Supplemental Information for

Modulating Endothelial Adhesion and Migration impacts Stem Cell Therapies Efficacy

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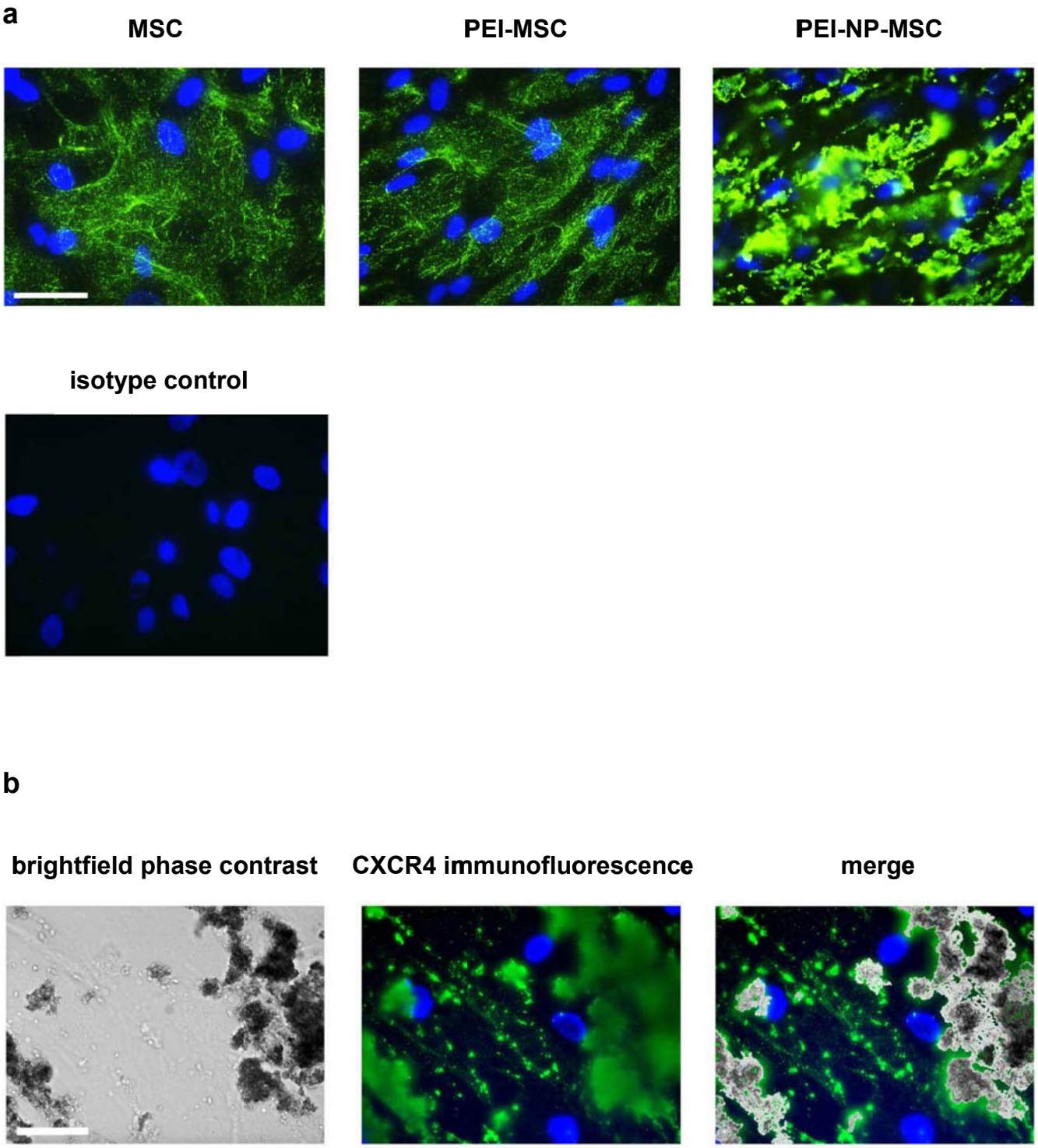
This file includes:

- Supplementary Figures 1-10
- Supplementary Tables 1+2
- Full Blots

Supplementary Figure 1



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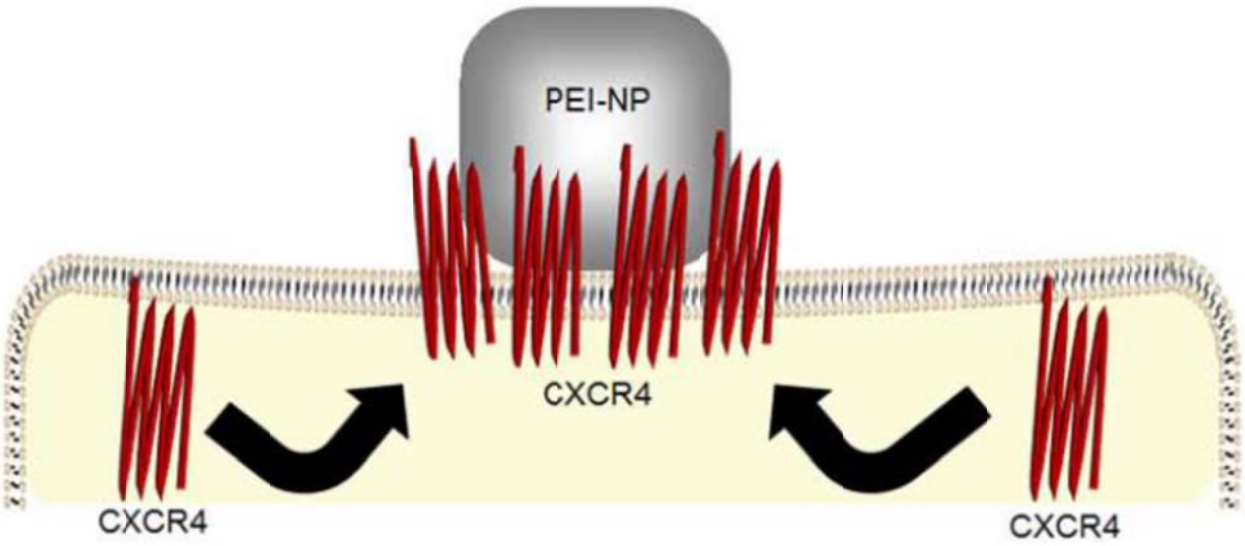
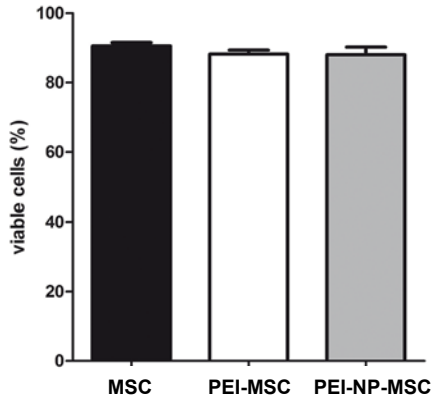


Supplementary Figure 1 CXCR4 expression pattern on human BM-MSC.

a, The overall expression of CXCR4 was not affected by treatment of MSC with PEI alone and an even distribution of CXCR4 molecules could be observed on the surface of untreated MSCs and MSCs treated with PEI alone. In contrast, the CXCR4 signal was strongly increased on MSCs treated with PEI in combination with NP. In particular, the CXCR4 molecules showed an aggregated distribution pattern on the cellular surface of PEI-NP-MSCs. The absence of green fluorescence in isotype control confirmed specificity of anti-CXCR4 antibodies and excluded unspecific auto-fluorescence of NP. Green: CXCR4; blue: DAPI; scale bar: 50 μm. **b**, PEI-NP-MSC: The increased CXCR4 expression was closely related to the localization of the PEI-NP complexes on the surface of MSC. The PEI-NP complexes in the merged microphotograph were highlighted in grey using Adobe Photoshop CS5.1; scale bar: 50 μm. **c**, Suggested mechanism of increased CXCR4 expression on PEI-NP-MSC: PEI-NP complexes trigger the inside-out flipping of CXCR4 molecules to the surface of MSC.

Supplementary Figure 2

a



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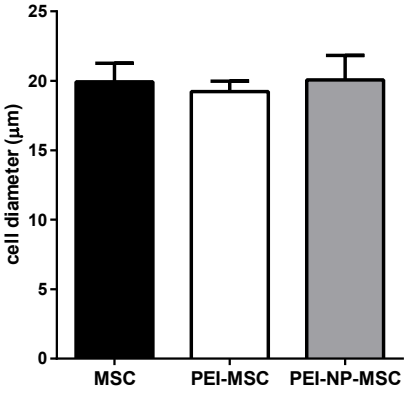

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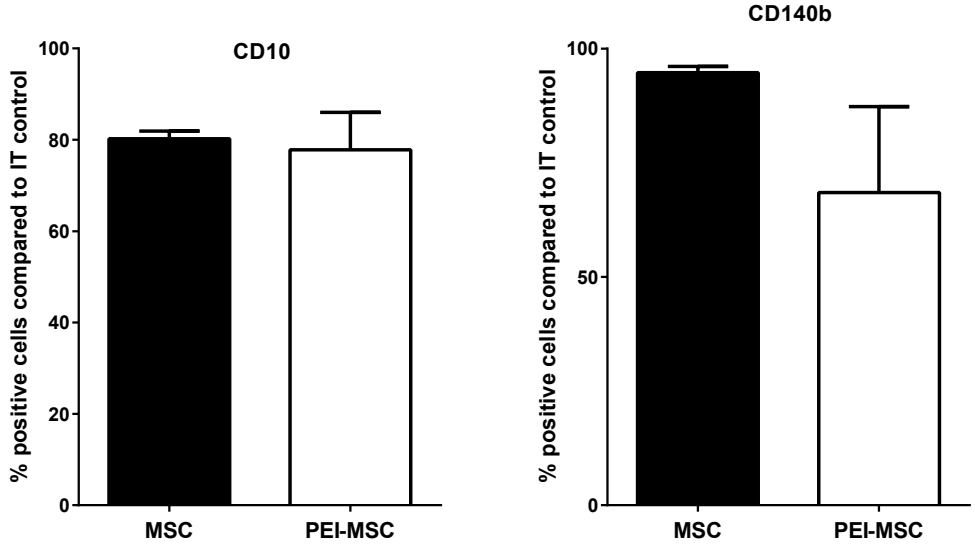
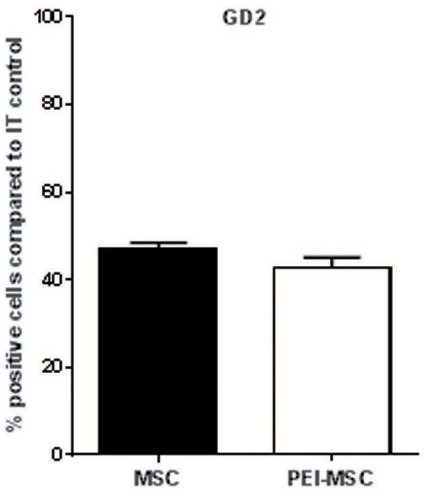
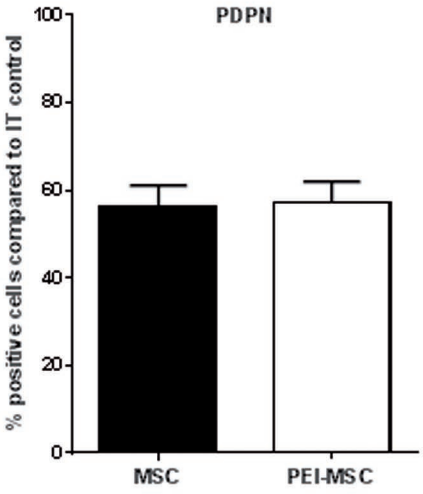
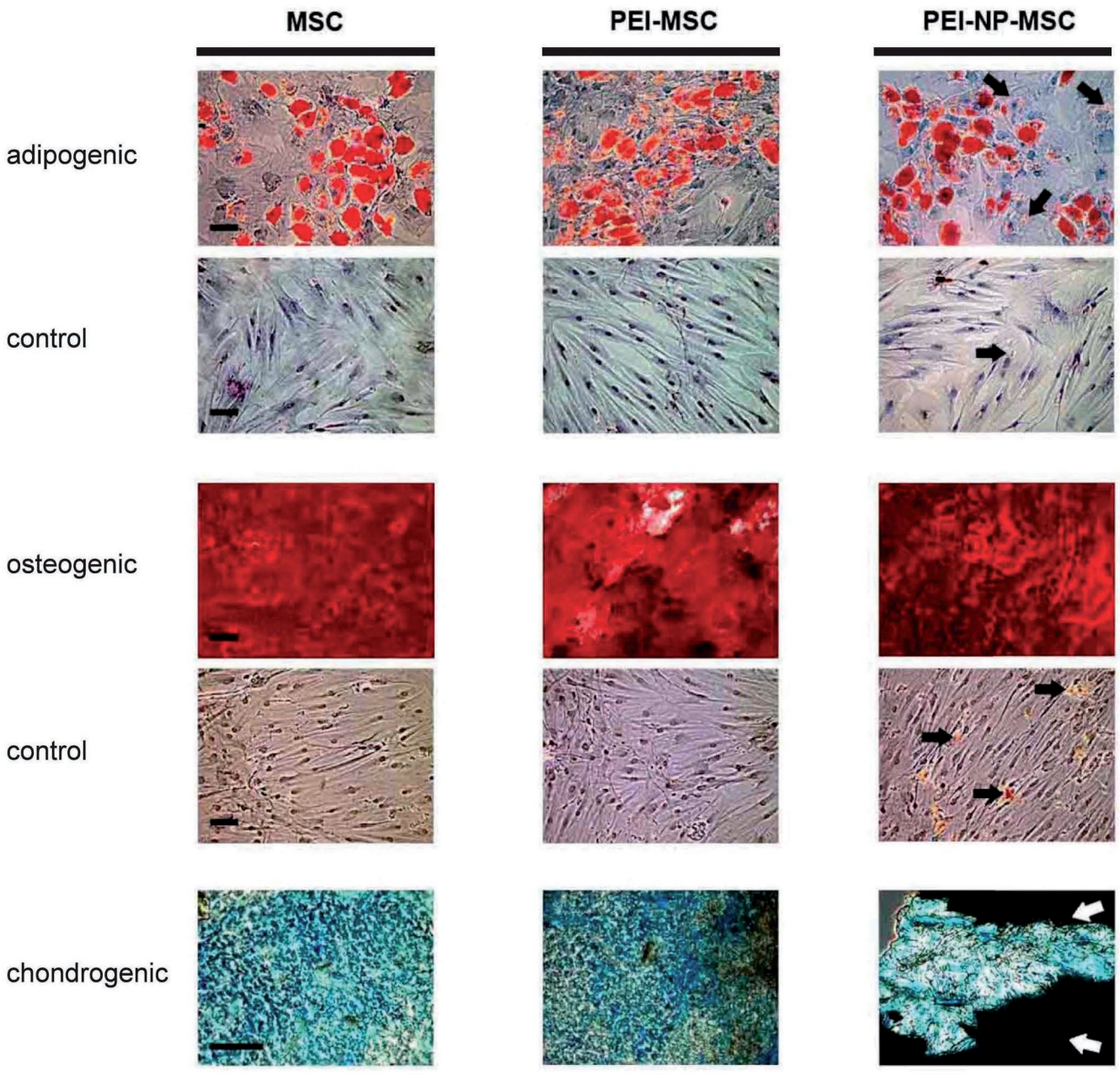


