Supplemental Table S1

	UNIGENE	GENE NAME			MG (/CTRL)	rMSC (/MG)	cMSC (/MG)
CELL SUBSETS	PTPRC	CD45	Protein tyrosine phosphatase, receptor type, C	in hematopoietic cells			
	CD20	CD20	CD20 molecule	in B cells	↑↑		↓
	CD4	CD4	CD4 molecule	in Taux cells			
	CD8A	CD8	CD8a molecule	in Tc cells			
	NCAM1	CD56	Neural cell adhesion molecule 1	in NK cells			
	ITGAM	CD11b	Integrin, alpha M	in monocytes	↓↓		
	CD14	CD14	CD14 molecule	in macrophages			
	CD1D	CD1D	CD1d molecule	in NKT cells			
	PECAM1	CD31	Platelet endothelial cell adhesion molecule 1	in endothelial cells			
TRANSCRIPTION FACTORS	PAX5	PAX5	Paired box 5	in naives B cells			
	XBP1	XBP1	X-box binding protein 1	plasma B cells differentiation			
	IRF4	IRF4	Interferon regulatory factor4	immune response regulation	↓↓		
	BCL6	BCL6	B-cell CLL/lymphoma 6	transcription factor TFH	↑		
	TBX21	t-bet	T-box 21	transcription factor TH1			
	GATA3	GATA3	GATA binding protein 3	transcription factor TH2	↑		
	RORC	RORc	RAR-related orphan receptor C	transcription factor TH17			
	FOXP3	FOXP3	Forkhead box P3	transcription factor Treg			
SIGNALIZATION MOLECULES	PRDM1	BLIMP1	PR domain containing 1, with ZNF domain	plasma B cells differentiation			
	STAT1	STAT1	Signal transducer and activator of transcription 1	transcription factor TH1			
	STAT4	STAT4	Signal transducer and activator of transcription 4	transcription factor TH1			
	STAT6	STAT6	Signal transducer and activator of transcription 6	transcription factor TH2	↑↑		

Supplemental Table S1

	UNIGENE	GENE NAME			MG (/CTRL)	rMSC (/MG)	cMSC (/MG)
ACCESSORY MOLECULES	CTLA4	CD152	cytotoxic T-lymphocyte-associated protein 4	on T cell, coinhibitor			
	CD80	B7-1	CD80 molecule	on APC			
	CD86	B7-2	CD86 molecule	on APC	↑		
	ICOSLG	CD275	Inducible T-cell co-stimulator ligand	on APC, costimulator			
	ICOS	ICOS	Inducible T-cell co-stimulator	on T cell			
	CD40L	CD154	CD40L molecule	on T cell, costimulator		↓	↓↓
	CD40	CD40	CD40 molecule	on APC cell	↑↑	↓	↓↓
	PD-L1	CD274	Programmed death-ligand 1	on APC, costimulator	↑↑		↓↓
	CD55	CD55	CD55 molecule	complement regulator			↑↑
CYCLE AND ACTIVATION MOLECULES	MKI67	MKI67	Marker Of Proliferation Ki-67	proliferating cells			↓↓
	CCNB1	cyclinB1	Cyclin B1	G2/M specific	↓		
	CCNE1	cyclinE1	Cyclin E1	G1/S specific			
	BCL2	BCL2	B cell lymphoma 2	anti apoptotic	↑		
	FAS	FAS	Fas (TNF receptor superfamily, member 6)	apoptose			
	CD69	CD69	CD69 molecule	activation	↑↑		
	CD25	CD25	CD25 molecule	activation			
	CD38	CD38	CD38 molecule	activation			
	CD27	CD27	CD27 molecule	activation			

