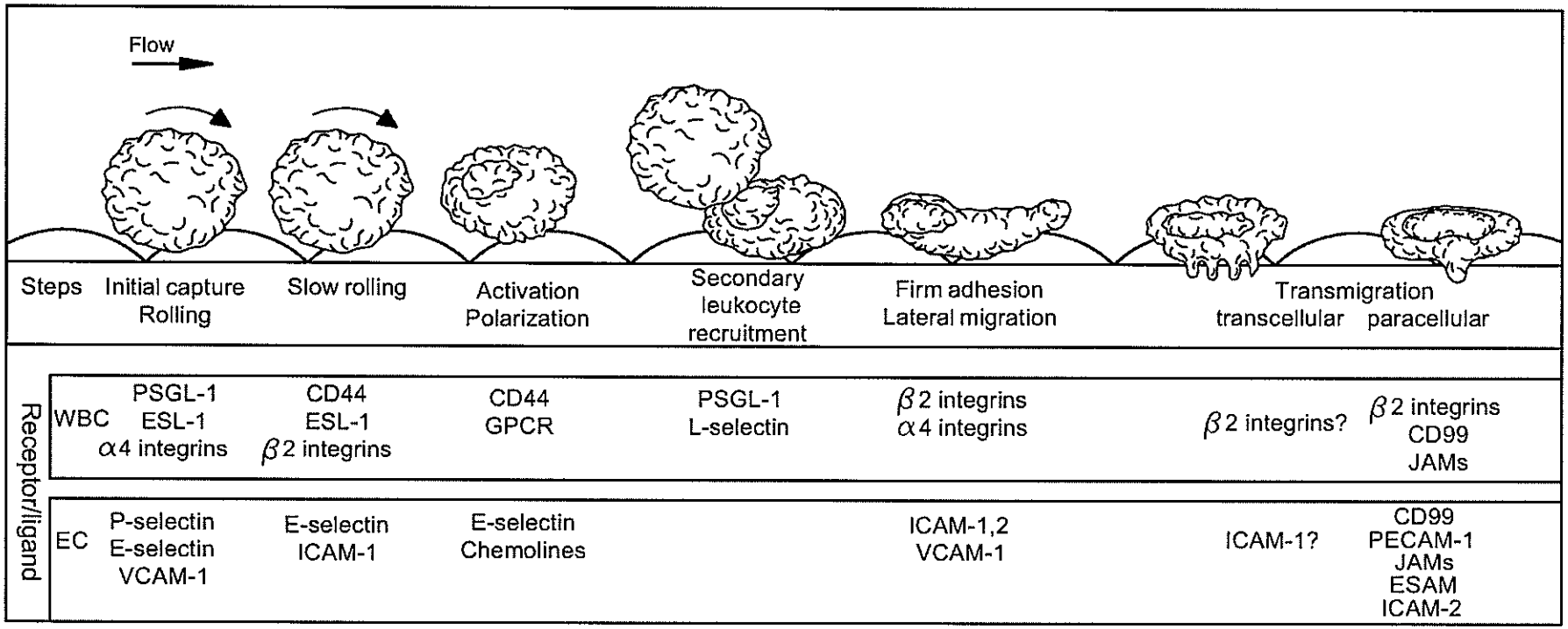

Flow
Steps
Initial capture Rolling
Slow rolling
Activation Polarization
Secondary leukocyte recruitment
Firm adhesion Lateral migration
Transmigration transcellular paracellular
Receptor/ligand
WBC
PSGL-1 ESL-1 α4 integrins
CD44 ESL-1 β2 integrins
CD44 GPCR
PSGL-1 L-selectin
β2 integrins α4 integrins
β2 integrins?
β2 integrins CD99 JAMs
EC
P-selectin E-selectin VCAM-1
E-selectin ICAM-1
E-selectin Chemolines
ICAM-1,2 VCAM-1
ICAM-1?
CD99 PECAM-1 JAMs ESAM ICAM-2

