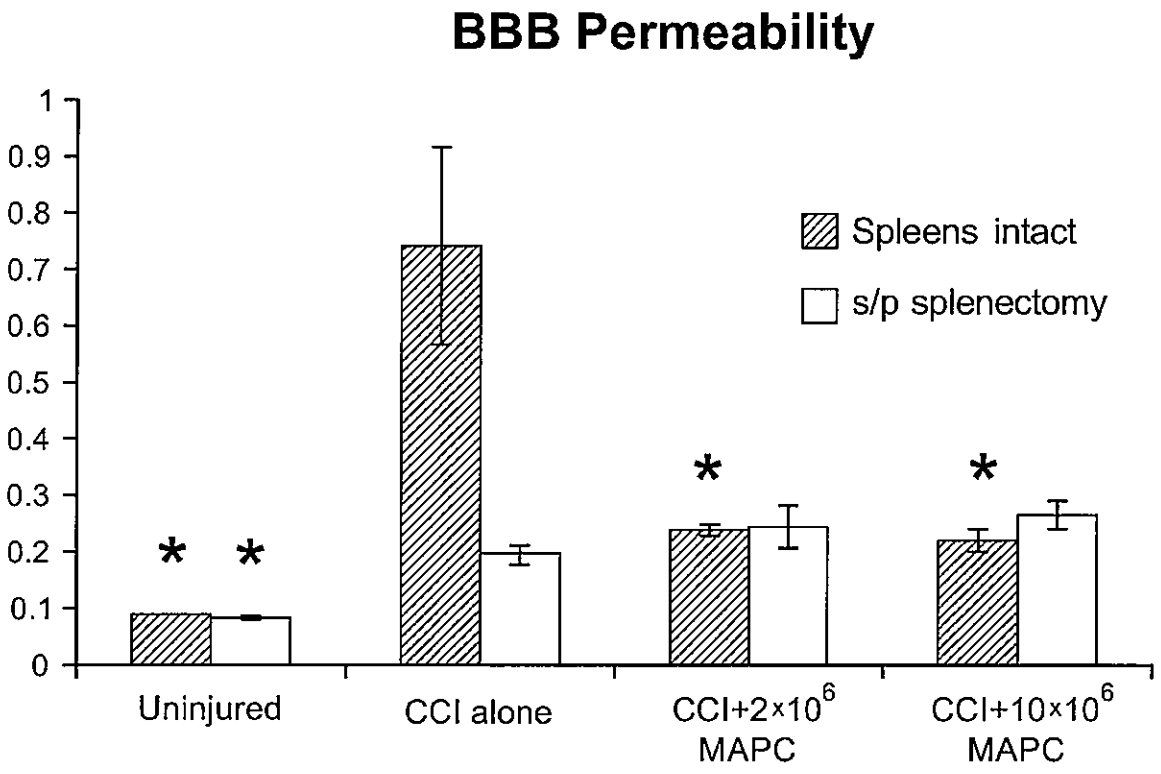

BBB Permeability
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Spleens intact
s/p splenectomy
*
*
*
*
Uninjured
CCI alone
CCI+2×10^6 MAPC
CCI+10×10^6 MAPC