Supplemental Table S1

	UNIGENE	GENE NAME			MG (/CTRL)	rMSC (/MG)	cMSC (/MG)
CHEMOKINES AND CHEMOKINES RECEPTORS	TNFSF13B	BAFF	Tumor necrosis factor (ligand) superfamily, member 13B	chemokine (GC)	↑↑		↓↓
	TNFSF13	APRIL	Tumor necrosis factor (ligand) superfamily, member 13	chemokine (GC)	↑		
	CXCL13	CXCL13	Chemokine (C-X-C motif) ligand 13	chemokine (GC)			
	CXCR3	CXCR3	Chemokine (C-X-C motif) receptor 3	chemokine receptor			
	CXCR5	CXCR5	Chemokine (C-X-C motif) receptor 5	chemokine receptor (GC)			
	CCR6	CCR6	Chemokine (C-C motif) receptor 6	chemokine receptor (TH17)			
	CCR8	CCR8	Chemokine (C-C motif) receptor 8	chemokine receptor (Th2)	↑		
	CCR9	CCR9	Chemokine (C-C motif) receptor 8	chemokine receptor			
	IL1B	IL1b	Interleukin 1, beta	interleukin, proinflammatory			
	IL2	IL2	Interleukin 2	interleukin	↑↑		
	IL6	IL6	Interleukin 6	interleukin (Th1)	↑↑		
	IL10	IL10	Interleukin 10	interleukin (Th2)			
	IL17A	IL17A	Interleukin 17A	interleukin (Th17)	↑↑		
	IL21	IL21	Interleukin 21	interleukin (TFH)	↓		
	IL7R	IL7R	Interleukin 7 receptor	interleukin receptor	↑↑		
	IL17RA	IL17RA	Interleukin 17 receptor A	interleukin receptor	↓↓		
	IFNG	IFNg	Interferon, gamma	cytokine (Th1)	↑↑		
	TNFA	TNFa	Tumor necrosis factor	cytokine (Th1)	↑↑	↓	↓↓

Global assessment of genes involved in activation, differentiation, and migration in the xenogeneic thymus. The gene expression was analyzed by real-time PCR in human grafted thymus samples. Three housekeeping genes (GAPD, GUSB, and PPIA) were used for normalization. Among the 57 genes explored, more than 20 were deregulated in the MG group compared to the CTRL group. Several of them were regulated after cMSC treatment. A single arrow, $p<0.10$, double arrow, $p<0.05$. Statistical analysis was performed by Student t test to compare CTRL to MG group, and by ANOVA test to compare MG, rMSC and cMSC groups.

Abs	Conjugate	Host		Reactivity	Clone	Supplier	
CD45	efluor450	mouse	IgG1	human	HI30	eBioscience	San Diego, CA, USA
CD4	FITC	mouse	IgG1	human	MT310	Dako	Trappes, France
CD8	APC	mouse	IgG2a	human	okt8	eBioscience	San Diego, CA, USA
CD19	FITC	mouse	IgG1	human	HIB19	eBioscience	San Diego, CA, USA
LiveDead	IR					LifeTechnologies	Saint-Aubin, France

Supplemental Table S2

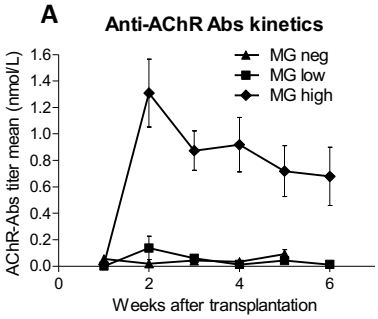
List of Abs used in flow cytometry experiments

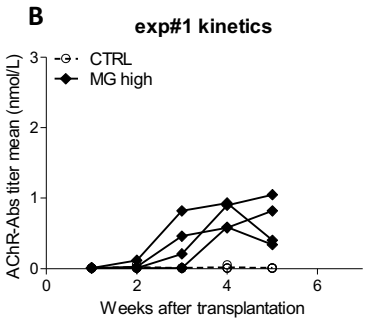
Abs	Conjugate	Host		Reactivity	Clone	Supplier	
Cytokeratin	purified	mouse	IgG1	human	EA1/EA3	Dako	Trappes, France
Cytokeratin	purified	mouse	IgG1	human	MNF116	Dako	Trappes, France
Fibronectin	purified	rabbit	-	human	polyclonal	Dako	Trappes, France
CD21	FITC	mouse	IgG1	human	BL13	immunotech	Marseille, France
CD4	FITC	mouse	IgG1	human	MT310	Dako	Trappes, France
CD8	FITC	mouse	IgG1	human	DK25	Dako	Trappes, France
KI-67	purified	rat	IgG1	human	5D7	AbCam	Cambridge, UK
LaminA/C	purified	mouse	IgG2b	human	636	Leica	Newcastle, UK