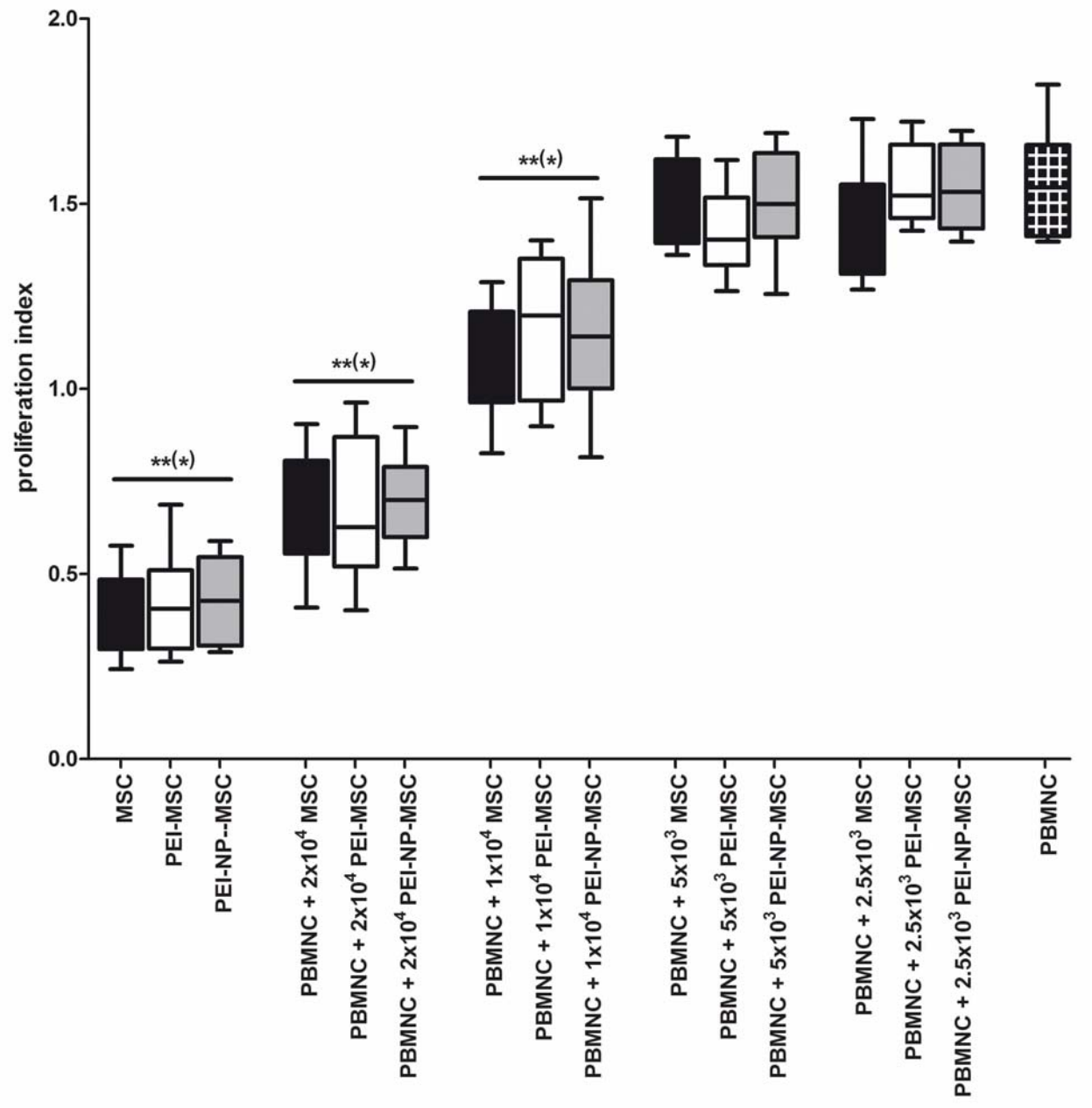

GD2
% positive cells compared to IT control
100
80
60
40
20
0
MSC
PEI-MSC


PDPN
% positive cells compared to IT control
100
80
60
40
20
0
MSC
PEI-MSC

d


MSC
PEI-MSC
PEI-NP-MSC
adipogenic
control
osteogenic
control
chondrogenic

e


proliferation index
2.0
1.5
1.0
0.5
0.0
**(*)
**(*)
**(*)
MSC
PEI-MSC
PEI-NP--MSC
PBMNC + 2x10^4 MSC
PBMNC + 2x10^4 PEI-MSC
PBMNC + 2x10^4 PEI-NP-MSC
PBMNC + 1x10^4 MSC
PBMNC + 1x10^4 PEI-MSC
PBMNC + 1x10^4 PEI-NP-MSC
PBMNC + 5x10^3 MSC
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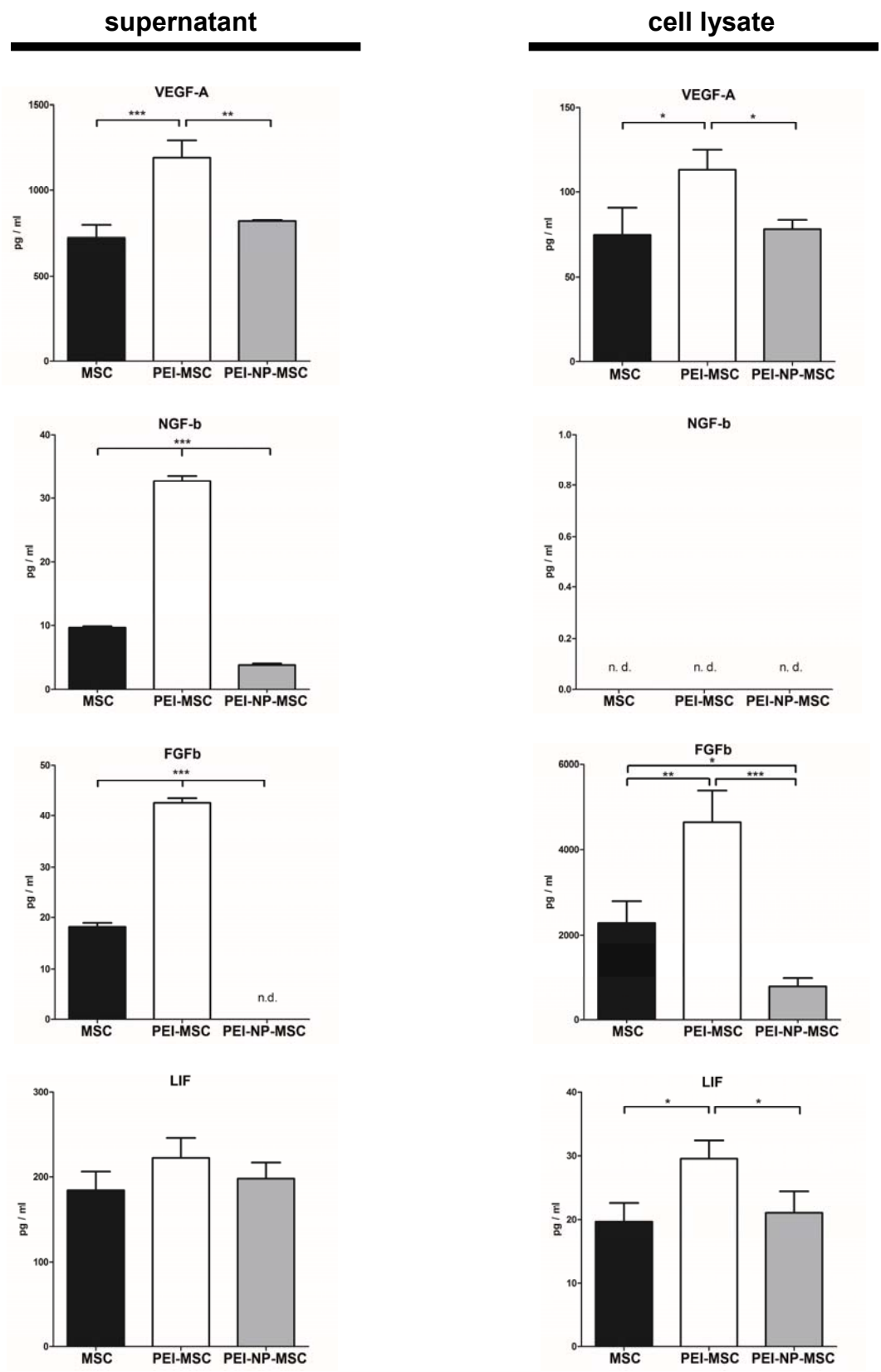
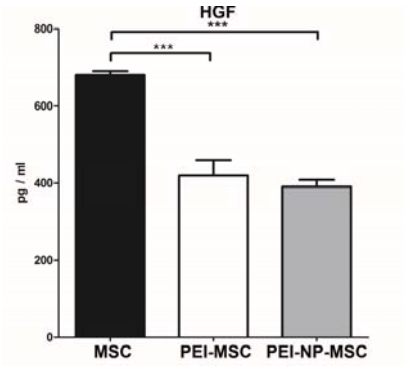
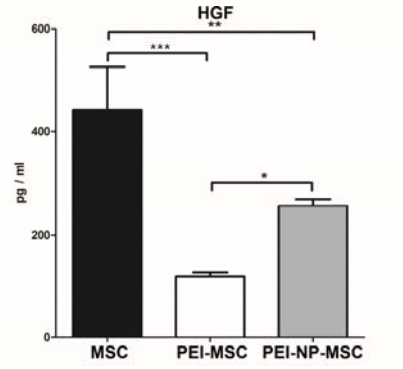
PBMNC + 2.5x10^3 PEI-NP-MSC
PBMNC

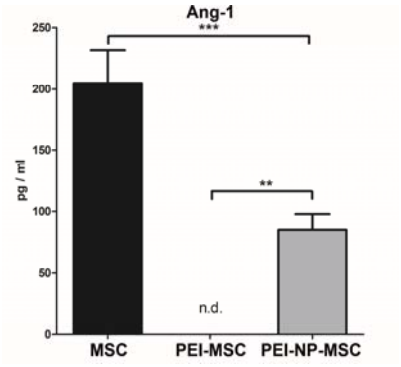
f

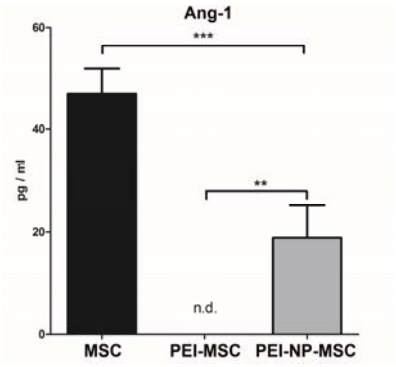

supernatant
cell lysate
VEGF-A
NGF-b
FGFb
LIF
pg / ml
MSC
PEI-MSC
PEI-NP-MSC
n. d.
n.d.