Figure 1

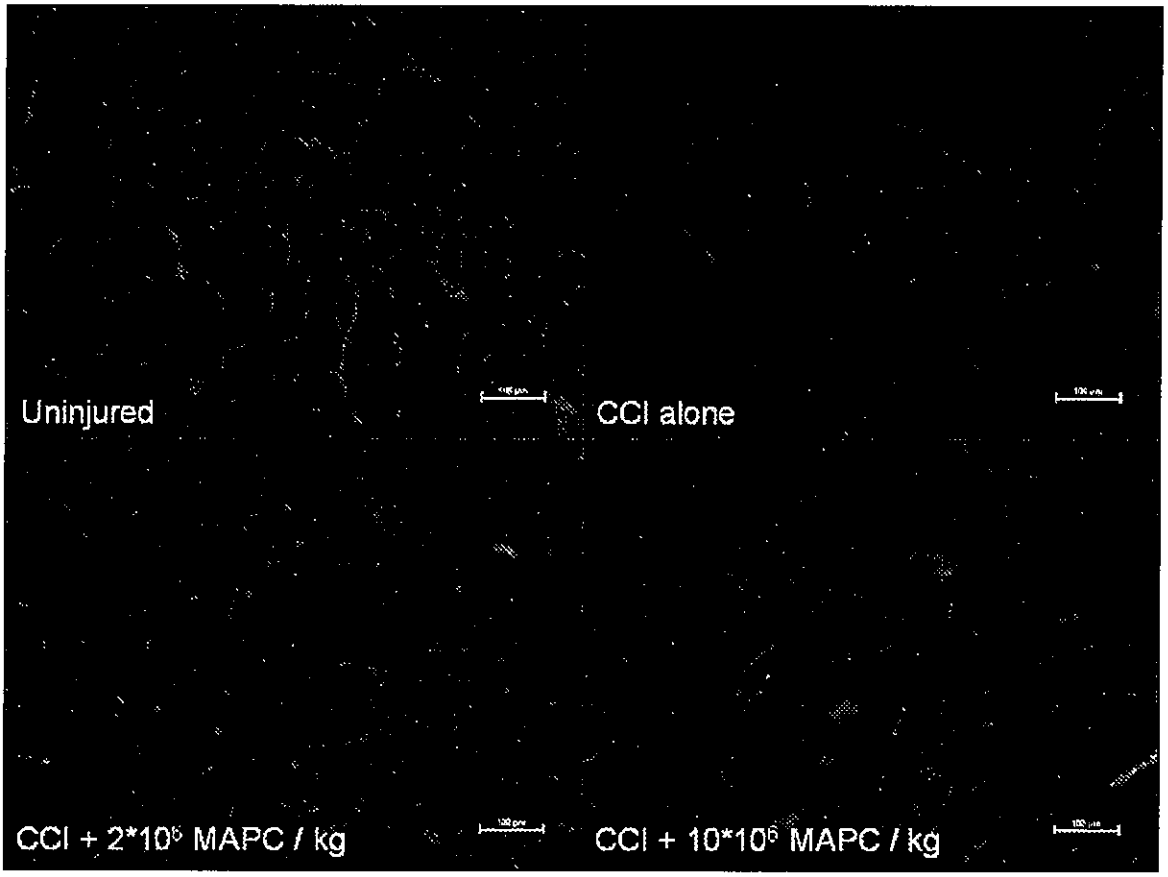


Figure 2

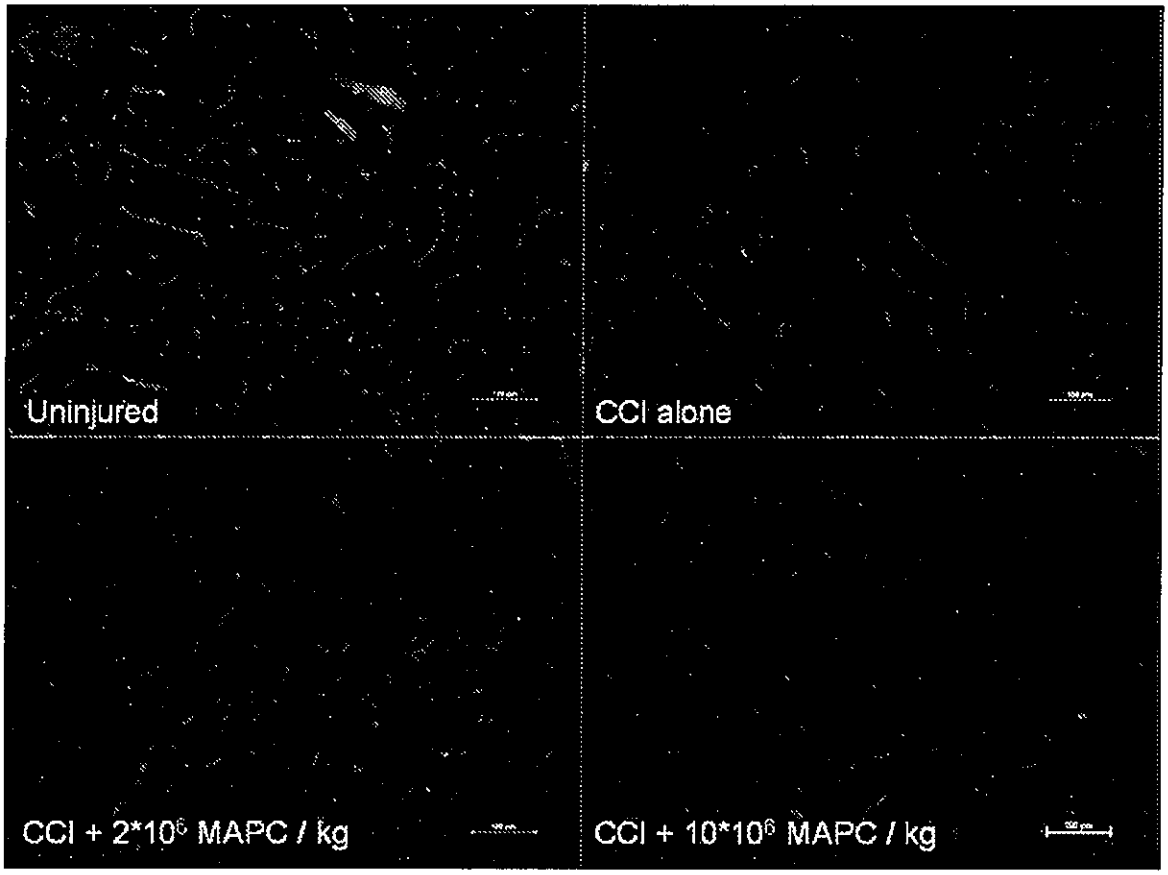
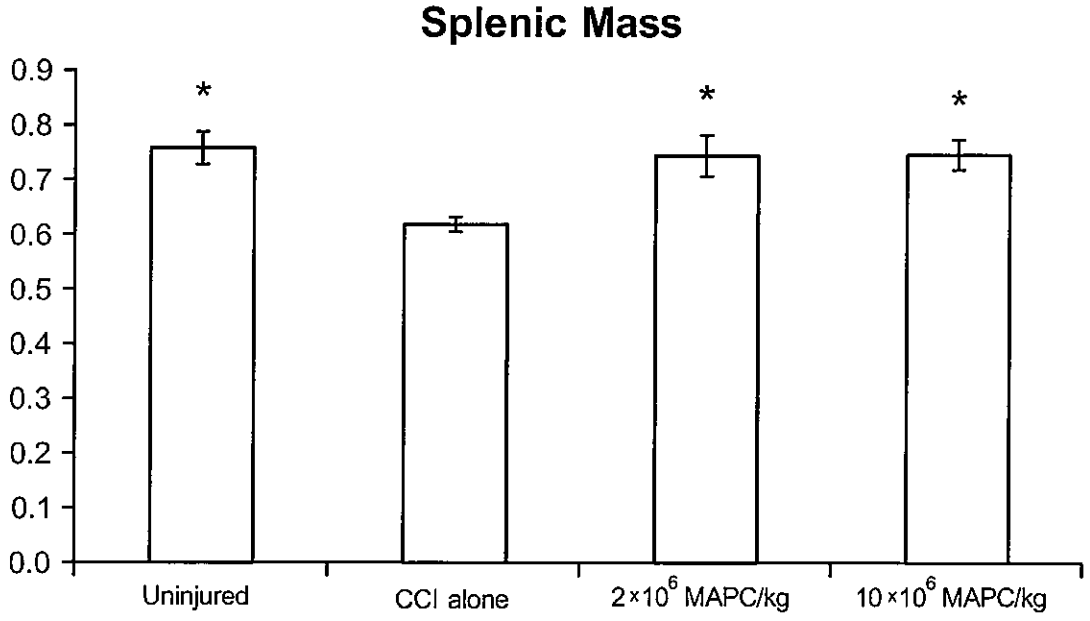


Figure 3

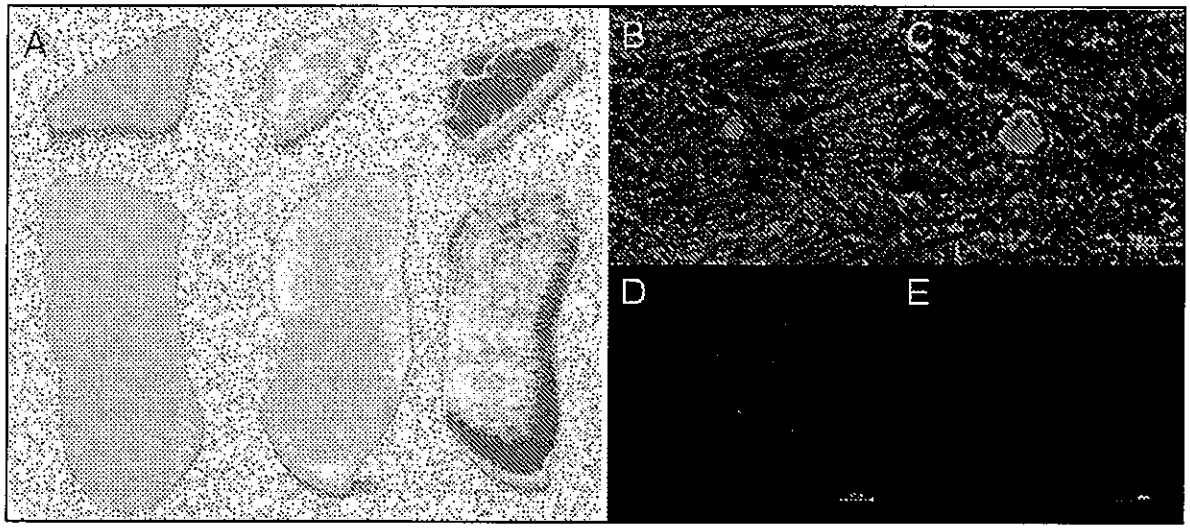
A



B

	Uninjured	CCI alone	CCI+2×10^6 MAPC/kg	CCI+10×10^6 MAPC/kg
CD3+/CD4+	18.6 +/- 0.90	18.9 +/- 0.93	21.4 +/- 0.57	24.2 +/- 1.1*
CD3+/CD8+	11.2 +/- 0.43	11.2 +/- 0.83	13.5 +/- 0.75	13.0 +/- 0.71
CD8+/CD4+	0.61 +/- 0.04	0.61 +/- 0.06	0.63 +/- 0.03	0.55 +/- 0.05