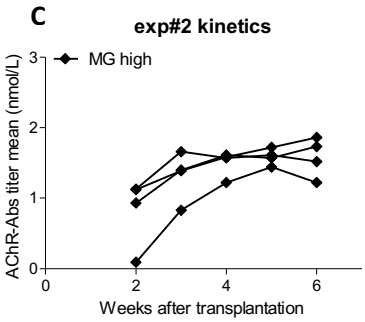
Secondary Abs	Conjugate	Host	Reactivity	Supplier	
	alexa 488	chicken	rat	LifeTechnologies	Saint-Aubin, France
	alexa 488	donkey	rabbit	LifeTechnologies	Saint-Aubin, France
	alexa 488	goat	mouse	LifeTechnologies	Saint-Aubin, France
	alexa 594	donkey	rat	LifeTechnologies	Saint-Aubin, France
	alexa 594	chicken	mouse	LifeTechnologies	Saint-Aubin, France
DAPI	blue	-	-	Dako	Trappes, France

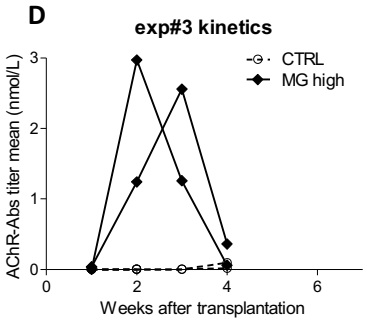
Supplemental Table S3

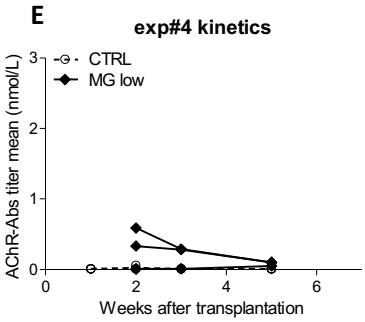
List of Abs used in IHC experiments

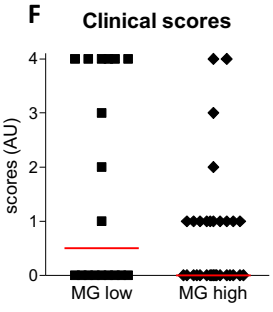

A
Anti-AChR Abs kinetics
MG neg
MG low
MG high
AChR-Abs titer mean (nmol/L)
Weeks after transplantation

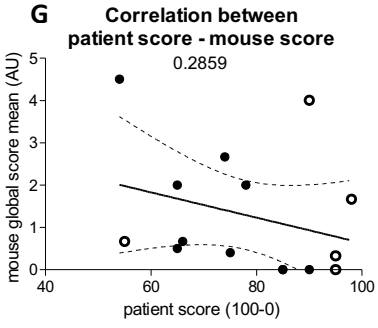

B
exp#1 kinetics
CTRL
MG high
AChR-Abs titer mean (nmol/L)
Weeks after transplantation


C
exp#2 kinetics
MG high
AChR-Abs titer mean (nmol/L)
Weeks after transplantation


D
exp#3 kinetics
CTRL
MG high
AChR-Abs titer mean (nmol/L)
Weeks after transplantation


E
exp#4 kinetics
CTRL
MG low
AChR-Abs titer mean (nmol/L)
Weeks after transplantation