supernatant **cell lysate**









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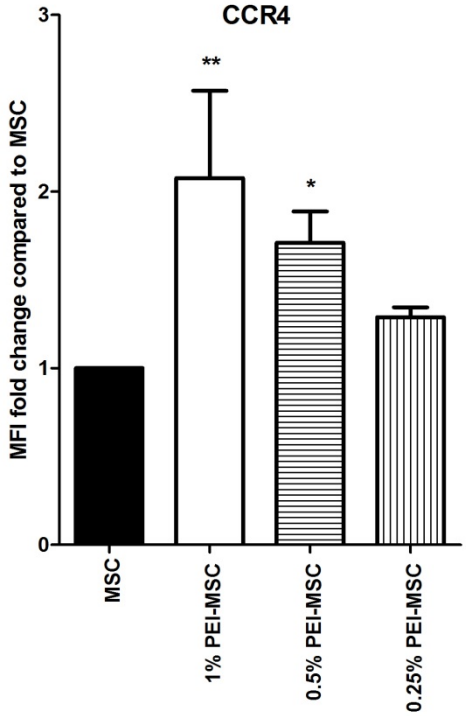
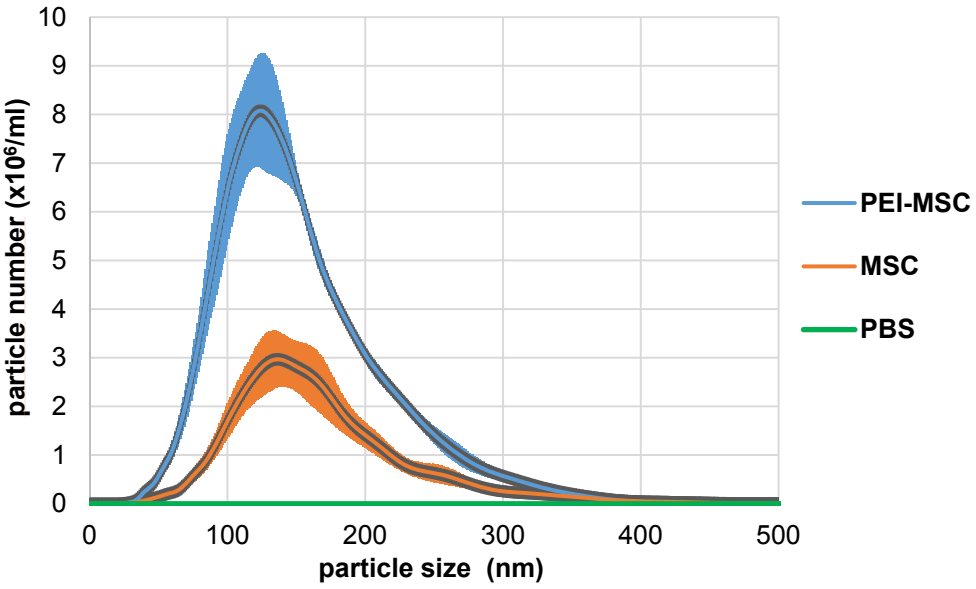


Supplementary Figure 2 Characterization of treated and untreated human BM-MSC.

a, MSC viability. The viability of MSC was not affected by treatment with PEI alone or in combination with NP. N=5; ANOVA analysis of variance. Error bars: SD. **b,** MSC diameter. The mean diameter of MSC, PEI-MSC and PEI-NP-MSC was not significantly different. N=6; ANOVA analysis of variance. Error bars: SD. **c,** Flow cytometry analyses of MSC phenotype. Treatment with PEI did not affect the percentages of MSC expressing CD10, CD140b (PDGFRb), GD2, or PDPN within the MSC preparation. N=2; two-tailed t-test. Error bars: SD. **d,** *In vitro* differentiation potential of MSC. After treatment with the respective differentiation media, the MSCs differentiated into cells of the adipogenic, osteogenic and chondrogenic lineage *in vitro.* Lipid vacuoles of adipogenic differentiated MSC are stained in red with Red-Oil-O (first row), undifferentiated MSC (second row). Calcium deposits of osteogenic differentiated MSC are stained in red with Alizarin Red (third row), undifferentiated MSC (fourth row). Mucopolysaccharides of chondrogenic differentiated MSC pellets are stained in bluish-green (fifth row). The treatment with PEI alone or in combination with NP did not affect the *in vitro* differentiation potential of the MSC (N=4). Arrows: PEI-NP complexes. Scale bars: 100 μm. **e,** Immunomodulatory capacities of MSC. The proliferation of $1*10^5$ PBMNC activated by PHA could be significantly suppressed by the addition of $0.1*10^5$ MSC or $0.2*10^5$ MSC, whereas the addition of $0.05*10^5$ MSC or $0.025*10^5$ MSC did not show an effect on the proliferation of PBMNC. No differences between the immunomodulatory capacities of untreated MSC, PEI-MSC, or PEI-NP-MSC could be observed within the same MSC-PBMNC ratios. ANOVA analysis of variance; stars indicate statistical comparisons of the respective MSC-PBMNC groups to PBMNCs alone; N=4 (**p <0.01; ***p <0.001). Error bars: SD. **f,** Profile of MSC trophic factors. Treatment of MSC with PEI alone resulted in increased secretion and/or production of vascular endothelial growth factor (VEGF)-A, nerve growth factor (NGF)-b, fibroblast growth factor basic (FGFb), and leukemia inhibitory factor (LIF). Notably, accumulated NGF-b could be detected only in the supernatants of untreated and

treated MSC but not in the respective cell lysates. Treatment of MSC with PEI with or without NP decreased the secretion and production of hepatocyte growth factor (HGF) and Angiopoietin-1. n.d.: not detectable. N=3; ANOVA analysis of variance (*p<0.05; **p <0.01; ***p <0.001). Error bars: SD. **g,** PEI dose effect on CCR4 expression of MSC. Increase of CCR4 expression was clearly dose depending with maximal fold change of CCR4 expression compared to untreated MSC of MSCs treated with 1% PEI (standard dose in this work), followed by 0.5% PEI and 0.25% PEI; ANOVA analysis of variance (*p <0.05; **p <0.01). Error bars: SD.

Supplementary Figure 3



	MSC	PEI-MSC
Mean size (nm)	172 +/-2.5	151 +/-3.5
Total number (10^8 particles/ml)	2.84 +/-0.7	8.48 +/-1.1

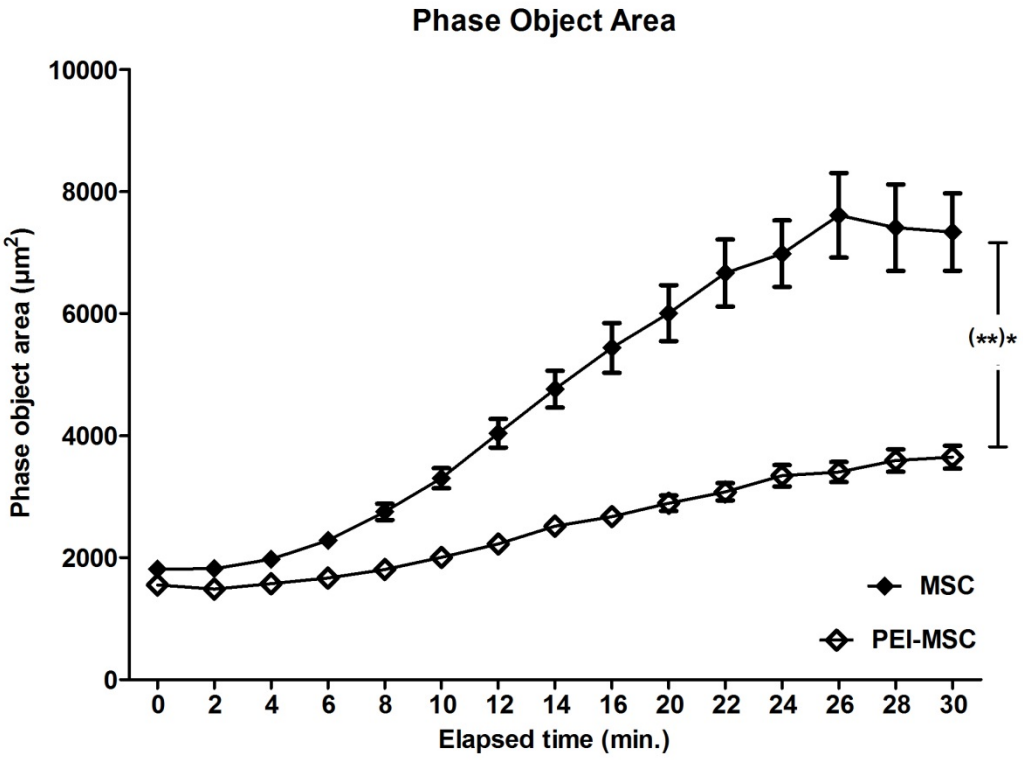
Supplementary Figure 3 Nanoparticle tracking analysis of Extracellular Vesicles (EVs)

Nanoparticle tracking analysis of Extracellular Vesicles (EVs) derived from untreated and PEI-treated human BM-MSC (N=3, different donors). PEI-treated MSC released significantly more EVs. EVs were isolated by differential centrifugation. Final 100.000 x g pellets were re-suspended in PBS and size-distribution of EVs was determined by laser based particle tracking.

Error bars: SEM. Mean particle size and the total number of particles (area under the curve) collected from each sample type are denoted in the table below the graph.

Supplementary Figure 4

a



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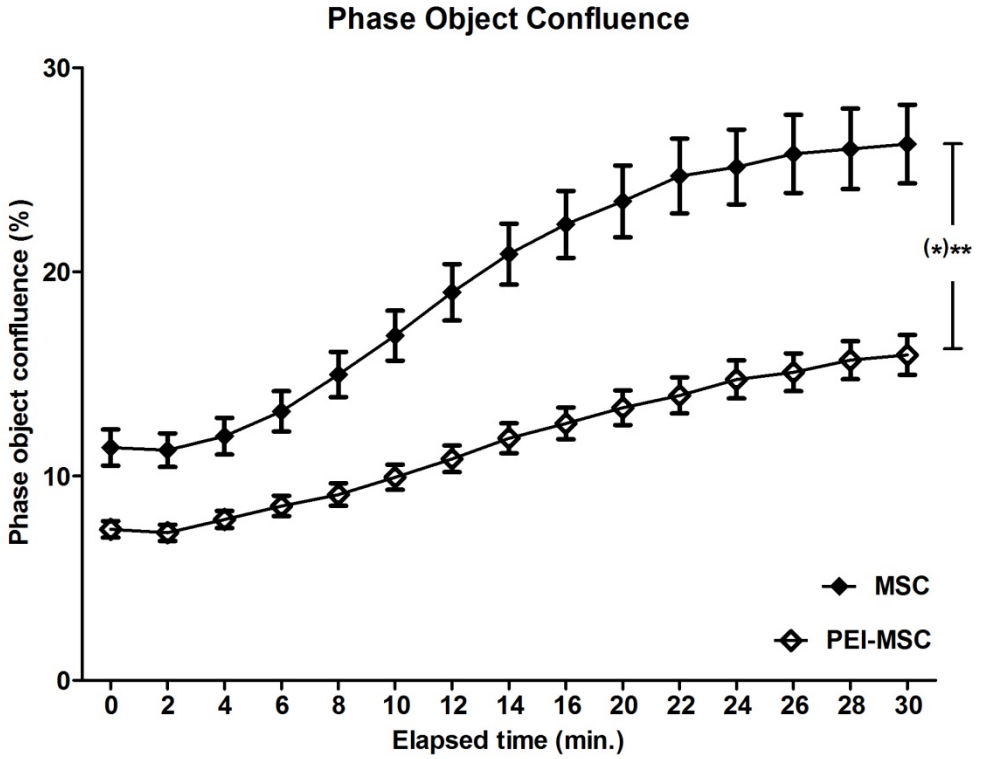


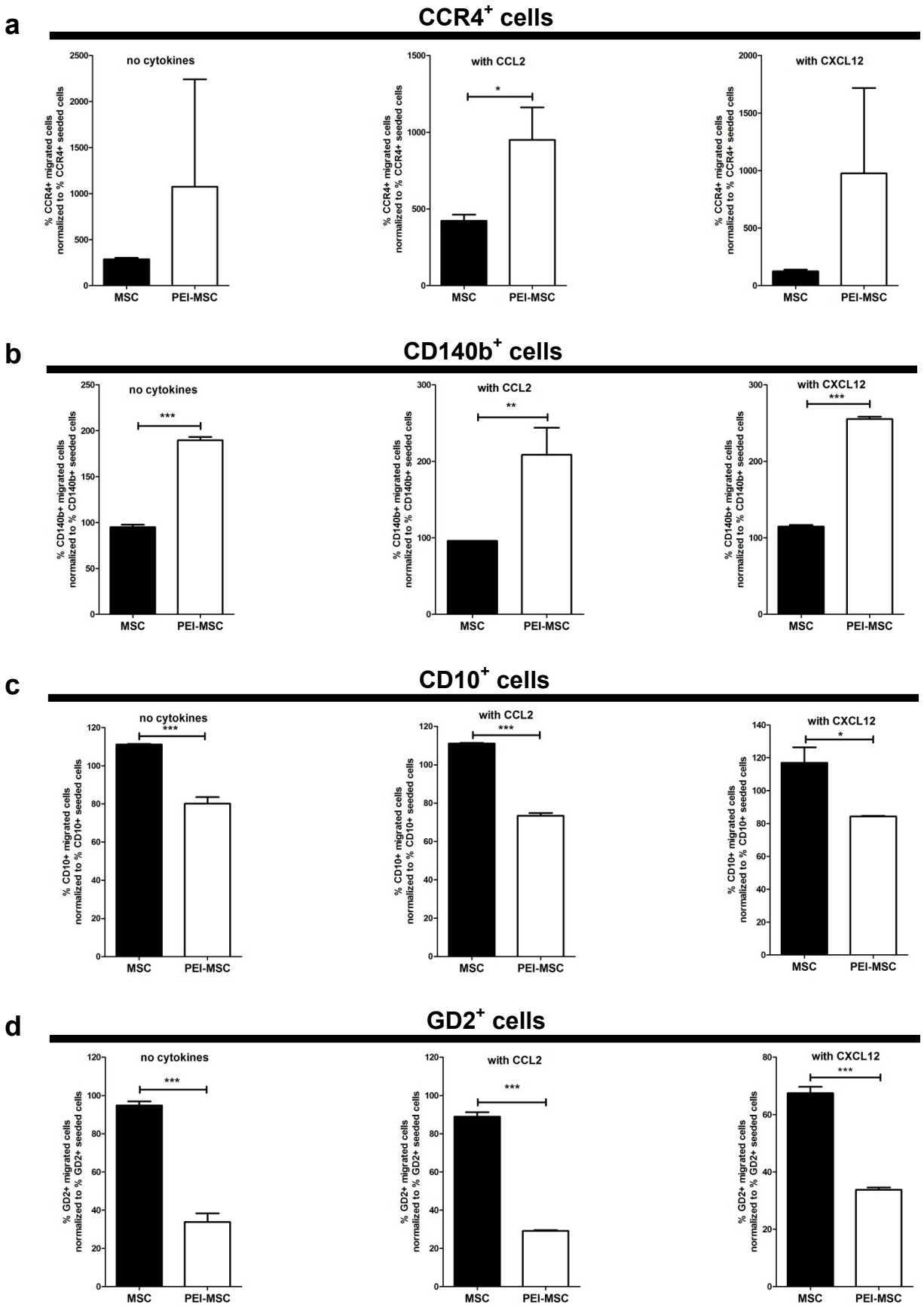
Supplementary Figure 4

Effects of PEI treatment on adhesion capacity dynamics of human BM-MSC *in vitro*.