Figure 4



CCI alone 2×10^6 MAPC/kg 10×10^6 MAPC/kg

Figure 5

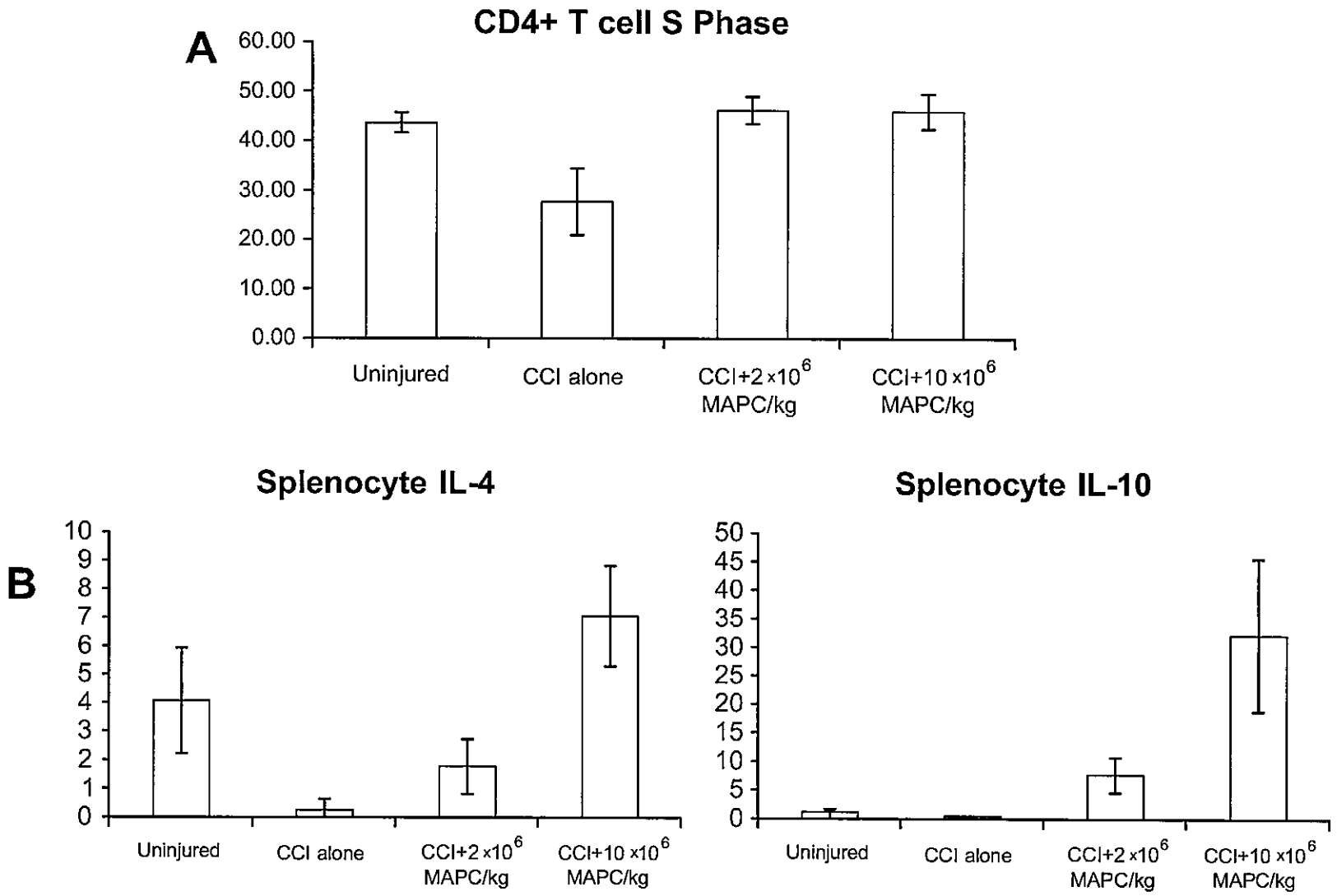

A
CD4+ T cell S Phase
60.00
50.00
40.00
30.00
20.00
10.00
0.00
Uninjured
CCI alone
CCI+2 x10^6 MAPC/kg
CCI+10 x10^6 MAPC/kg
B
Splenocyte IL-4
10
9
8
7
6
5
4
3
2
1
0
Uninjured
CCI alone
CCI+2 x10^6 MAPC/kg
CCI+10 x10^6 MAPC/kg
Splenocyte IL-10
50
45
40
35
30
25
20
15
10
5
0
Uninjured
CCI alone
CCI+2 x10^6 MAPC/kg
CCI+10 x10^6 MAPC/kg

Figure 6

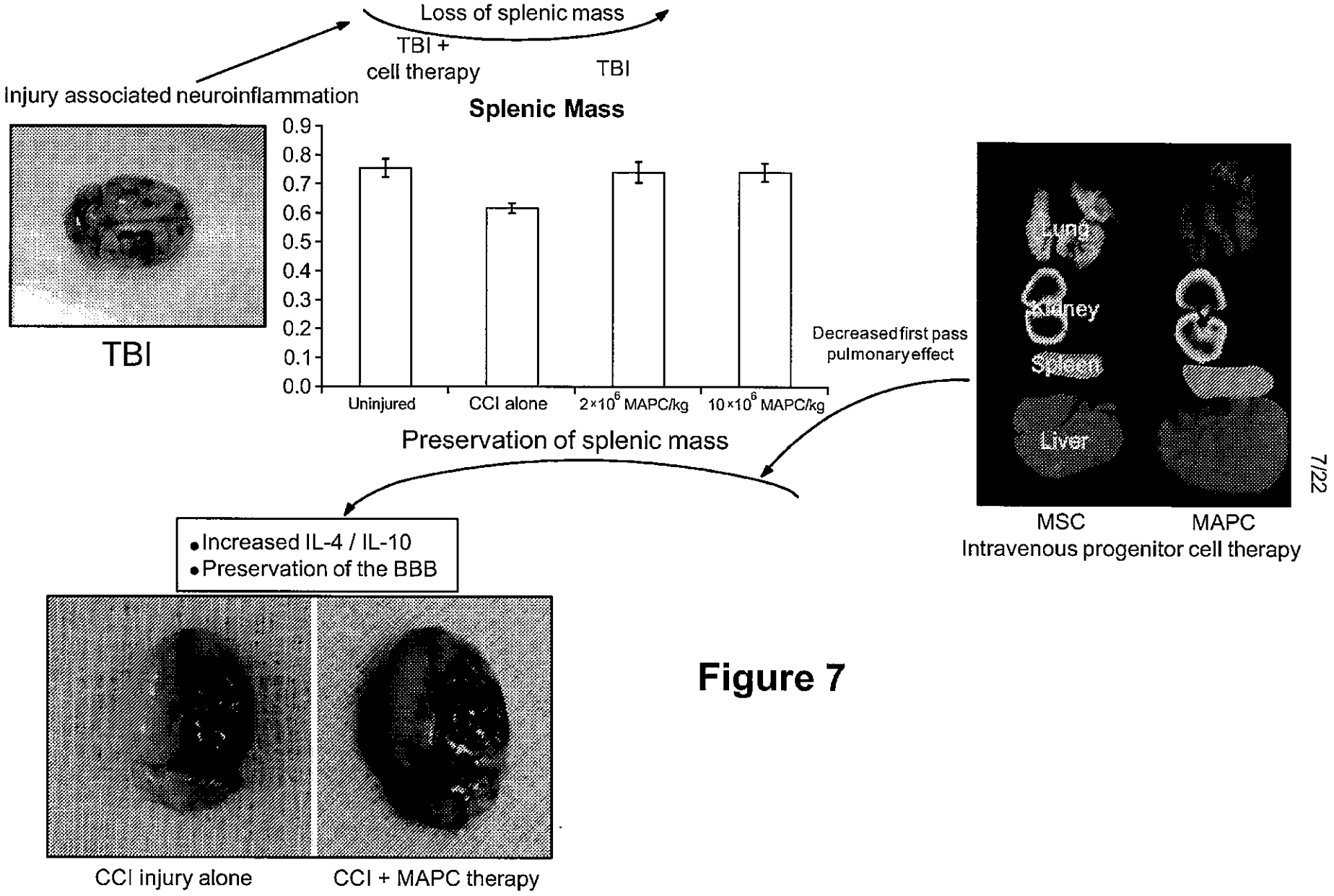

Loss of splenic mass
TBI +
cell therapy
TBI
Injury associated neuroinflammation
Splenic Mass
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Uninjured
CCI alone
2×10^6 MAPC/kg
10×10^6 MAPC/kg
TBI
Decreased first pass
pulmonary effect
Lung
Kidney
Spleen
Liver
MSC
MAPC
Intravenous progenitor cell therapy
Preservation of splenic mass
•Increased IL-4 / IL-10
•Preservation of the BBB
CCI injury alone
CCI + MAPC therapy

Figure 7

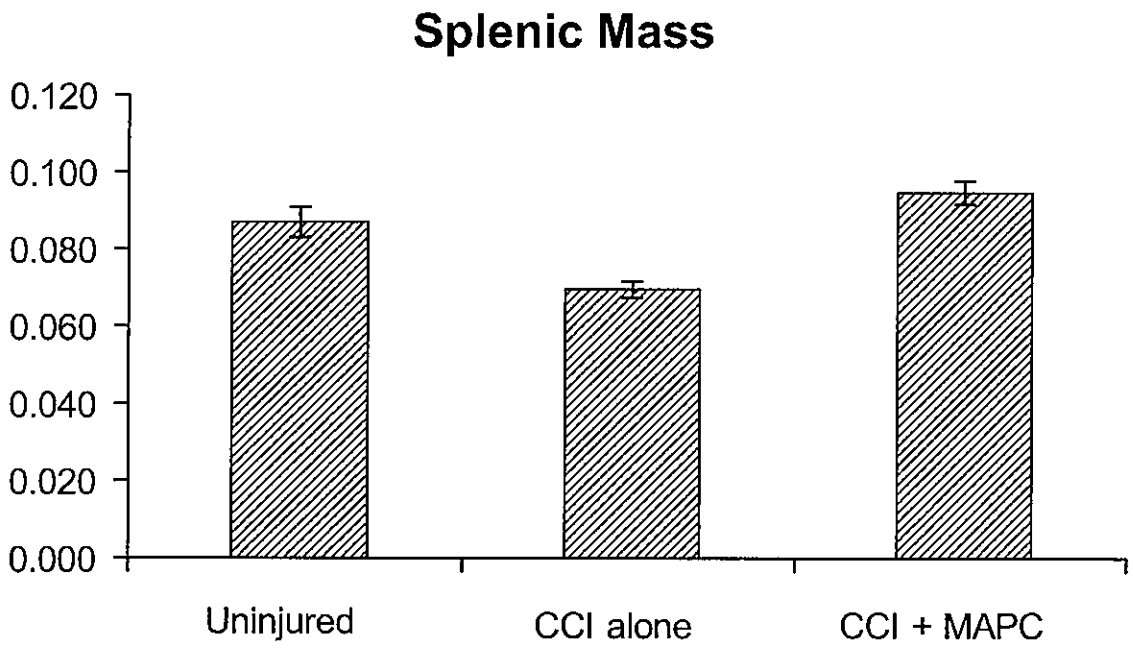

Splenic Mass
0.120
0.100
0.080
0.060
0.040
0.020
0.000
Uninjured
CCI alone
CCI + MAPC