F
Clinical scores
scores (AU)
MG low
MG high

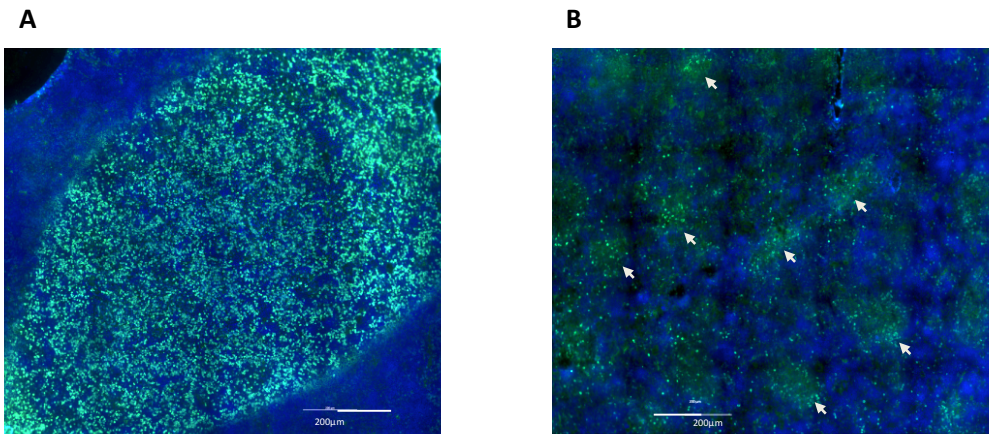

G
Correlation between
patient score - mouse score
0.2859
mouse global score mean (AU)
patient score (100-0)

Supplemental Figure S1. NSG-MG model characterization

A-E. Human Anti-AChR Abs kinetics in mice. A. The curves represent the mean value of human AChR-specific Abs titers (nmol/L) measured by RIA in the serum of mice grafted with thymus fragments from MG patients (day 7: 8 mice, 2 experiments; day 21: 27 mice, 8 experiments; day 28: 36 mice, 10 experiments; day 35: 11 mice, 3 experiments and day 42: 16 mice; 4 experiments). **The titers reach a plateau 3 to 4 weeks after graft.** B-E. Four individual experiments are shown. The curves represent the value of human AChR-specific Abs titers in the serum of each mice in a given graft experiment (Exp1 to 4).

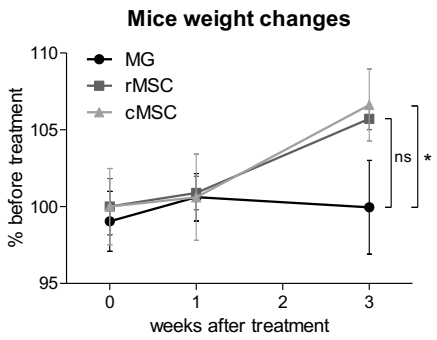
F. MG severity is relatively similar in MG low and MG high mice. MG mice were clinically scored as described in MM. Each symbol represents one mouse (MG low, closed squares, n=18 and MG high, closed diamonds, n=31) and red bars represent the median value in each group.

G. Corticosteroid-treated patients do not display a correlation between the patient score and the mouse score (r^2=0.09). Each symbol represents the score of MG patient and the corresponding mean score attributed in mice for each experiment (open circle = treated patients). While untreated patients have a good correlation between their clinical score in the patient and the mouse (Fig 1F), this is not the case for treated patients. The likely explanation is the discontinuation of the treatment in the mice after grafting. Indeed some patients (MG4 and MG11) had a good MG score under treatment but had a significant clinical score in mice.



