

Supplemental Data and information for:

Improving the therapeutic efficacy of mesenchymal stromal cells to restore perfusion in critical limb ischemia through pulsed focused ultrasound

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Supplemental Table 1: List of Abbreviations

bFGF	Basic Fibroblast Growth Factor
BMSC	Bone Marrow Stromal Cells
CAM	Cell Adhesion Molecules
CCTF	Cytokines, Chemokines, Trophic Factors
FUS	Focused Ultrasound
GCSF	Granulocyte Colony-Stimulating Factor
GMCSF	Granulocyte Macrophage Colony-Stimulating Factor
HSP-70	Heat Shock Protein 70
ICAM	Intercellular Adhesion Molecule
IFN γ	Interferon Gamma
IGF-1	Insulin-like Growth Factor
IL1 α	Interleukin-1 Alpha
IL1 β	Interleukin-1 Beta
IL2	Interleukin-2
IL3	Interleukin 3
IL4	Interleukin 4
IL5	Interleukin 5
IL6	Interleukin 6
IL9	Interleukin 9
IL10	Interleukin 10
IL12p40	Interleukin 12 (p40 subunit)
IL12p70	Interleukin 12 (p70 subunit)
IL13	Interleukin 13
IL15	Interleukin 15
IL17	Interleukin 17
IL18	Interleukin 18
KC	Keratinocyte-derived Chemokine or Keratinocyte Chemoattractant
LIF	Leukemia Inhibitory Factor
MSC	Mesenchymal Stem Cell
MCP1	Monocyte Chemoattractant Protein-1
MCSF	Monocyte Colony Stimulating Factor
MIG	Monokine Induced by Gamma-Interferon
MIP1 α	Macrophage Inflammatory Protein 1 Alpha
MIP1 β	Macrophage Inflammatory Protein 1 Beta
MIP2	Macrophage Inflammatory Protein 2
NF κ B	Nuclear Factor Kappa-Light-Chain-Enhancer of Activated B Cells
PDGF	Platelet-Derived Growth Factor
pFUS	Pulsed Focused Ultrasound
RANTES	Regulated on Activation, Normal T-Cell Expressed and Secreted
SCF	Stem Cell Factor

SDF-1 α	Stromal Cell-Derived Factor 1 Alpha
TNF α	Tumor Necrosis Factor Alpha
VCAM	Vascular Cell Adhesion Molecule
VEGF	Vascular Endothelial Growth Factor

Supplemental Table 2: Pre-clinical PAD studie

Ref #	Animal Model	Age	Ischemia Model	Cell type	Route of admin.	Time of Cell Admin Post-PAD	Outcome-first day increase in perfusion
45	C57BL/6 m; CD4 ^{-/-} m	12w k	Acute	mCD4 ⁺ cells, mCD4 depleted spleenocytes	IV	Day 3	Day 28
48	Athymic nude m	8- 10w k	Critical	CM-Dil- labeled hEPC	IV	Day 0	Day 21
46	Nude KSN/Slc m	8wk	Acute	h-VPC	IA	Day -1	Day 14
N/A *	Immunodeficient m	NR	Critical	hBM-EC, hiPSC-EC, hESC-CE	IM	Day 0	Day 14
18	Syngenic FVB m	10- 12w k	Acute	mMNC	IM IM	Day 0	NS
	C57BL/6 m	10- 12w k	Acute	mMNC	IV	Day 0	NS
15	Athymic nude r	5 wk	Acute	hEPC + SW	IV	3wk	2 wk post treatment
19	C57BL/6 m	6-8 wk	Acute	mMNC	IM	Day 0	Day 7
16	Athymic nu r	8wk	Acute	hEPC	IM	Day28 Day 31 Day 34	Day 42
20	C57BL/6J m	8wk	Acute	mMSC + Simvastatin (for 21 days) rEPC;	IM	Day 0	Day 21
17	Fisher F344 r	NR	Acute	UM-SDF-1 + rEPC	IV	Day 14	Day 28
13	NOD/SCID β 2M null or NOD/SCID/MPSVII m	NR	Acute	hMNC, ALDHlo, ALDHhi cells, CD14 ⁺ cells	IV	Day 0- 1	Day 7

Reference	Animal Model	Age	Ischemia Model	Cell type	Route	Time of Cell Admin Post-PAD	Outcome-initial day of significant increase in perfusion
47	C nude m	8-10wk	Critical	mADSC	IM	Day 1	Day 14
21	C57BL/6J m	NR	Acute	mMSC	IM	Day 0	Day 7
22	C57BL/6J m	12-16wk	Acute	mMAPC-U, mBMC, mMAPC-VP	IM	Day 0	Day 4
	BALB/C-nu/nu	12-16wk	Critical	mMAPC-U, mBMC-U2, hMAPC-VP mBMC, mCD34 ⁺ /M	IM	Day 5	Day 9
14	ApoE ^{-/-}	8-15m	Acute	cad ⁺ BMC mCD34 ⁻ /Mcad ⁺ BMC	IA	Day 0	Day 0

* Lai, W.H. *et al.* PLoS One 2013;8:e57876

m - mouse; h - human; r - rat; rb - rabbit; nu - nude; IM - intramuscular; IV- intravenous; IA - intra-arterial; EP - electroporation; CM - conditioning media; NR-not reported; NS-not significant; SW-shock wave; wk- week(s); admin-administration, MSCs – mesenchymal stem cell, EPC – endothelial progenitor cell, EC – endothelial progenitor cell, EC – endothelial-like cell, EC – endothelial-like cell, iPSC – induced pluripotent stem cell, BM - bone marrow mononuclear cells, ESC– embryonic stem cells, MNC – bone marrow– derived mononuclear cells, MSC – mesenchymal stem cells, UM – ultrasound-mediated, SDF-1 – stromal cell derived factor-1, lo – low, hi-high, ALDH – aldehyde dehydrogenase, ADSC – adipose-derived stromal cell, MAPC – multipotent adult progenitor cells, MAPC-U – undifferentiated MAPCs, MAPC-VP – MAPC-derived vascular pro-genitors, MAPC – derived vascular pro-genitors, BMC – bone marrow stem/progenitor cells, ApoE^{-/-} – hypercholesterolemic mouse, CD34⁺/Mcad⁺ BMC – BMC expressing both CD34 and M- cadherin surface molecules, CD34⁻/Mcad⁺ BMC – BMC expressing M- cadherin surface molecules, CD34⁺/Mcad⁻ BMC – BMC expressing both CD34 surface molecules

Supplemental Figure 1: Primary data of proteomic responses to critical limb ischemia (CLI) and pulsed focused ultrasound (pFUS). * $p < 0.05$ using one-way ANOVA with Bonferroni correction; $n = 6$ mice/group. Data are means \pm SD. See Supplemental Table 1 above for abbreviations.