Figure 8

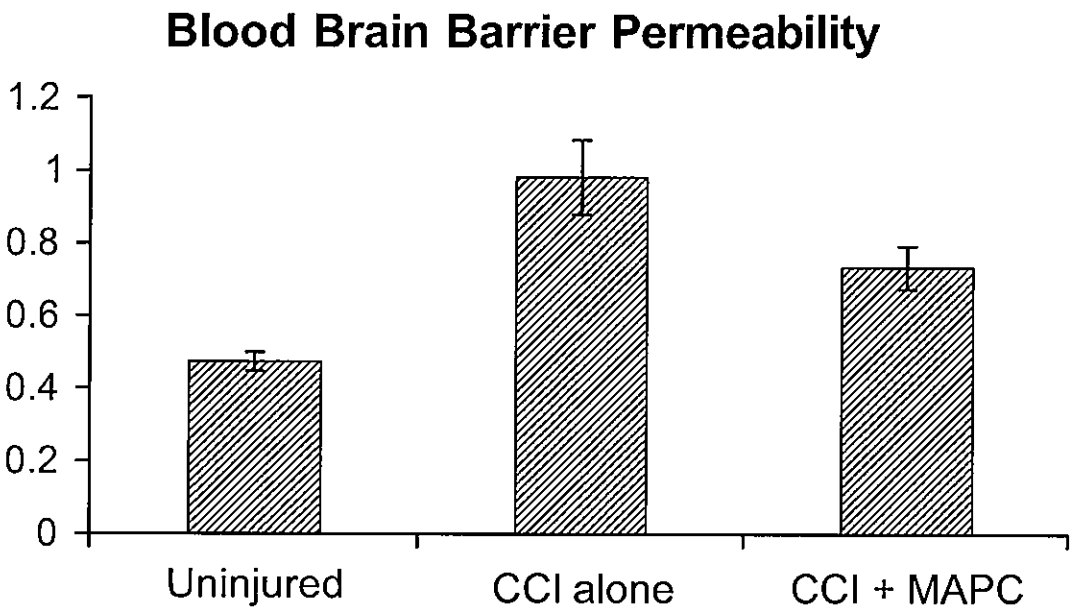

Blood Brain Barrier Permeability
1.2
1
0.8
0.6
0.4
0.2
0
Uninjured
CCI alone
CCI + MAPC

Figure 9

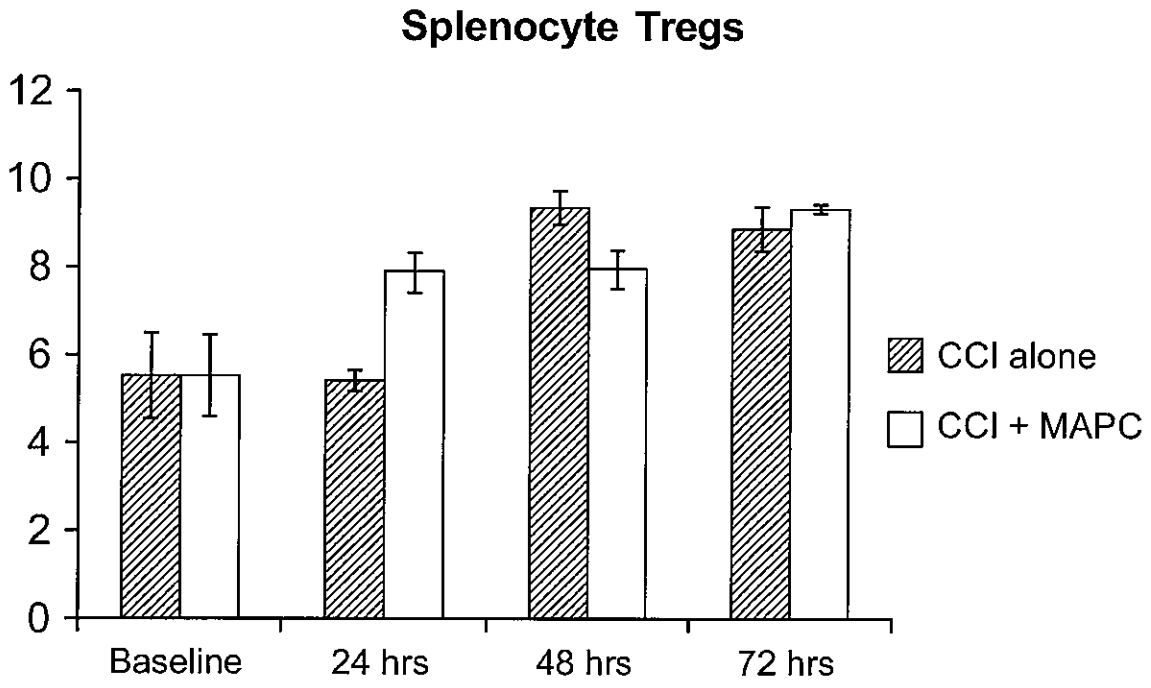

Splenocyte Tregs
12
10
8
6
4
2
0
Baseline
24 hrs
48 hrs
72 hrs
CCI alone
CCI + MAPC

Figure 10

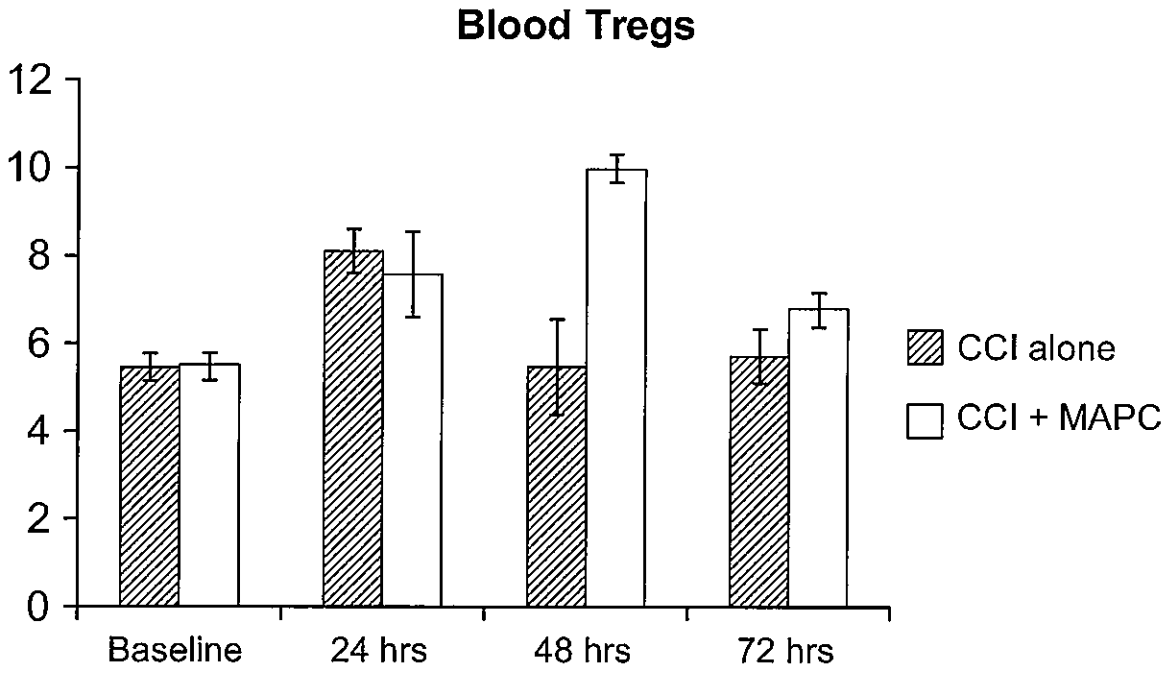

Blood Tregs
12
10
8
6
4
2
0
Baseline
24 hrs
48 hrs
72 hrs
CCI alone
CCI + MAPC

Figure 11

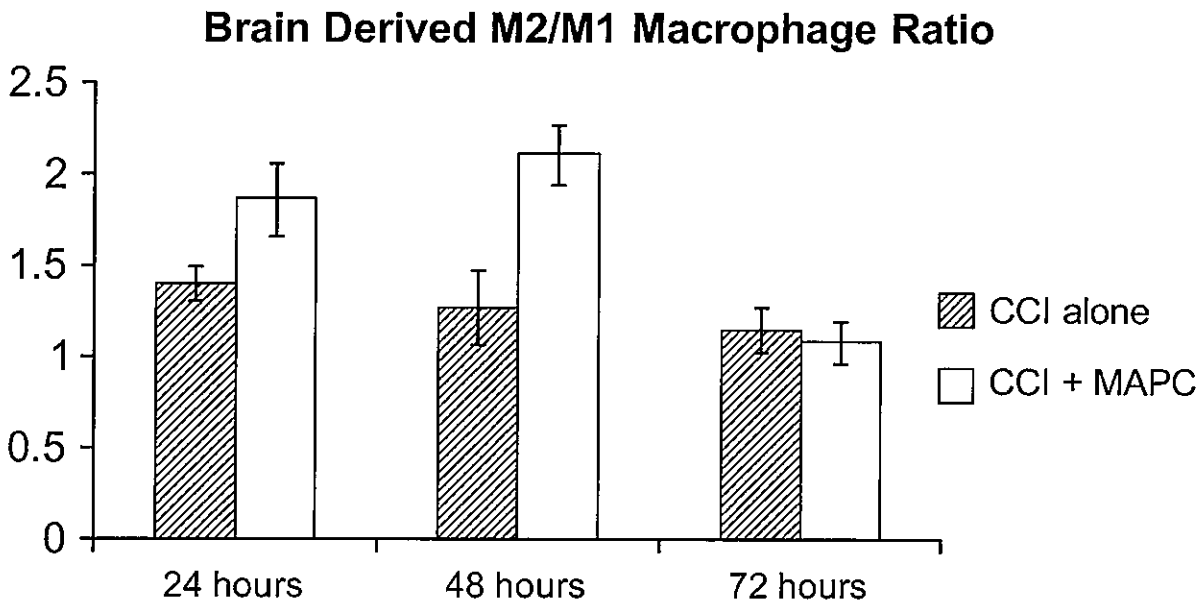

Brain Derived M2/M1 Macrophage Ratio
2.5
2
1.5
1
0.5
0
24 hours
48 hours
72 hours
CCI alone
CCI + MAPC