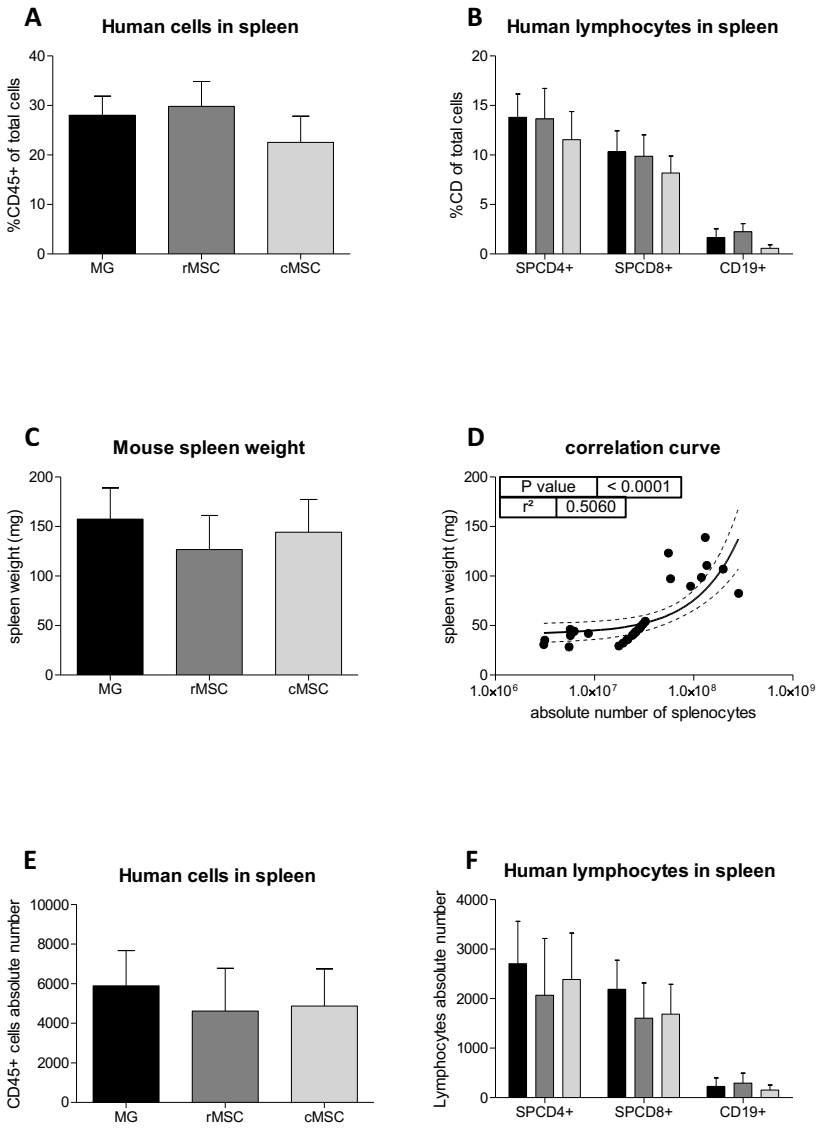
Supplemental Figure S2. Human cells home in the spleen of mice

Immunohistochemistry was performed on spleen sections showing human cells (laminA/C positive cells, in green) and the nucleus in blue (DAPI coloration) in two mice (A and B) grafted with the same MG thymus. Control sections with secondary antibody were negative (not shown).



Supplemental Figure S3. MSC treatment promoted animal weight gain.

Data are normalized using each mice weight before treatment. Symbols represent the mean value ± SEM of the weight change at the indicated time point for the MG group (n=18 to 20), for the rMSC group (n=16 to 19) and for the cMSC group (n=14).



Supplemental Figure S4. MSC treatment did not modify T and B cell number in the spleen of MG thymus-grafted animals.

A. MSC treatment does not modify the percentage of CD45 positive cells in the spleen. FACS analysis of human CD45 expression among splenocytes in MG (n=19), rMSC (n=15) and cMSC (n=13) groups. Histograms represent the mean value ± SEM for each group.

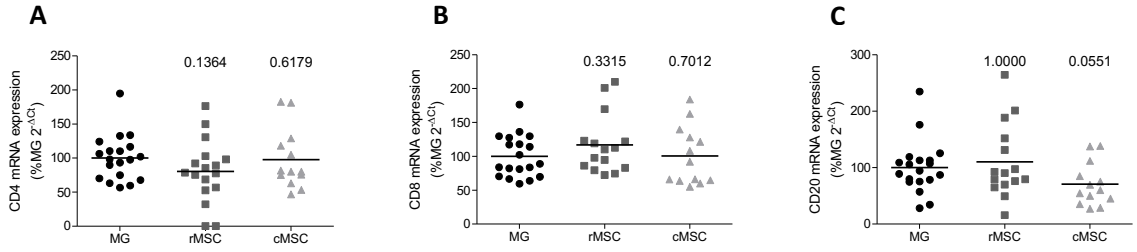
B. MSC treatment does not modify the percentage of T and B cells in the spleen. FACS analysis of human CD4, CD8 and CD19 expression among splenocytes in MG (n=15), rMSC (n=13) and cMSC (n=13) groups. Histograms represent the mean value ± SEM for each group.

