
4961.55328	5	P.SVSLPPPAQVSSVPSLNQPYGEGLCVSLDPLPPLPPLPPLPPEDPEQP.P	3.761
4961.55328	5	P.SVSLPPPAQVSSVPSLNQPYGEGLCVSLDPLPPLPPLPPLPPEDPEQP.P	3.611