Figure 12

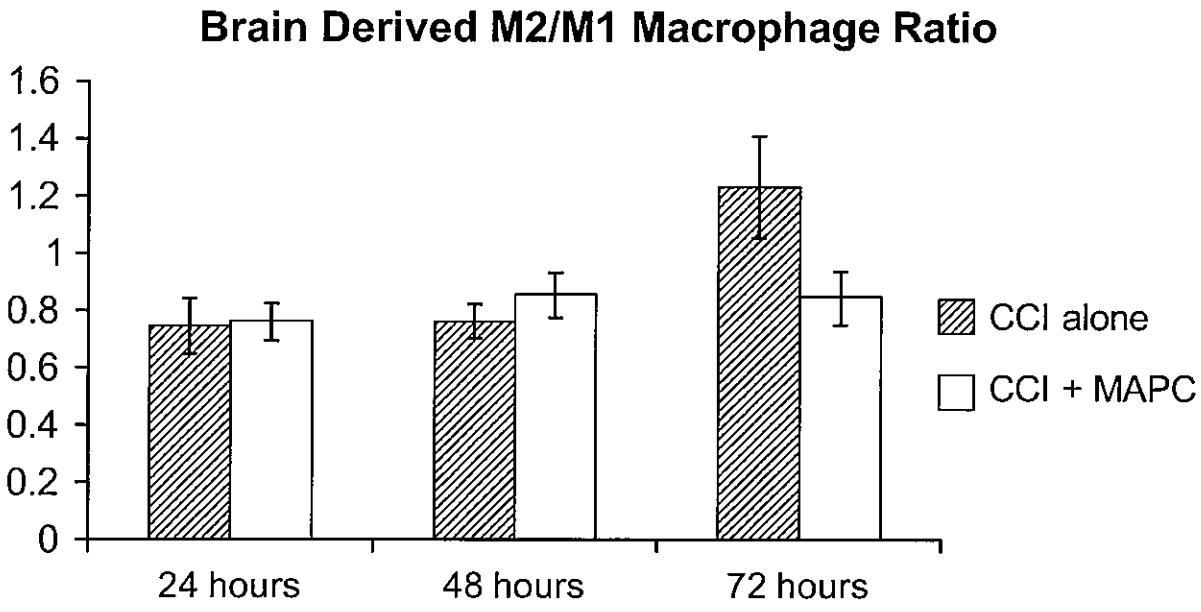

Brain Derived M2/M1 Macrophage Ratio
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
24 hours
48 hours
72 hours
CCI alone
CCI + MAPC

Figure 13

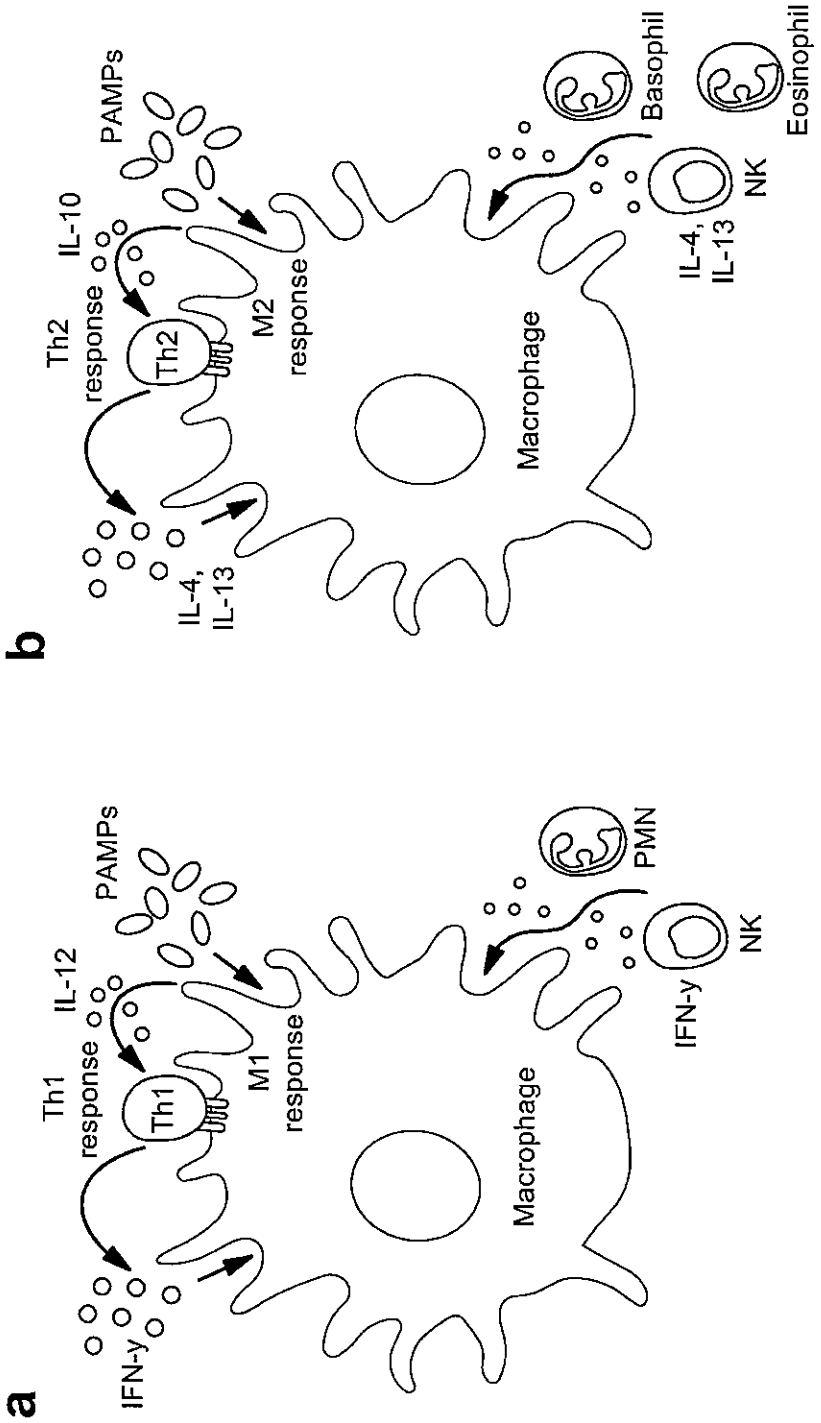

a
IFN-y
Th1
response
IL-12
Th1
PAMPs
M1
response
Macrophage
IFN-y
NK
PMN
b
IL-4,
IL-13
Th2
response
IL-10
Th2
PAMPs
M2
response
Macrophage
IL-4,
IL-13
NK
Basophil
Eosinophil