C. MSC treatment does not modify spleen weight of MG thymus-grafted animals. Spleens of treated (rMSC, n=7; cMSC, n=10) and untreated (MG, n=10) were weighted. Histograms represent the mean value ± SEM for each group.

D. The absolute number of splenocytes correlates with the spleen weight. Each symbol represents one mouse (n=32), and three experiments are included. P-value is determined using the linear regression test.

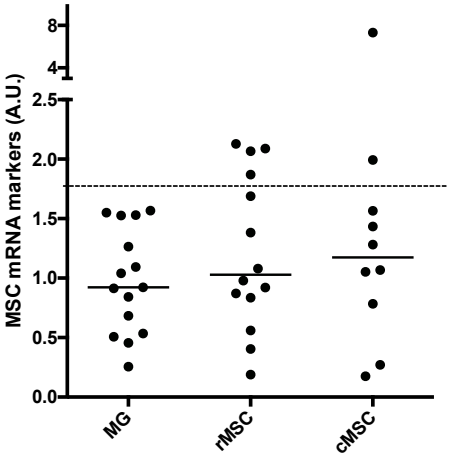
E. MSC treatment does not modify the number of CD45 positive cells in the spleen. Since the absolute number of cells in the spleen of grafted animals was not numerated in all experiments and it correlates with the spleen weight, we extrapolated the number of CD45 positive cells according to the correlation curve (MG, n=10; rMSC, n=7, and cMSC, n=10). Histograms represent the mean value ± SEM for each group ($x10^{-4}$).

F. MSC treatment does not modify the number of T and B cells in the spleen. An extrapolated absolute number of CD4, CD8, and CD20 positive cells was calculated according to the correlation curve (MG, n=10; rMSC, n=7 and cMSC, n=10). Histograms represent the mean value ± SEM for each group ($x10^{-4}$).



Supplemental Figure S5.

CD4 (A), CD8 (B) and CD20 (C) mRNA expression were analyzed by q-PCR in xenogeneic thymus. 2^-ΔCt data of the MG, rMSC and cMSC group are normalized using 2^-ΔCt mean values of the MG group (levels set at 100%). Each symbol represents the 2^-ΔCt normalized value of each mouse and bars represent the mean values in each group. P-values were determined according to Mann Whitney t test (MG, n=19; rMSC, n=15; cMSC, n=13)



Supplemental Figure S6

Analysis of MSC markers in the grafted thymus. We used two MSC-expressed markers, Serpin 2 (Crigler et al., 2006) and collagen 6A3 (Harvey et al. 2013) that we analyzed by real-time PCR at the end of the experiment (about 2 months after graft). We first validated that these markers were highly expressed in MSC but not in the human thymus. The ratio of expression MSC/human thymus was higher than 50.

We calculated a mean value of 4 values; each of these markers was normalized to 2 house-keeping genes (GAPD and TBP). For pure cultured MSC, this value was about 110 A.U., while the grafted MG thymus was less than 1.8 A.U. Two months after MSC therapy, only one mouse has a mean value of 8 in the group of cMSC, five mice (1 in the cMSC group, and 4 in the rMSC group) had a value just above the level of controls (grafted MG thymus without MSC therapy), and 18 mice (8 in the cMSC, 10 in the rMSC group) had levels equivalent to controls.

- Crigler, L., Robey, R.C., Asawachaicharn, A., Gaupp, D., and Phinney, D.G. 2006. Human mesenchymal stem cell subpopulations express a variety of neuro-regulatory molecules and promote neuronal cell survival and neuritogenesis. *Exp Neurol* 198:54-64.
- Harvey, A., Yen, T.Y., Aizman, I., Tate, C., and Case, C. 2013. Proteomic analysis of the extracellular matrix produced by mesenchymal stromal cells: implications for cell therapy mechanism. *PLoS One* 8:e79283.