Adhesion capacity dynamics of human BM-MSC were assessed by live cell imaging of covered area and confluence in 2 minute-intervals for up to 30 minutes.

a, b, Covered area and confluence. Over the recorded time PEI-MSC covered a smaller area hereby reaching a lower degree of confluence. PEI treatment resulted in delayed adhesion capacity of MSC compared to untreated MSC; two-tailed t-test (*$p<0.05$; **$p<0.01$; ***$p<0.001$). Error bars: SEM.

Supplementary Figure 5



Supplementary Figure 5

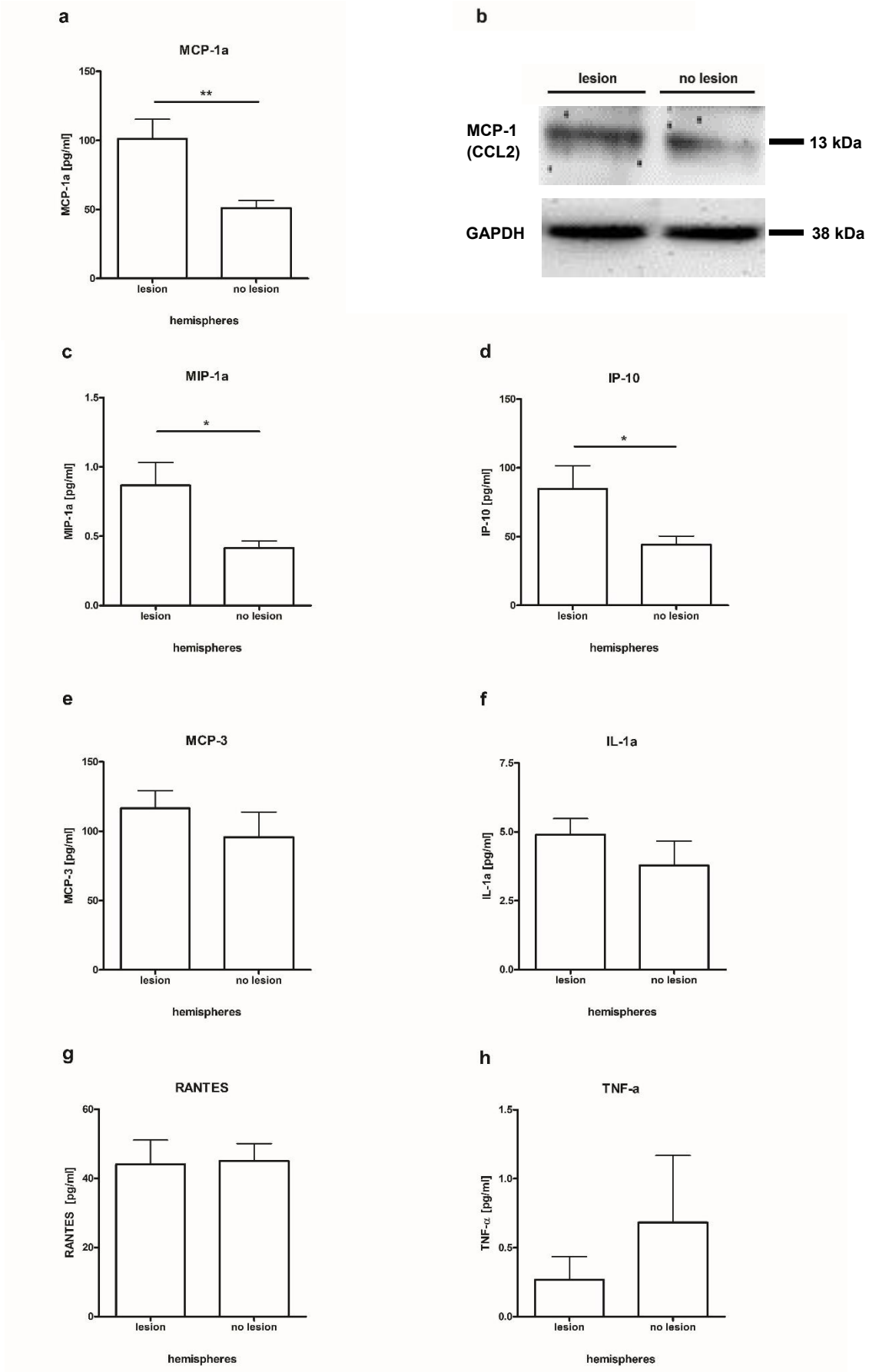
Effects of PEI treatment on migration of human BM-MSC subpopulations *in vitro*.

Migrated MSC subpopulations were identified by expression of CCR4, CD140b, CD10, or GD2 by flow cytometry under three conditions *in vitro*. Effects of PEI treatment on BM-MSC subpopulations was assessed by analyses of percent migrated antigen positive cells normalized to percent antigen positive cells that were initially seeded.

a, b, PEI treatment promoted *in vitro* migration of CCR4+ and CD140b+ human BM-MSC subpopulations; N=2-3 technical replicates out of one experiment per subpopulation marker; two-tailed t-test (*$p < 0.05$; **$p < 0.01$; ***$p<0.001$). Error bars: SD.

c, d, PEI treatment did not promote but appeared to inhibit *in vitro* migration of CD10+ and GD2+ human BM-MSC subpopulations; N=2-3 technical replicates out of one experiment per subpopulation marker; two-tailed t-test (*$p < 0.05$; ***$p<0.001$). Error bars: SD.

Supplementary Figure 6



Supplementary Figure 6

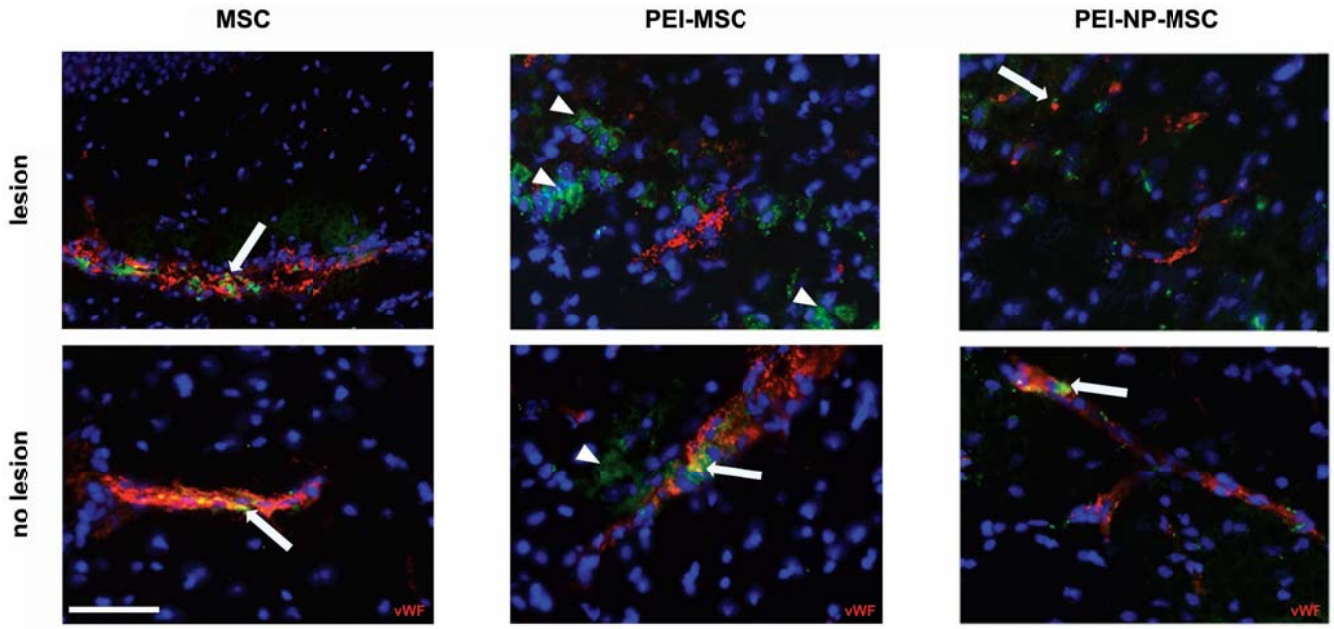
***In vivo* cytokine expressions in the brain after quinolinic acid lesion.**

After unilateral application of quinolinic acid (QA) into the hippocampal region brain lesioned and non-lesioned hemispheres were analyzed separately by multiplex protein quantification assays (a, c-h) or Western blot (b). **a,b**, the lesioned hemispheres contained higher concentrations of the CCR4 ligand MCP-1a (CCL2) as confirmed by two technologies. **c,d**, more MIP-1a and IP-10 protein could be detected in the lesioned hemispheres compared to the non-lesioned hemispheres. **e-h**, no differences in the concentrations of MCP-3, IL-1a, RANTES, and TNF-α were observed.

Two-tailed t-test (*p <0.05; **p <0.01). N=5; Error bars: SD.

Supplementary Figure 7

a



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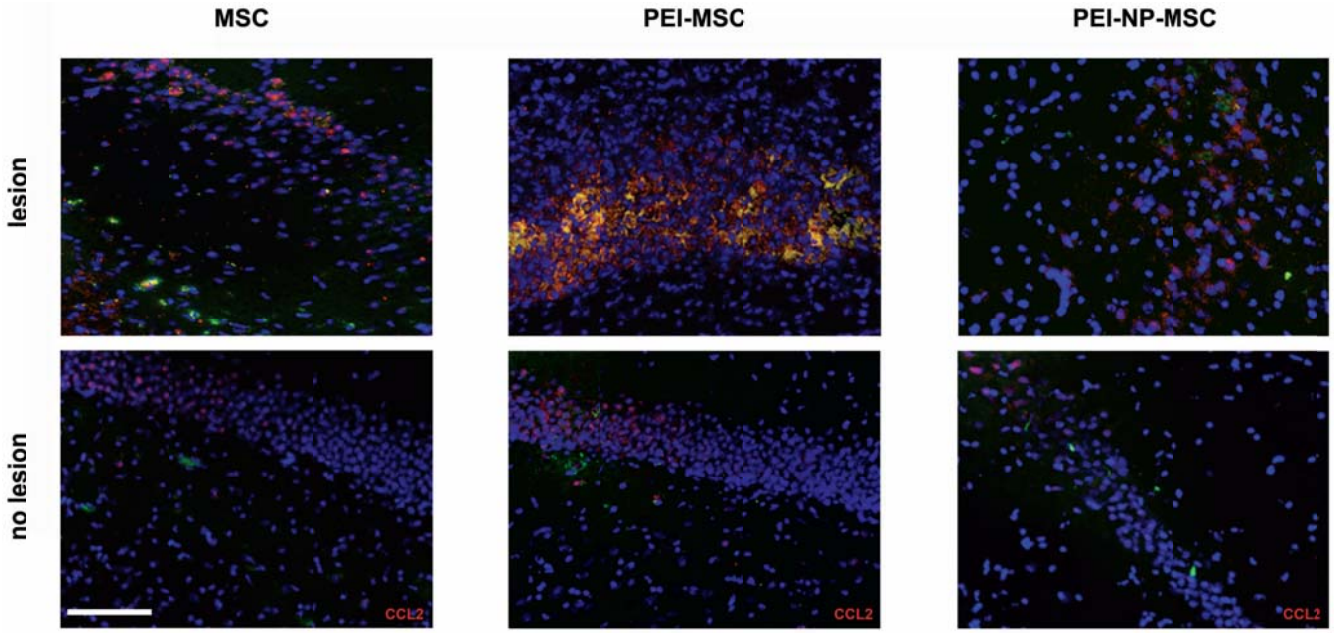


Supplementary Figure 7 Distribution of untreated and treated green fluorescent protein (GFP) positive human BM-MSC in the QA lesioned and non-lesioned hippocampal region.

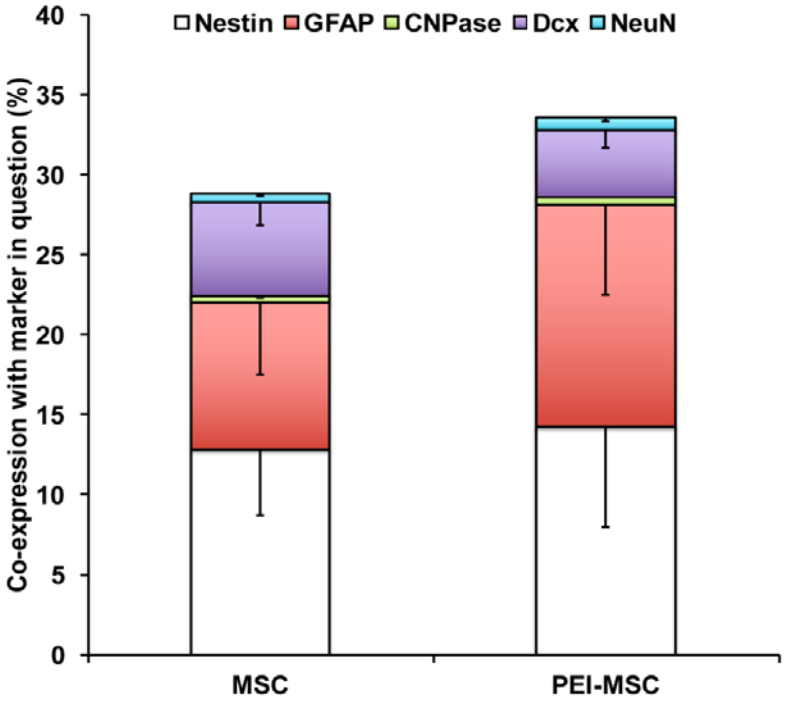
Treated and untreated eGFP+MSC could be detected in the brain with relationship to the vasculature, marked by vWF+ endothelial cells.

a, In the lesioned hippocampus, we observed more MSC that transmigrated from the vessels into the brain parenchyme (arrowheads) than MSC remaining in intravascular position (arrows). *von Willebrand Factor* (vWF): red; eGFP: green; DAPI: blue; scale bar: 50 μm.

b, Corresponding to the multiplex analysis more CCL2 protein was detected in the lesioned hippocampus/hemisphere and in particular, PEI-MSC accumulated in areas of high CCL2 protein expression. CCL2: red; eGFP: green; DAPI: blue; scale bar: 100 μm.