Figure 14

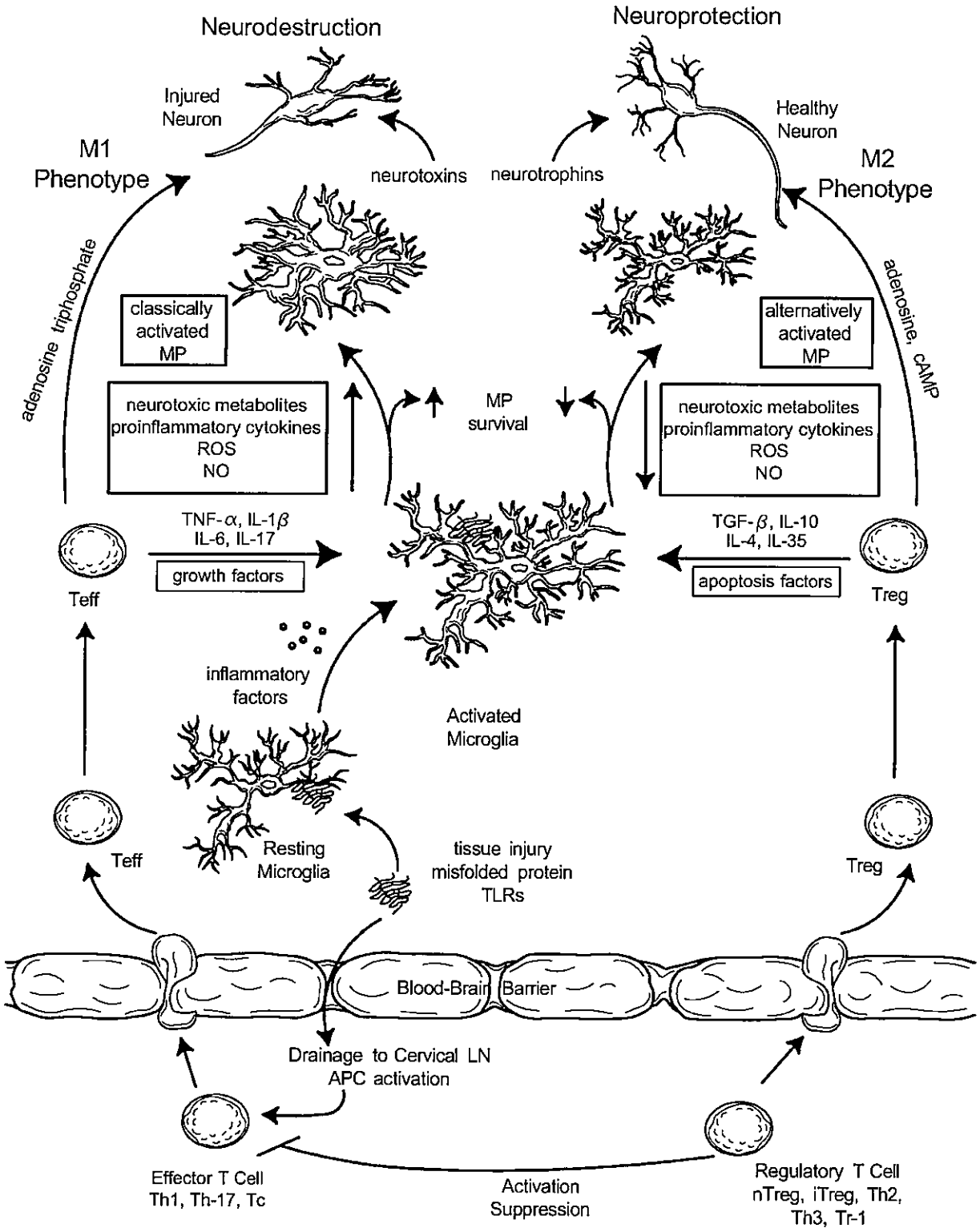

Neurodestruction
Neuroprotection
Injured Neuron
Healthy Neuron
M1 Phenotype
M2 Phenotype
neurotoxins
neurotrophins
adenosine triphosphate
adenosine, cAMP
classically activated MP
alternatively activated MP
neurotoxic metabolites
proinflammatory cytokines
ROS
NO
MP survival
TNF-α, IL-1β
IL-6, IL-17
growth factors
TGF-β, IL-10
IL-4, IL-35
apoptosis factors
Teff
Treg
inflammatory factors
Activated Microglia
Resting Microglia
tissue injury
misfolded protein
TLRs
Blood-Brain Barrier
Drainage to Cervical LN
APC activation
Effector T Cell
Th1, Th-17, Tc
Activation
Suppression
Regulatory T Cell
nTreg, iTreg, Th2,
Th3, Tr-1

Figure 15

Experiments:

- Animals: Long-Evans Rats, Male, 300-320g
- Ischemic Stroke Model: CCAo /MCAo for 3 hrs
- Cells dosing and route: $1.2x10^7$/kg, iv
- Timing: Cell/saline infusion at 24 hours after Stroke
- Behavior test: Cylinder test
- Endpoints:
  - Behavioral tests up to 28 days post-MCAo
  - Lesion size measurements at 28 days post-MCAo
  - Serum cytokines measured 3 days post-treatment
  - Spleen mass measured at 3 days post-treatment
  - IL-10 gene level changes by microarray at 3 days post-treatment

Figure 16

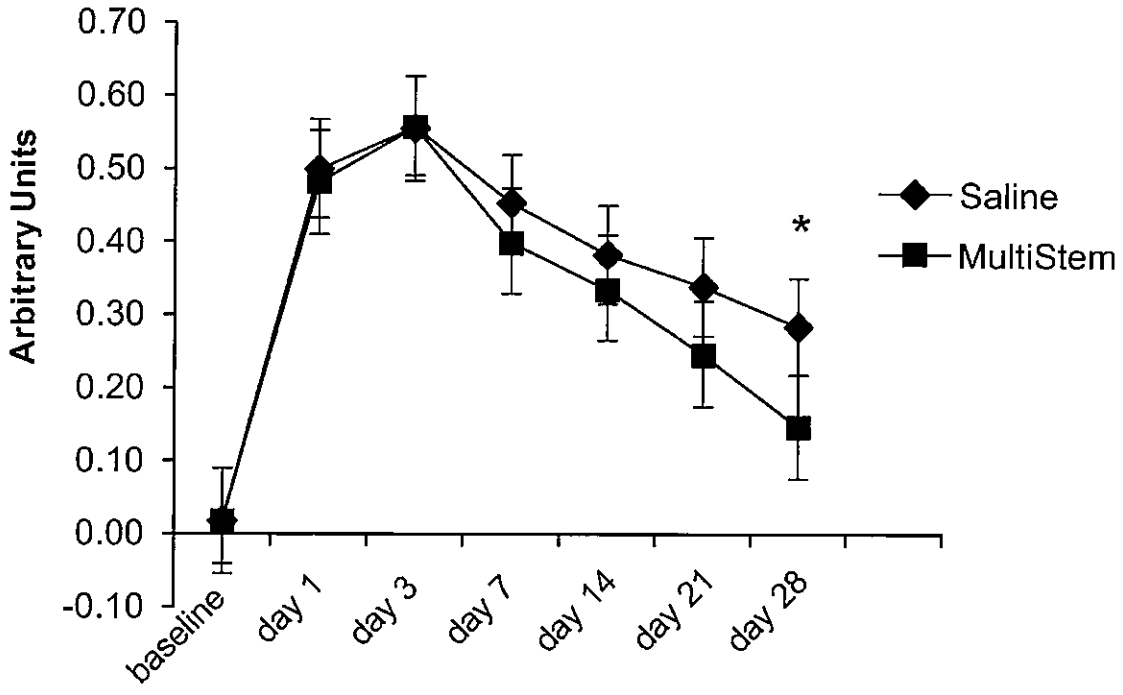
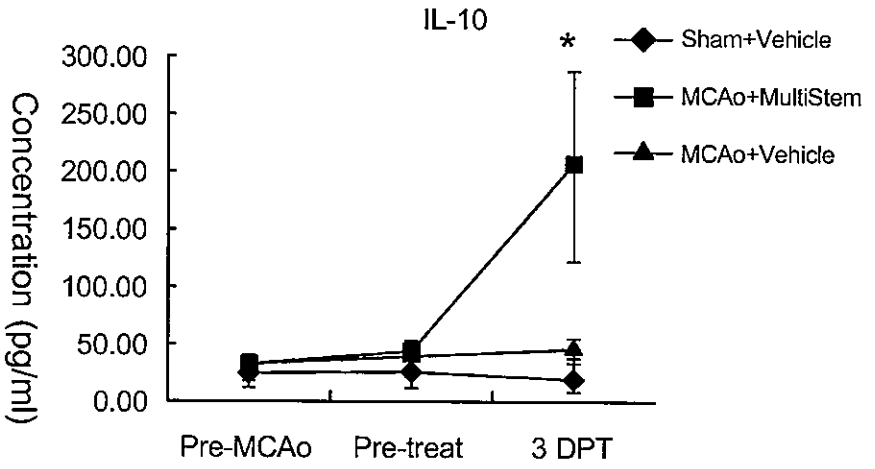
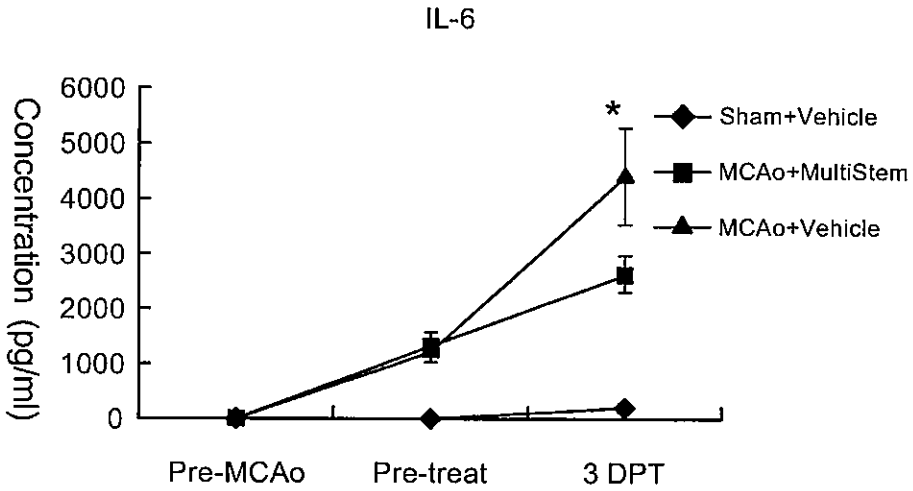

0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
-0.10
Arbitrary Units
baseline
day 1
day 3
day 7
day 14
day 21
day 28
*
Saline
MultiStem

Figure 17

Saline n=10: MultiStem n=12: Sham n=10
***:p<0.05**





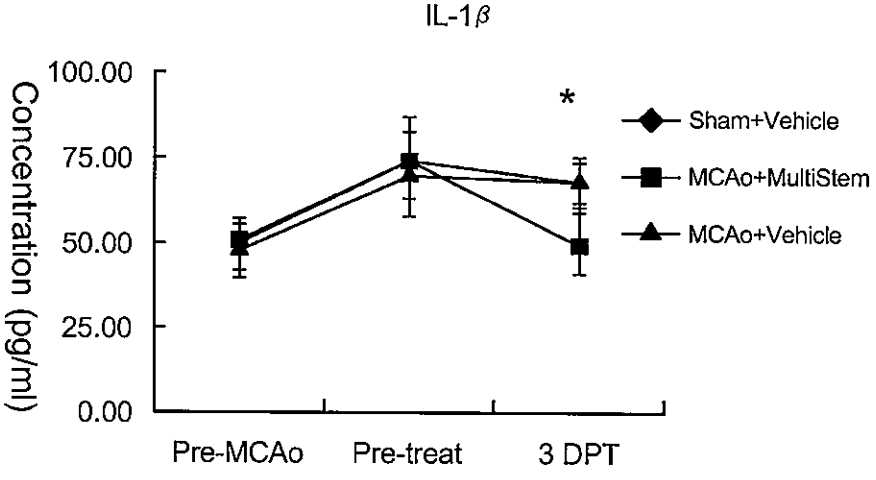
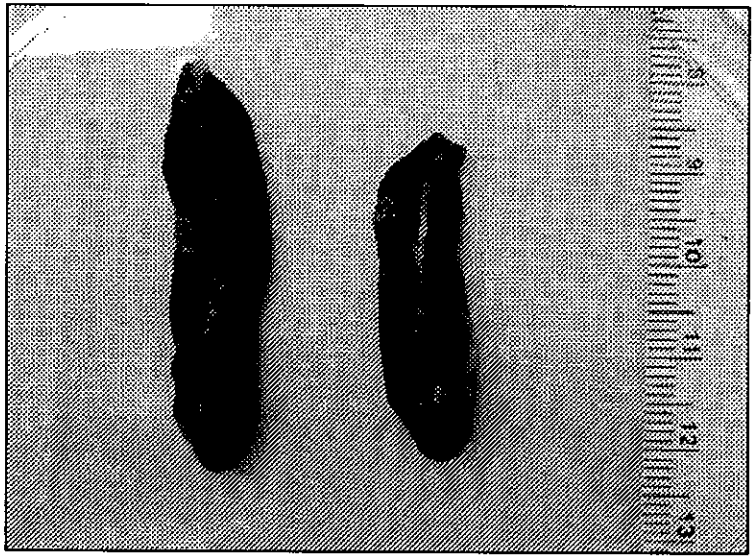
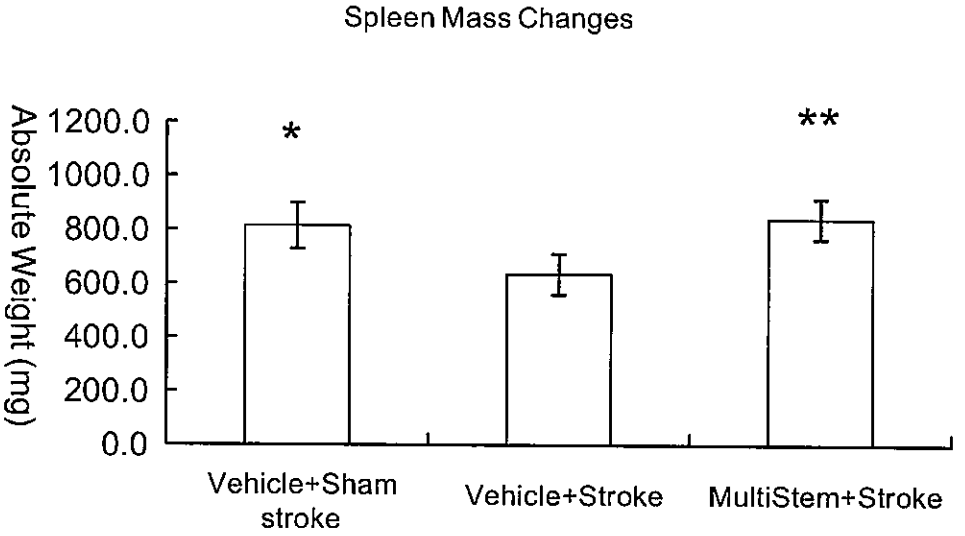


Figure 18



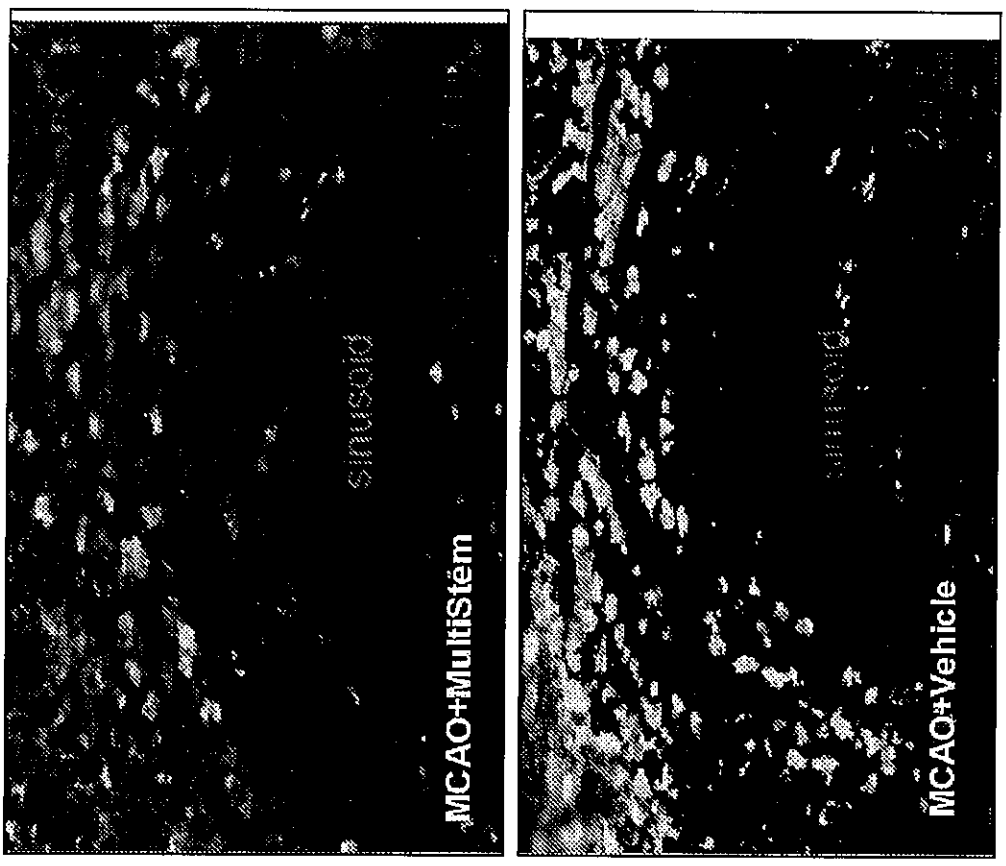
MultiStem Vehicle



MEAN (mg)	MCAO		Sham	
	Multistem	Vehicle	Vehicle	
	838.5	636.9	815.2	
SD	144.5	140.8	115.2	
n	12	11	10	