Supplementary Figure 8

a



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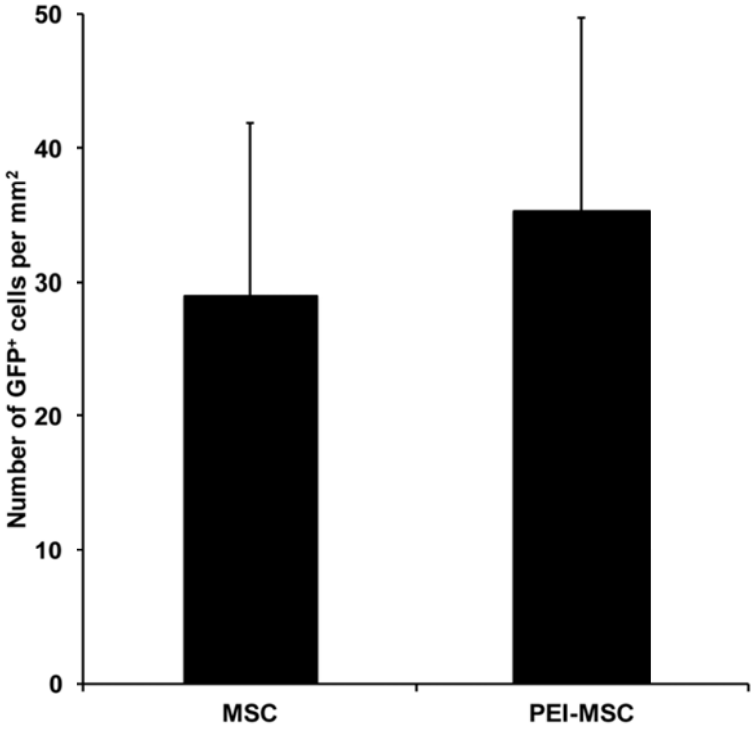
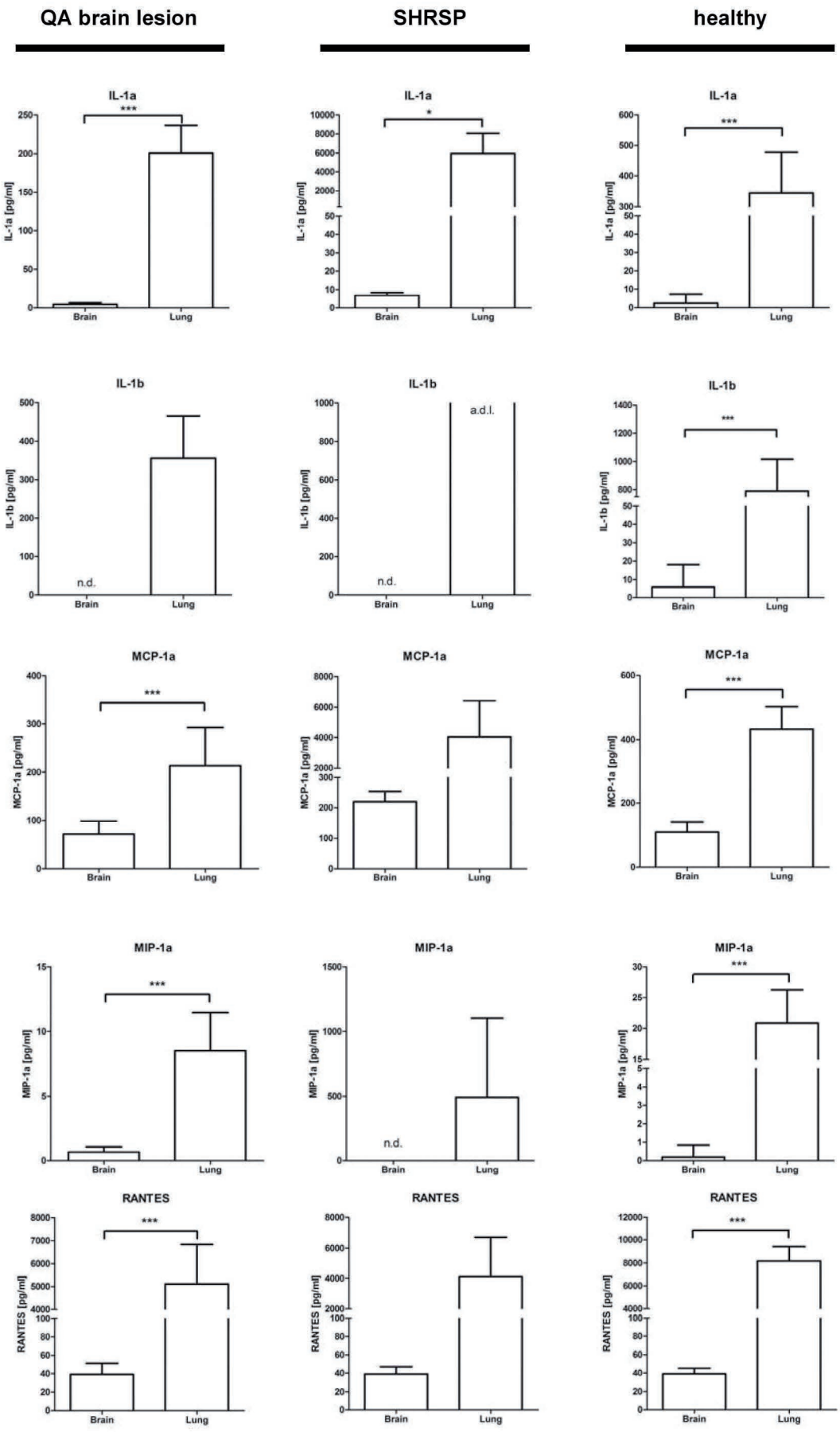
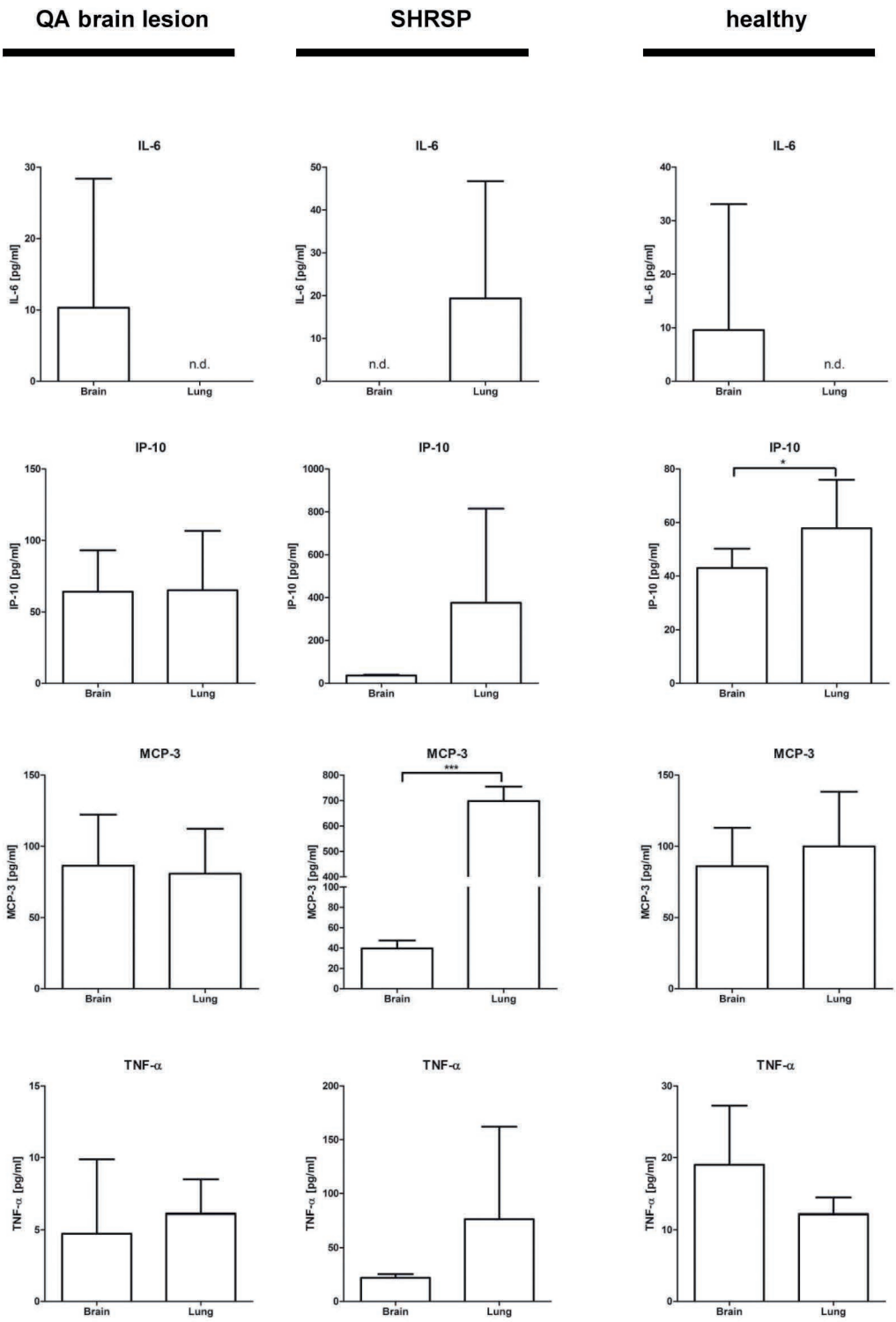


Supplementary Figure 8 Quantitative analysis of transplanted eGFP positive human BM-MSC and their *in vivo* phenotype assessment in the post-ischemic brain. Mice were exposed to transient focal cerebral ischemia followed by intravenous delivery of untreated MSC or PEI-MSC expressing eGFP for cell tracking as described in materials and methods. Thereafter, mice were sacrificed on day 28 post-stroke and sections for subsequent immunohistochemical GFP staining and immunohistochemical co-stainings against nestin, glial fibrillary acidic protein (GFAP), 2',3'-Cyclic-nucleotide 3'-phosphodiesterase (CNPase), doublercortin (DCX) or NeuN were performed. **a**, **b**, Except for DCX and CNPase, the PEI-MSC group showed a general trend to higher cell numbers but no significant differences between the two groups were observed. Error bars: SD.

Supplementary Figure 9



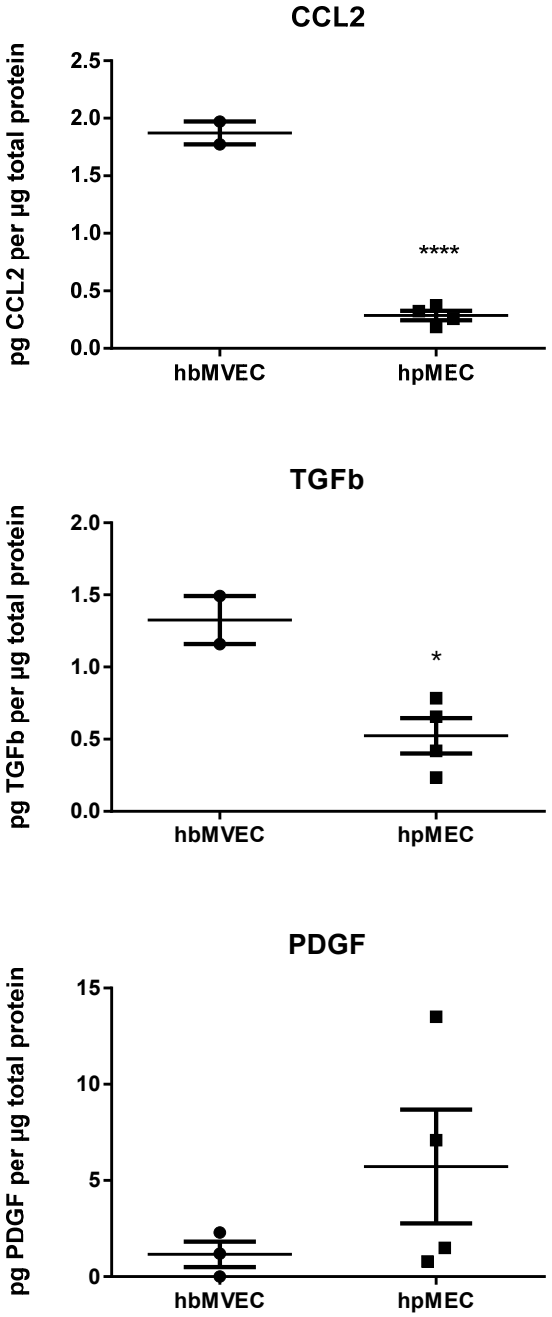

QA brain lesion
SHRSP
healthy
IL-6
IL-6 [pg/ml]
n.d.
Brain
Lung
IP-10
IP-10 [pg/ml]
*
MCP-3
MCP-3 [pg/ml]
***
TNF-α
TNF-α [pg/ml]

Supplementary Figure 9

Expressions of pro-migratory cytokines in lung and brain *in vivo*.