*	p<0.05	p=0.014
**	p<0.01	p=0.005

Figure 19



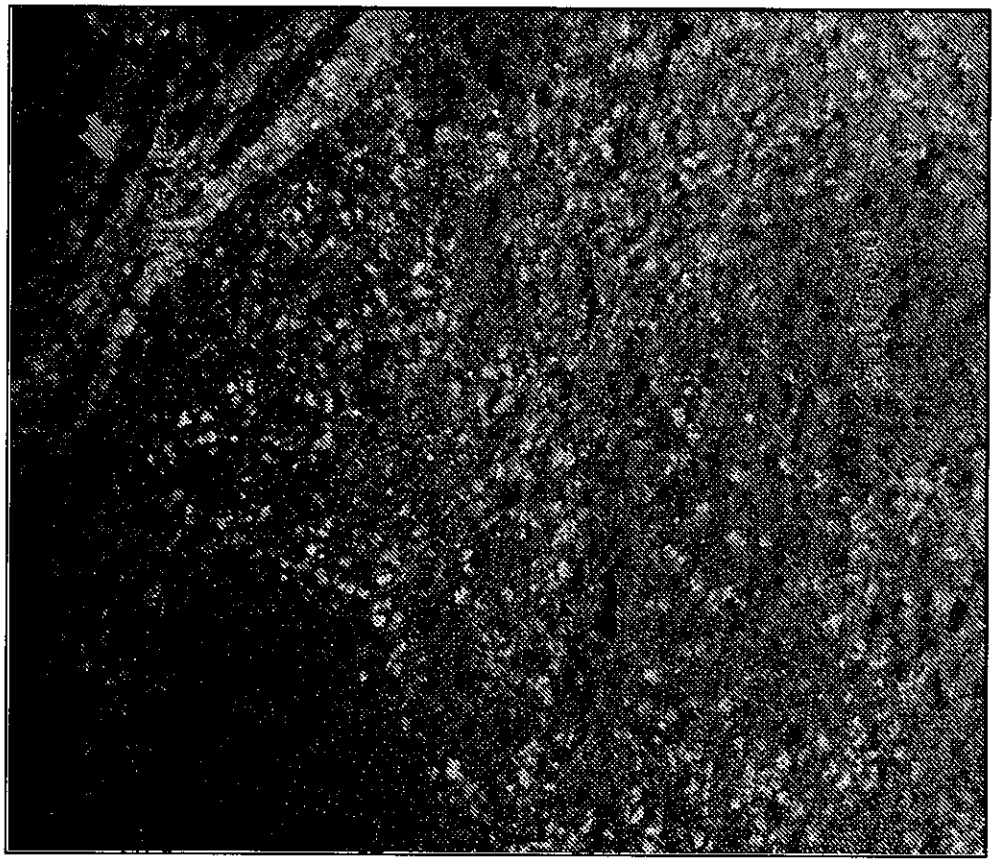
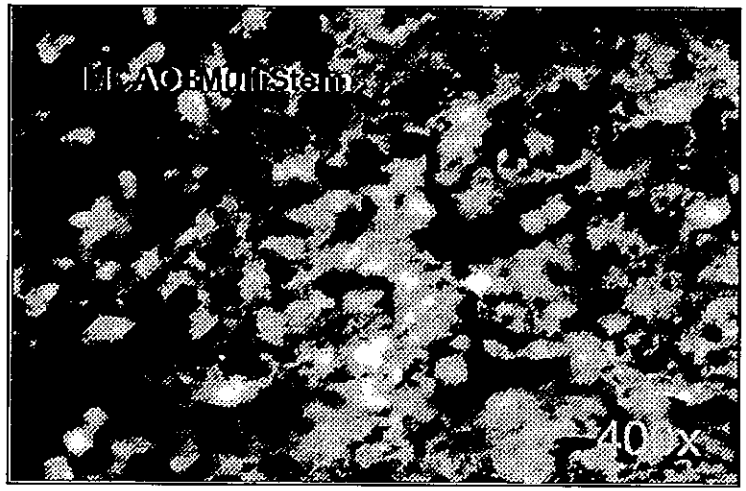
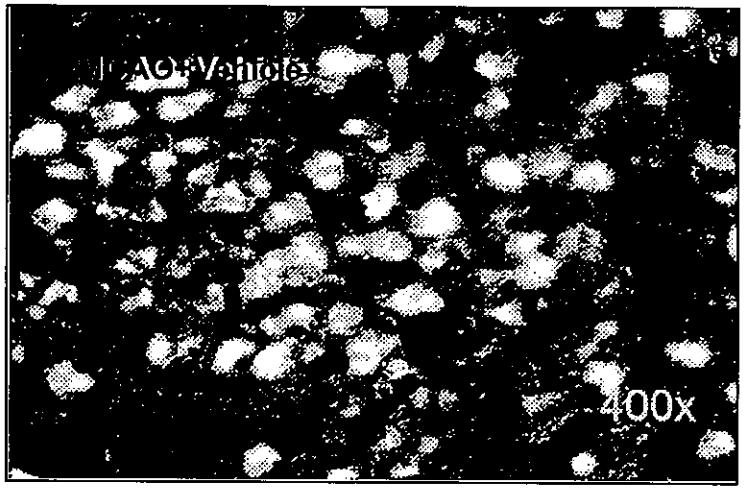


Figure 20





	MultiStem	Vehicle
MEAN	18	49.33
SD	6.63	15.15

*: p=0.010
(n=3 each group)

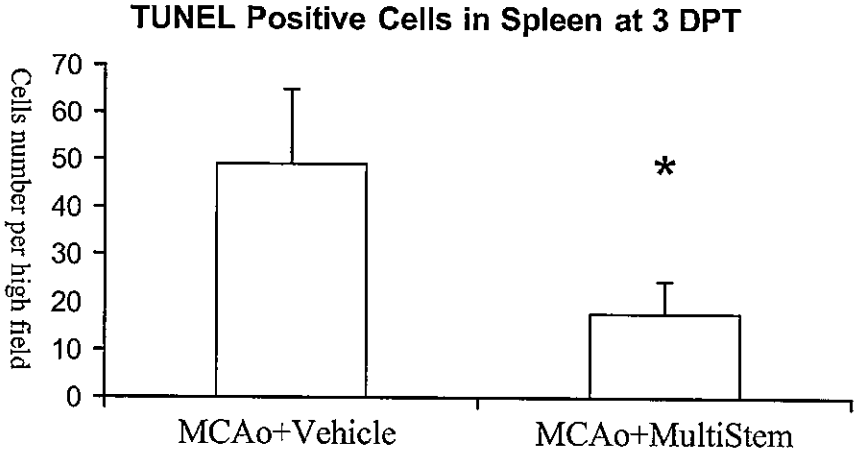
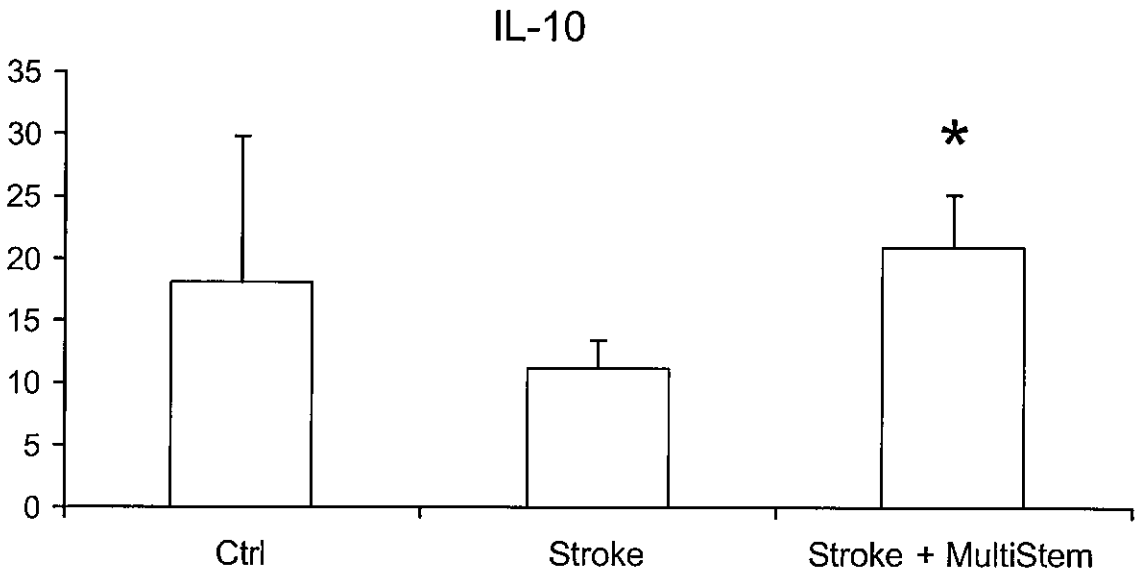


Figure 21



*:p<0.05

Figure 22