Multiplex analysis of *in vivo* protein expressions of pro-migratory cytokines were quantified in lungs and brains of rats with cerebral QA lesion (N=5 per organ group), stroke-prone spontaneously hypertensive rats (SHRSP) (N=3 [brain], N=2 [lung]) and healthy rats (N=6 per organ group). Except for IL-6 and TNF-α, pro-migratory cytokines could be detected at higher concentrations in the lungs compared to the brains without obvious differences between the animal models; two-tailed t-test (*$p < 0.05$; ***$p<0.001$). Error bars: SD. n.d. = not detactable; a.d.l. = above detection limit.

Supplementary Figure 10



Supplementary Figure 10 Pro-migratory cytokines in human endothelial cells.

Analyses of pro-migratory cytokines showed greater expression of CCL2, TGF-β and PDGF in endothelial cells derived from human brain (hbMVEC) compared to endothelial cells derived from human lung (hpMEC); N=2-4, each data point represents one biological replicate per group; two-tailed t-test (*$p < 0.05$; ****$p<0.0001$). Error bars: SEM.

Supplementary Table 1

	MSC (supernatant)	PEI-MSC (supernatant)	PEI-NP-MSC (supernatant)	MSC (lysate)
CD44 protein (ng/mL)	not detectable	not detectable	not detectable	6.2

Detection limit: 0.02 ng / mL

Supplementary Table 1 CD44 ELISA analysis of treated and untreated MSC.

To investigate potential shedding of CD44 molecules from MSC surface after PEI or PEI-NP treatment total MSC protein and supernatants of untreated and treated MSC were analyzed by CD44 ELISA. CD44 protein was detectable only in total MSC protein but not in supernatants indicating that CD44 molecules were not shedded by PEI or PEI-NP treatment.

Supplementary Table 2

Descriptive statistics for comparisons with low sample sizes (N≤4).

Figure	Test details	Mean difference	95% CI of difference
Figure 1 a CD44	MSC vs. PEI-MSC	30.1	7.206 to 52.99
	MSC vs. PEI-NP-MSC	17.88	-5.019 to 40.77
	PEI-MSC vs. PEI-NP-MSC	-12.23	-35.12 to 10.67
Figure 1 a CD105	MSC vs. PEI-MSC	44.31	8.307 to 80.31
	MSC vs. PEI-NP-MSC	-0.6362	-36.64 to 35.37
	PEI-MSC vs. PEI-NP-MSC	-44.95	-80.95 to -8.943
Figure 1 a CD106	MSC vs. PEI-MSC	17.1	5.144 to 29.05
	MSC vs. PEI-NP-MSC	-10.74	-22.70 to 1.208
	PEI-MSC vs. PEI-NP-MSC	-27.84	-39.79 to -15.89
Figure 1 a CD49a	MSC vs. PEI-MSC	23.76	2.224 to 45.29
	MSC vs. PEI-NP-MSC	23.95	2.420 to 45.48
	PEI-MSC vs. PEI-NP-MSC	0.1964	-21.34 to 21.73
Figure 1 a CCR4	MSC vs. PEI-MSC	-94.01	-167.8 to -20.26
	MSC vs. PEI-NP-MSC	-21.18	-156.0 to 113.6
	PEI-MSC vs. PEI-NP-MSC	72.83	-98.83 to 244.5
Figure 1 a CXCR4	MSC vs. PEI-MSC	1.179	-22.32 to 24.68
	MSC vs. PEI-NP-MSC	-32.9	-56.39 to -9.396
	PEI-MSC vs. PEI-NP-MSC	-34.07	-57.57 to -10.58
Figure 1 a CD62P	MSC vs. PEI-MSC	-3.508	-32.00 to 24.98
	MSC vs. PEI-NP-MSC	-17.48	-45.97 to 11.01
	PEI-MSC vs. PEI-NP-MSC	-13.97	-42.46 to 14.52
Figure 1 a CD49d	MSC vs. PEI-MSC	5.809	-19.32 to 30.94
	MSC vs. PEI-NP-MSC	21.93	-3.194 to 47.06
	PEI-MSC vs. PEI-NP-MSC	16.12	-9.003 to 41.25
Figure 1 a CD29	MSC vs. PEI-MSC	17.83	-13.10 to 48.76
	MSC vs. PEI-NP-MSC	4.103	-26.83 to 35.03
	PEI-MSC vs. PEI-NP-MSC	-13.72	-44.65 to 17.21
Figure 1 a CCR9	MSC vs. PEI-MSC	7.485	-17.11 to 32.08
	MSC vs. PEI-NP-MSC	-16.67	-41.26 to 7.930
	PEI-MSC vs. PEI-NP-MSC	-24.15	-48.75 to 0.4448

Figure	Test details	Mean difference	95% CI of difference
Figure 2 d	MSC+TNF vs. MSC -TNF	69.53	58.44 to 80.63
	MSC+TNF vs. MSC on CHO+TNF	84.39	66.58 to 102.2
	MSC -TNF vs. MSC on CHO+TNF	14.86	-3.840 to 33.56
Figure 2 e	MSC+TNF vs. MSC+TNF+aCD44	-57.71	-73.62 to -41.80
	PEI-NP-MSC+TNF vs. PEI-NP-MSC+TNF+aCD44	-72.46	-101.5 to -43.41

Figure	Test details	Mean difference	95% CI of difference
Figure 3 a PDGF	MSC vs. PEI-MSC	-6.807	-13.57 to -0.04265
Figure 3 a CCL2	MSC vs. PEI-MSC	-2.696	-6.910 to 1.518
Figure 3 a HPL	MSC vs. PEI-MSC	-3.719	-12.34 to 4.899

Figure	Test details	Mean difference	95% CI of difference
Supplementary Figure 2 c CD10	MSC vs. PEI-MSC	-2.4	-91.34 to 86.54
Supplementary Figure 2 c CD140b	MSC vs. PEI-MSC	-26.25	-207.3 to 154.8
Supplementary Figure 2 c GD2	MSC vs. PEI-MSC	-4.2	-38.51 to 30.11
Supplementary Figure 2 c PDPN	MSC vs. PEI-MSC	1.05	-85.99 to 88.09

Figure	Test details	Mean difference	95% CI of difference
Supplementary Figure 2 e	MSC vs. PEI-NP--MSC	-0.03292	-0.2350 to 0.1691
	MSC vs. PEI-MSC	-0.02325	-0.2253 to 0.1788
	MSC vs. PBMNC + $2x10^4$ MSC	-0.2888	-0.4908 to -0.08670
	MSC vs. PBMNC + $2x10^4$ PEI-NP-MSC	-0.3048	-0.5069 to -0.1028
	MSC vs. PBMNC + $2x10^4$ PEI-MSC	-0.2718	-0.4784 to -0.06519
	MSC vs. PBMNC + $1x10^4$ MSC	-0.6927	-0.8947 to -0.4906
	MSC vs. PBMNC + $1x10^4$ PEI-NP-MSC	-0.7606	-0.9626 to -0.5585
	MSC vs. PBMNC + $1x10^4$ PEI--MSC	-0.7725	-0.9746 to -0.5704
	MSC vs. PBMNC + $5x10^3$ MSC	-1.109	-1.311 to -0.9071
	MSC vs. PBMNC + $5x10^3$ PEI-NP-MSC	-1.115	-1.317 to -0.9131
	MSC vs. PBMNC + $5x10^3$ PEI-MSC	-1.032	-1.244 to -0.8197
	MSC vs. PBMNC + $2.5x10^3$ MSC	-1.067	-1.274 to -0.8608
	MSC vs. PBMNC + $2.5x10^3$ PEI-NP-MSC	-1.145	-1.352 to -0.9385
	MSC vs. PBMNC + $2.5x10^3$ PEI--MSC	-1.16	-1.362 to -0.9580
	MSC vs. PBMNC	-1.16	-1.362 to -0.9575
	PEI-NP--MSC vs. PEI-MSC	0.009667	-0.1924 to 0.2117
	PEI-NP--MSC vs. PBMNC + $2x10^4$ MSC	-0.2558	-0.4579 to -0.05378

	PEI-NP--MSC vs. PBMNC + $2x10^4$ PEI-NP-MSC	-0.2719	-0.4740 to -0.06986
	PEI-NP--MSC vs. PBMNC + $2x10^4$ PEI-MSC	-0.2389	-0.4455 to -0.03228
	PEI-NP--MSC vs. PBMNC + $1x10^4$ MSC	-0.6598	-0.8618 to -0.4577
	PEI-NP--MSC vs. PBMNC + $1x10^4$ PEI-NP-MSC	-0.7277	-0.9297 to -0.5256
	PEI-NP--MSC vs. PBMNC + $1x10^4$ PEI--MSC	-0.7396	-0.9416 to -0.5375
	PEI-NP--MSC vs. PBMNC + $5x10^3$ MSC	-1.076	-1.278 to -0.8742
	PEI-NP--MSC vs. PBMNC + $5x10^3$ PEI-NP-MSC	-1.082	-1.284 to -0.8802
	PEI-NP--MSC vs. PBMNC + $5x10^3$ PEI-MSC	-0.9987	-1.211 to -0.7868
	PEI-NP--MSC vs. PBMNC + $2.5x10^3$ MSC	-1.035	-1.241 to -0.8279
	PEI-NP--MSC vs. PBMNC + $2.5x10^3$ PEI-NP-MSC	-1.112	-1.319 to -0.9055
	PEI-NP--MSC vs. PBMNC + $2.5x10^3$ PEI--MSC	-1.127	-1.329 to -0.9251
	PEI-NP--MSC vs. PBMNC	-1.127	-1.329 to -0.9246
	PEI-MSC vs. PBMNC + $2x10^4$ MSC	-0.2655	-0.4676 to -0.06345
	PEI-MSC vs. PBMNC + $2x10^4$ PEI-NP-MSC	-0.2816	-0.4836 to -0.07953
	PEI-MSC vs. PBMNC + $2x10^4$ PEI-MSC	-0.2485	-0.4551 to -0.04194
	PEI-MSC vs. PBMNC + $1x10^4$ MSC	-0.6694	-0.8715 to -0.4674
	PEI-MSC vs. PBMNC + $1x10^4$ PEI-NP-MSC	-0.7373	-0.9394 to -0.5353
	PEI-MSC vs. PBMNC + $1x10^4$ PEI—MSC	-0.7493	-0.9513 to -0.5472
	PEI-MSC vs. PBMNC + $5x10^3$ MSC	-1.086	-1.288 to -0.8839
	PEI-MSC vs. PBMNC + $5x10^3$ PEI-NP-MSC	-1.092	-1.294 to -0.8899
	PEI-MSC vs. PBMNC + $5x10^3$ PEI-MSC	-1.008	-1.220 to -0.7965
	PEI-MSC vs. PBMNC + $2.5x10^3$ MSC	-1.044	-1.251 to -0.8376
	PEI-MSC vs. PBMNC + $2.5x10^3$ PEI-NP-MSC	-1.122	-1.328 to -0.9152
	PEI-MSC vs. PBMNC + $2.5x10^3$ PEI--MSC	-1.137	-1.339 to -0.9348
	PEI-MSC vs. PBMNC	-1.136	-1.338 to -0.9343
	PBMNC + $2x10^4$ MSC vs. PBMNC + $2x10^4$ PEI-NP-MSC	-0.01608	-0.2181 to 0.1860
	PBMNC + $2x10^4$ MSC vs. PBMNC + $2x10^4$ PEI-MSC	0.01696	-0.1896 to 0.2236
	PBMNC + $2x10^4$ MSC vs. PBMNC + $1x10^4$ MSC	-0.4039	-0.6060 to -0.2019
	PBMNC + $2x10^4$ MSC vs. PBMNC + $1x10^4$ PEI-NP-MSC	-0.4718	-0.6739 to -0.2698
	PBMNC + $2x10^4$ MSC vs. PBMNC + $1x10^4$ PEI--MSC	-0.4838	-0.6858 to -0.2817
	PBMNC + $2x10^4$ MSC vs. PBMNC + $5x10^3$ MSC	-0.8204	-1.022 to -0.6184

Supplementary Figure 2 e	PBMNC + $2x10^4$ MSC vs. PBMNC + $5x10^3$ PEI-NP-MSC	-0.8264	-1.028 to -0.6244
	PBMNC + $2x10^4$ MSC vs. PBMNC + $5x10^3$ PEI-MSC	-0.7429	-0.9548 to -0.5310
	PBMNC + $2x10^4$ MSC vs. PBMNC + $2.5x10^3$ MSC	-0.7787	-0.9853 to -0.5721
	PBMNC + $2x10^4$ MSC vs. PBMNC + $2.5x10^3$ PEI-NP-MSC	-0.8563	-1.063 to -0.6497
	PBMNC + $2x10^4$ MSC vs. PBMNC + $2.5x10^3$ PEI--MSC	-0.8713	-1.073 to -0.6693
	PBMNC + $2x10^4$ MSC vs. PBMNC	-0.8708	-1.073 to -0.6688
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $2x10^4$ PEI-MSC	0.03305	-0.1735 to 0.2396
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $1x10^4$ MSC	-0.3878	-0.5899 to -0.1858
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $1x10^4$ PEI-NP-MSC	-0.4558	-0.6578 to -0.2537
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $1x10^4$ PEI--MSC	-0.4677	-0.6697 to -0.2656
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $5x10^3$ MSC	-0.8043	-1.006 to -0.6023
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $5x10^3$ PEI-NP-MSC	-0.8103	-1.012 to -0.6083
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $5x10^3$ PEI-MSC	-0.7268	-0.9387 to -0.5149
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $2.5x10^3$ MSC	-0.7626	-0.9692 to -0.5560
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $2.5x10^3$ PEI-NP-MSC	-0.8402	-1.047 to -0.6336
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC + $2.5x10^3$ PEI--MSC	-0.8553	-1.057 to -0.6532
	PBMNC + $2x10^4$ PEI-NP-MSC vs. PBMNC	-0.8548	-1.057 to -0.6527
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $1x10^4$ MSC	-0.4209	-0.6275 to -0.2143
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $1x10^4$ PEI-NP-MSC	-0.4888	-0.6954 to -0.2822
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $1x10^4$ PEI--MSC	-0.5007	-0.7073 to -0.2941
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $5x10^3$ MSC	-0.8374	-1.044 to -0.6308
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $5x10^3$ PEI-NP-MSC	-0.8434	-1.050 to -0.6368
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $5x10^3$ PEI-MSC	-0.7598	-0.9761 to -0.5436
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $2.5x10^3$ MSC	-0.7956	-1.007 to -0.5846
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $2.5x10^3$ PEI-NP-MSC	-0.8733	-1.084 to -0.6622
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC + $2.5x10^3$ PEI--MSC	-0.8883	-1.095 to -0.6817
	PBMNC + $2x10^4$ PEI-MSC vs. PBMNC	-0.8878	-1.094 to -0.6812
	PBMNC + $1x10^4$ MSC vs. PBMNC + $1x10^4$ PEI-NP-MSC	-0.06792	-0.2700 to 0.1341
	PBMNC + $1x10^4$ MSC vs. PBMNC + $1x10^4$ PEI--MSC	-0.07983	-0.2819 to 0.1222
	PBMNC + $1x10^4$ MSC vs. PBMNC + $5x10^3$ MSC	-0.4165	-0.6186 to -0.2144
	PBMNC + $1x10^4$ MSC vs. PBMNC	-0.4225	-0.6246 to -0.2204

Supplementary Figure 2 e	+ 5x10^3 PEI-NP-MSC		
	PBMNC + 1x10^4 MSC vs. PBMNC + 5x10^3 PEI-MSC	-0.339	-0.5509 to -0.1271
	PBMNC + 1x10^4 MSC vs. PBMNC + 2.5x10^3 MSC	-0.3748	-0.5814 to -0.1682
	PBMNC + 1x10^4 MSC vs. PBMNC + 2.5x10^3 PEI-NP-MSC	-0.4524	-0.6590 to -0.2458
	PBMNC + 1x10^4 MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.4674	-0.6695 to -0.2654
	PBMNC + 1x10^4 MSC vs. PBMNC	-0.4669	-0.6690 to -0.2649
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC + 1x10^4 PEI--MSC	-0.01192	-0.2140 to 0.1901
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC + 5x10^3 MSC	-0.3486	-0.5506 to -0.1465
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC + 5x10^3 PEI-NP-MSC	-0.3546	-0.5566 to -0.1525
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC + 5x10^3 PEI-MSC	-0.2711	-0.4830 to -0.05913
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC + 2.5x10^3 MSC	-0.3068	-0.5134 to -0.1002
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC + 2.5x10^3 PEI-NP-MSC	-0.3845	-0.5911 to -0.1779
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.3995	-0.6016 to -0.1974
	PBMNC + 1x10^4 PEI-NP-MSC vs. PBMNC	-0.399	-0.6011 to -0.1969
	PBMNC + 1x10^4 PEI--MSC vs. PBMNC + 5x10^3 MSC	-0.3367	-0.5387 to -0.1346
	PBMNC + 1x10^4 PEI--MSC vs. PBMNC + 5x10^3 PEI-NP-MSC	-0.3427	-0.5447 to -0.1406
	PBMNC + 1x10^4 PEI--MSC vs. PBMNC + 5x10^3 PEI-MSC	-0.2591	-0.4710 to -0.04722
	PBMNC + 1x10^4 PEI--MSC vs. PBMNC + 2.5x10^3 MSC	-0.2949	-0.5015 to -0.08833
	PBMNC + 1x10^4 PEI--MSC vs. PBMNC + 2.5x10^3 PEI-NP-MSC	-0.3726	-0.5792 to -0.1660
	PBMNC + 1x10^4 PEI--MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.3876	-0.5896 to -0.1855
	PBMNC + 1x10^4 PEI--MSC vs. PBMNC	-0.3871	-0.5891 to -0.1850
	PBMNC + 5x10^3 MSC vs. PBMNC + 5x10^3 PEI-NP-MSC	-0.006	-0.2081 to 0.1961
	PBMNC + 5x10^3 MSC vs. PBMNC + 5x10^3 PEI-MSC	0.07753	-0.1344 to 0.2894
	PBMNC + 5x10^3 MSC vs. PBMNC + 2.5x10^3 MSC	0.04174	-0.1649 to 0.2483
	PBMNC + 5x10^3 MSC vs. PBMNC + 2.5x10^3 PEI-NP-MSC	-0.03589	-0.2425 to 0.1707
	PBMNC + 5x10^3 MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.05092	-0.2530 to 0.1511
	PBMNC + 5x10^3 MSC vs. PBMNC	-0.05042	-0.2525 to 0.1516
	PBMNC + 5x10^3 PEI-NP-MSC vs. PBMNC + 5x10^3 PEI-MSC	0.08353	-0.1284 to 0.2954
	PBMNC + 5x10^3 PEI-NP-MSC vs. PBMNC + 2.5x10^3 MSC	0.04774	-0.1589 to 0.2543
	PBMNC + 5x10^3 PEI-NP-MSC vs. PBMNC + 2.5x10^3 PEI-NP-MSC	-0.02989	-0.2365 to 0.1767
	PBMNC + 5x10^3 PEI-NP-MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.04492	-0.2470 to 0.1571

Supplementary Figure 2 e	PBMNC + 5x10^3 PEI-NP-MSC vs. PBMNC	-0.04442	-0.2465 to 0.1576
	PBMNC + 5x10^3 PEI-MSC vs. PBMNC + 2.5x10^3 MSC	-0.03579	-0.2520 to 0.1805
	PBMNC + 5x10^3 PEI-MSC vs. PBMNC + 2.5x10^3 PEI-NP-MSC	-0.1134	-0.3297 to 0.1028
	PBMNC + 5x10^3 PEI-MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.1285	-0.3404 to 0.08347
	PBMNC + 5x10^3 PEI-MSC vs. PBMNC	-0.128	-0.3399 to 0.08397
	PBMNC + 2.5x10^3 MSC vs. PBMNC + 2.5x10^3 PEI-NP-MSC	-0.07764	-0.2887 to 0.1334
	PBMNC + 2.5x10^3 MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.09266	-0.2993 to 0.1139
	PBMNC + 2.5x10^3 MSC vs. PBMNC	-0.09216	-0.2988 to 0.1144
	PBMNC + 2.5x10^3 PEI-NP-MSC vs. PBMNC + 2.5x10^3 PEI--MSC	-0.01502	-0.2216 to 0.1916
	PBMNC + 2.5x10^3 PEI-NP-MSC vs. PBMNC	-0.01452	-0.2211 to 0.1921
	PBMNC + 2.5x10^3 PEI--MSC vs. PBMNC	0.0005	-0.2016 to 0.2026

Figure	**Test details**	**Mean difference**	**95% CI of difference**
Supplementary Figure 2 f VEGF-A supernatant	MSC vs. PEI-MSC	-467.5	-653.1 to -281.9
	MSC vs. PEI-NP-MSC	-97	-282.6 to 88.63
	PEI-MSC vs. PEI-NP-MSC	370.5	184.9 to 556.1
Supplementary Figure 2 f VEGF-A lysate	MSC vs. PEI-MSC	-38.35	-68.79 to -7.911
	MSC vs. PEI-NP-MSC	-3.367	-33.81 to 27.07
	PEI-MSC vs. PEI-NP-MSC	34.98	4.544 to 65.42
Supplementary Figure 2 f NGFb supernatant	MSC vs. PEI-MSC	-23.05	-24.29 to -21.81
	MSC vs. PEI-NP-MSC	5.81	4.573 to 7.047
	PEI-MSC vs. PEI-NP-MSC	28.86	27.62 to 30.10
Supplementary Figure 2 f FGFb supernatant	MSC vs. PEI-MSC	-24.42	-26.15 to -22.69
	MSC vs. PEI-NP-MSC	18.18	16.45 to 19.91
	PEI-MSC vs. PEI-NP-MSC	42.6	40.87 to 44.33
Supplementary Figure 2 f FGFb lysate	MSC vs. PEI-MSC	-2360	-3702 to -1018
	MSC vs. PEI-NP-MSC	1494	151.5 to 2836
	PEI-MSC vs. PEI-NP-MSC	3854	2511 to 5196
Supplementary Figure 2 f LIF supernatant	MSC vs. PEI-MSC	-38	-92.85 to 16.85
	MSC vs. PEI-NP-MSC	-13.33	-68.18 to 41.52
	PEI-MSC vs. PEI-NP-MSC	24.67	-30.18 to 79.52
Supplementary Figure 2 f LIF lysate	MSC vs. PEI-MSC	-9.883	-17.61 to -2.154
	MSC vs. PEI-NP-MSC	-1.367	-9.096 to 6.362
	PEI-MSC vs. PEI-NP-MSC	8.517	0.7877 to 16.25
Supplementary Figure 2 f HGF supernatant	MSC vs. PEI-MSC	262.3	196.2 to 328.5
	MSC vs. PEI-NP-MSC	290.3	224.2 to 356.5
	PEI-MSC vs. PEI-NP-MSC	28	-38.14 to 94.14

Supplementary Figure 2 f HGF lysate	MSC vs. PEI-MSC	323.2	200.8 to 445.5
	MSC vs. PEI-NP-MSC	186.8	64.45 to 309.2
	PEI-MSC vs. PEI-NP-MSC	-136.3	-258.7 to -13.95
Supplementary Figure 2 f ANG-1 supernatant	MSC vs. PEI-MSC	205	162.9 to 247.2
	MSC vs. PEI-NP-MSC	119.9	77.76 to 162.0
	PEI-MSC vs. PEI-NP-MSC	-85.13	-127.3 to -42.99
Supplementary Figure 2 f ANG-1 lysate	MSC vs. PEI-MSC	47.03	35.36 to 58.71
	MSC vs. PEI-NP-MSC	28.17	16.49 to 39.85
	PEI-MSC vs. PEI-NP-MSC	-18.86	-30.54 to -7.186

Figure	Test details	Mean difference	95% CI of difference
Supplementary Figure 5 a CCR4 no ck	MSC vs. PEI-MSC	-788.4	-2745 to 1169
Supplementary Figure 5 a CCR4 with CCL2	MSC vs. PEI-MSC	-527.1	-895.0 to -159.1
Supplementary Figure 5 a CCR4 with CXCL12	MSC vs. PEI-MSC	-851.3	-2097 to 394.5
Supplementary Figure 5 a CD140b no ck	MSC vs. PEI-MSC	-94.65	-103.5 to -85.85
Supplementary Figure 5 a CD140b with CCL2	MSC vs. PEI-MSC	-112.6	-171.8 to -53.39
Supplementary Figure 5 a CD140b with CXCL12	MSC vs. PEI-MSC	-140.5	-148.0 to -133.1
Supplementary Figure 5 a CD10 no ck	MSC vs. PEI-MSC	30.98	25.18 to 36.77
Supplementary Figure 5 a CD10 with CCL2	MSC vs. PEI-MSC	37.66	35.24 to 40.09
Supplementary Figure 5 a CD10 with CXCL12	MSC vs. PEI-MSC	32.58	10.19 to 54.96
Supplementary Figure 5 a GD2 no ck	MSC vs. PEI-MSC	60.95	51.76 to 70.14

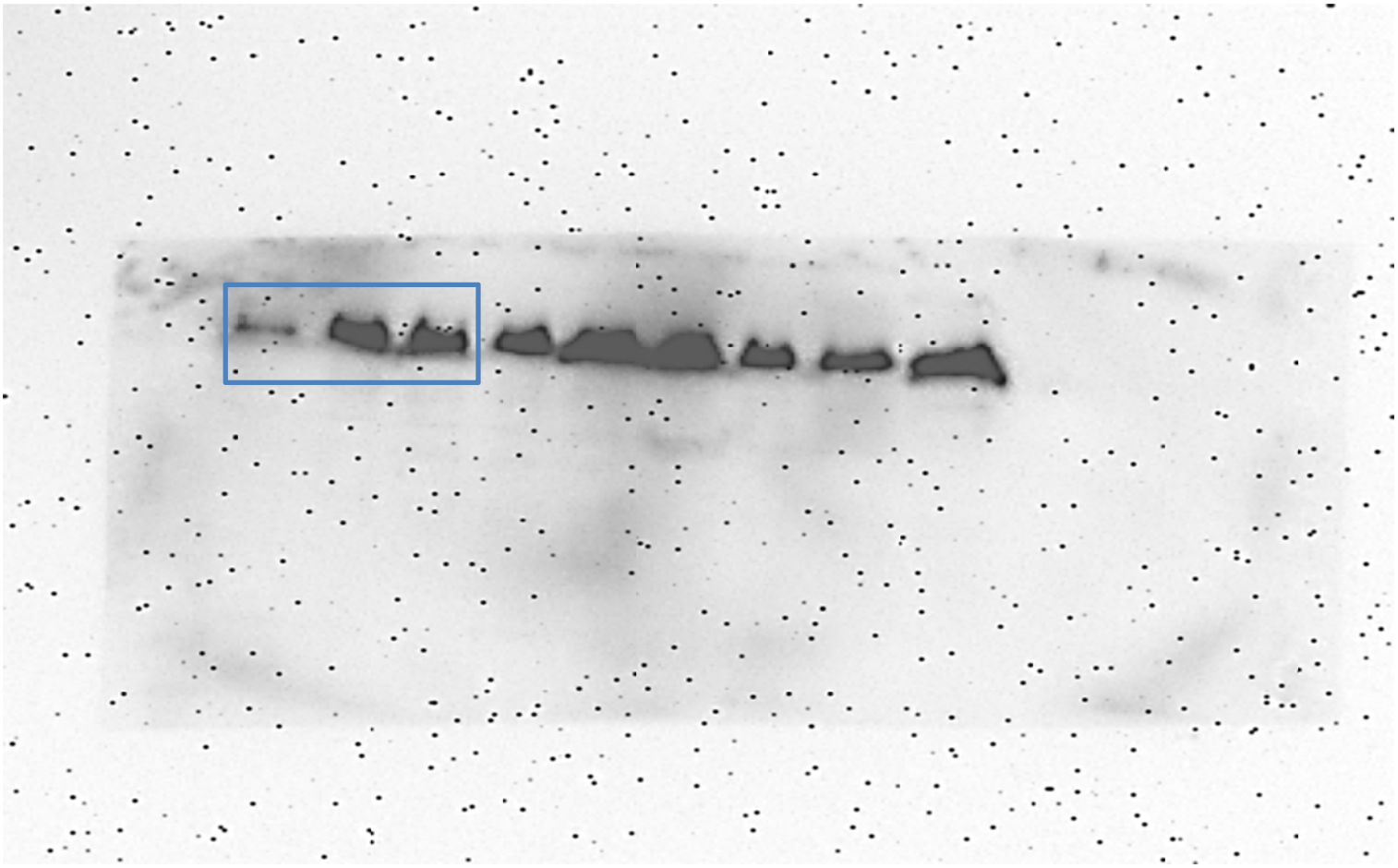
Supplementary Figure 5 a GD2 with CCL2	MSC vs. PEI-MSC	59.74	54.18 to 65.30
Supplementary Figure 5 a GD2 with CXCL12	MSC vs. PEI-MSC	33.66	28.25 to 39.07

Figure	Test details	Mean difference	95% CI of difference
Supplementary Figure 10 CCL2	hbMVEC vs. hpMEC	-1.587	-1.825 to -1.348
Supplementary Figure 10 TGFb	hbMVEC vs. hpMEC	-0.803	-1.386 to -0.2202
Supplementary Figure 10 PDGF	hbMVEC vs. hpMEC	4.56	-4.542 to 13.66

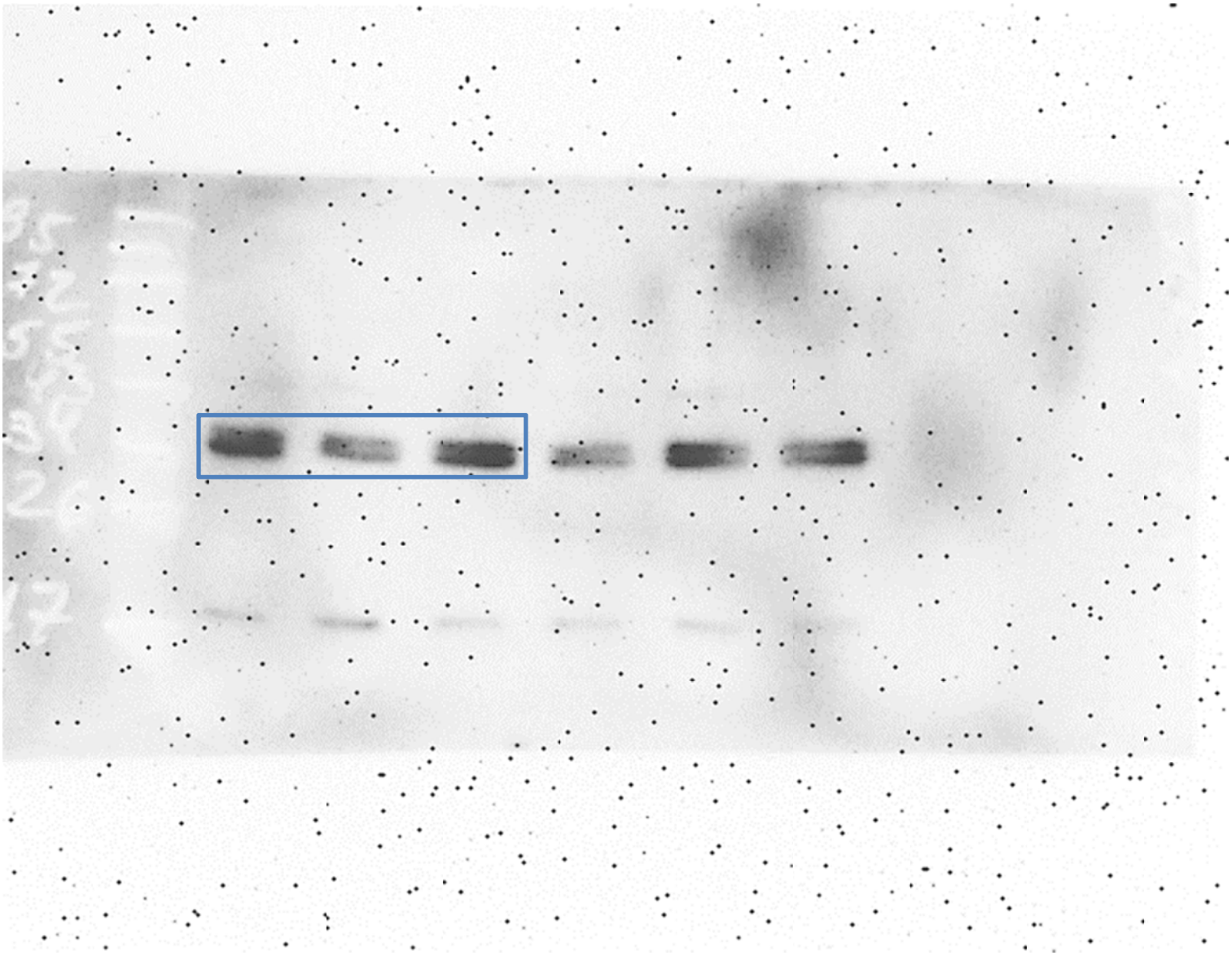
Full Western Blots

The blue frames indicate the areas shown in the Figures.

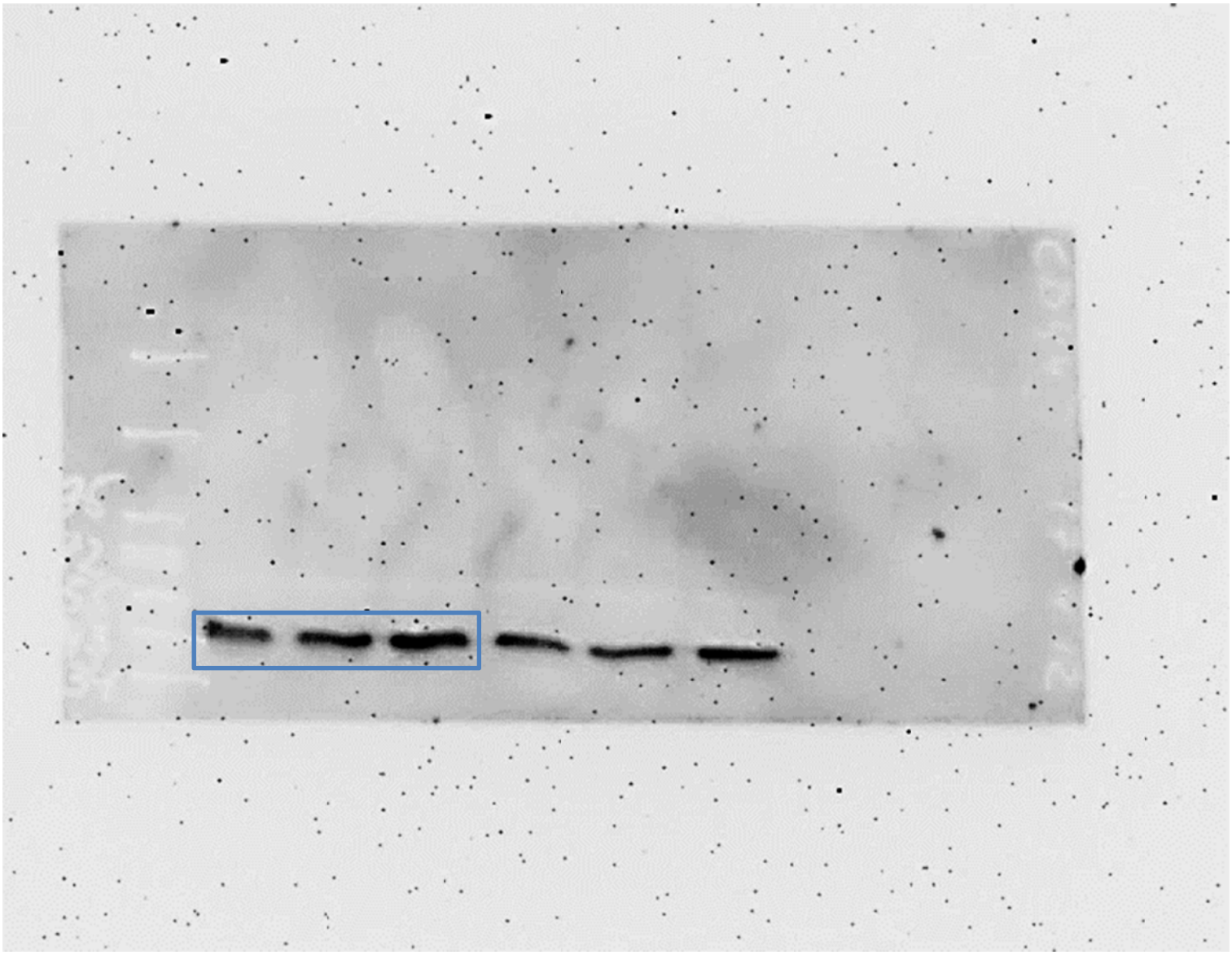
CD44 Fig.1b



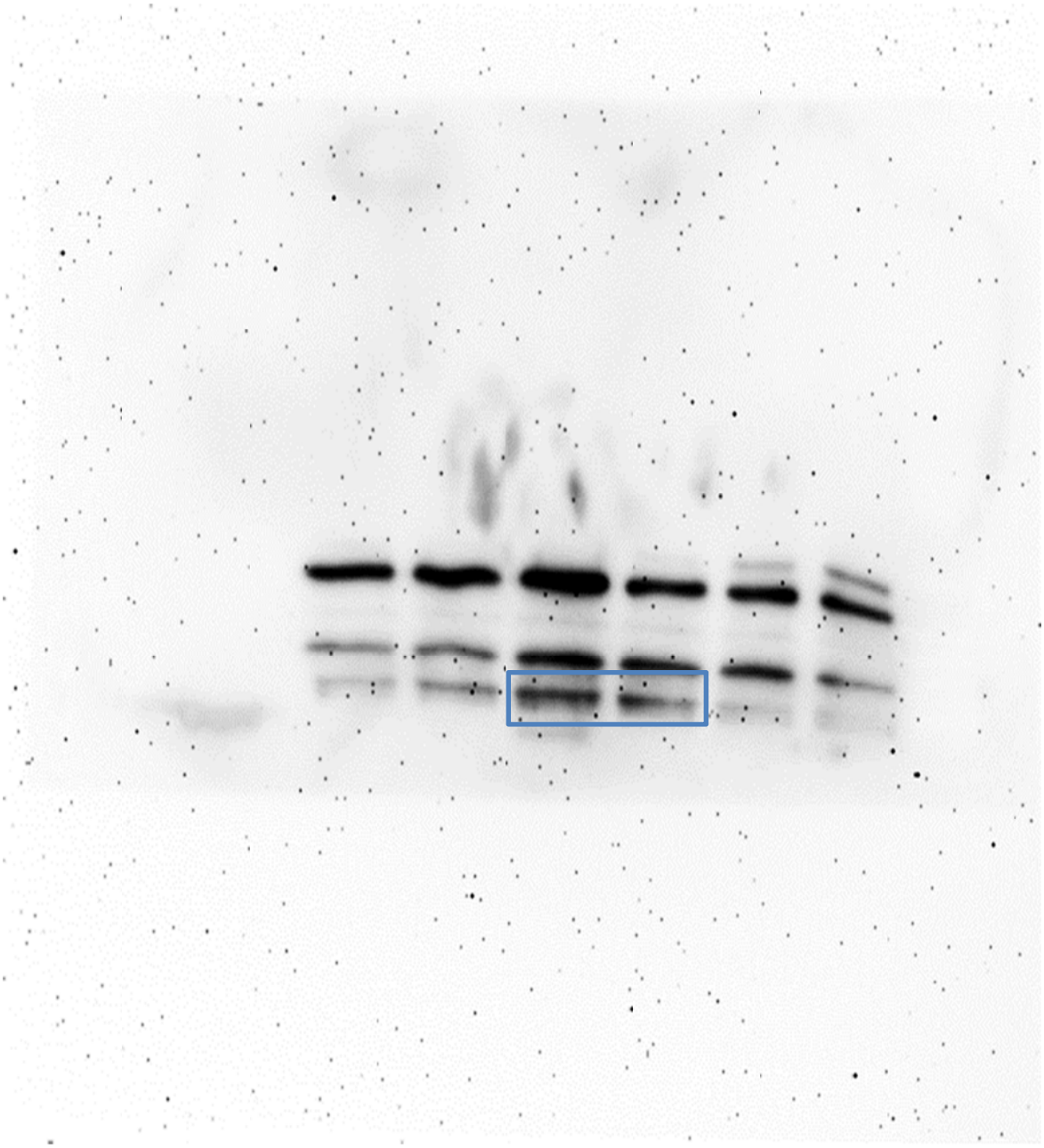
CXCR4 Fig.1b



GAPDH Fig.1b



CCL2 Suppl Fig.6



GAPDH Suppl Fig.6