Figure 1

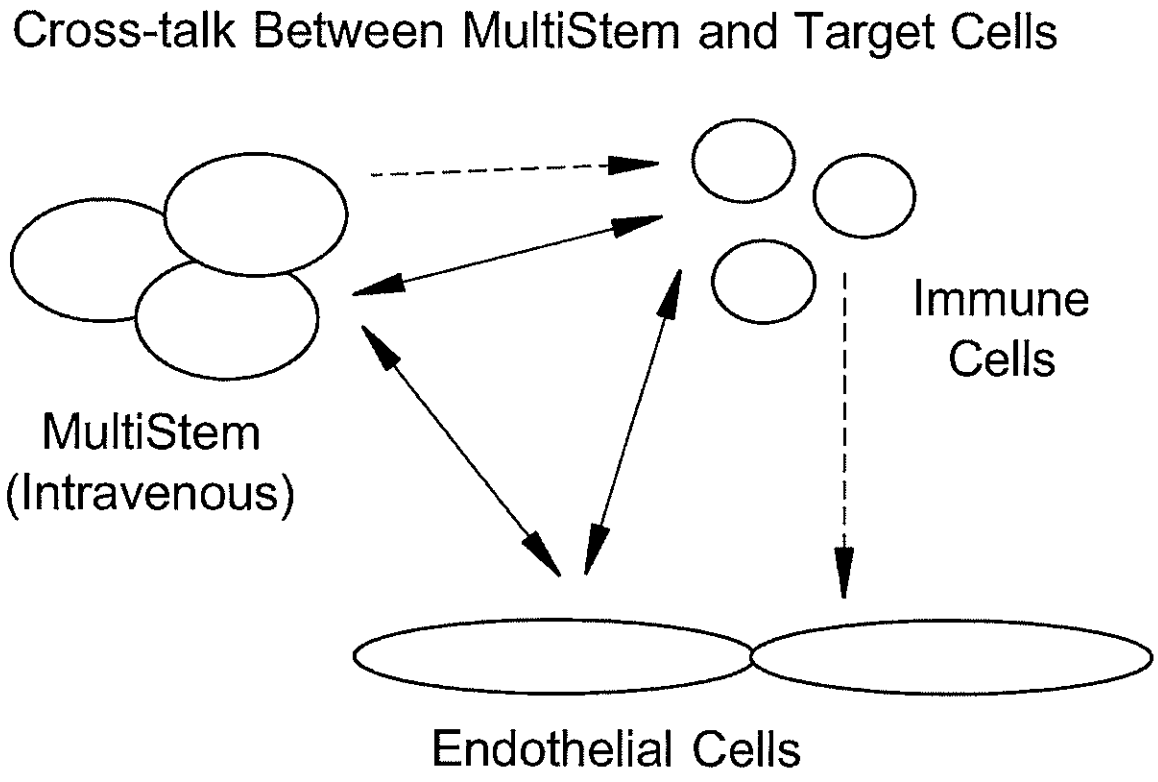

Cross-talk Between MultiStem and Target Cells
Immune Cells
MultiStem (Intravenous)
Endothelial Cells

Figure 2

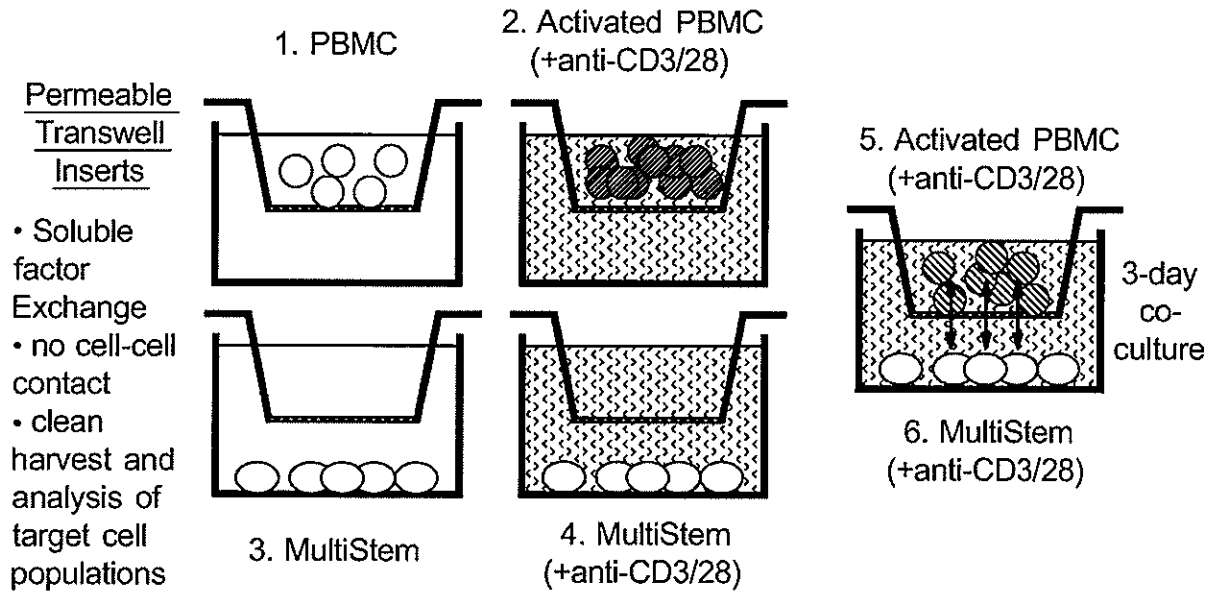

Permeable Transwell Inserts
• Soluble factor Exchange
• no cell-cell contact
• clean harvest and analysis of target cell populations
1. PBMC
2. Activated PBMC (+anti-CD3/28)
3. MultiStem
4. MultiStem (+anti-CD3/28)
5. Activated PBMC (+anti-CD3/28)
3-day co-culture
6. MultiStem (+anti-CD3/28)

Figure 3

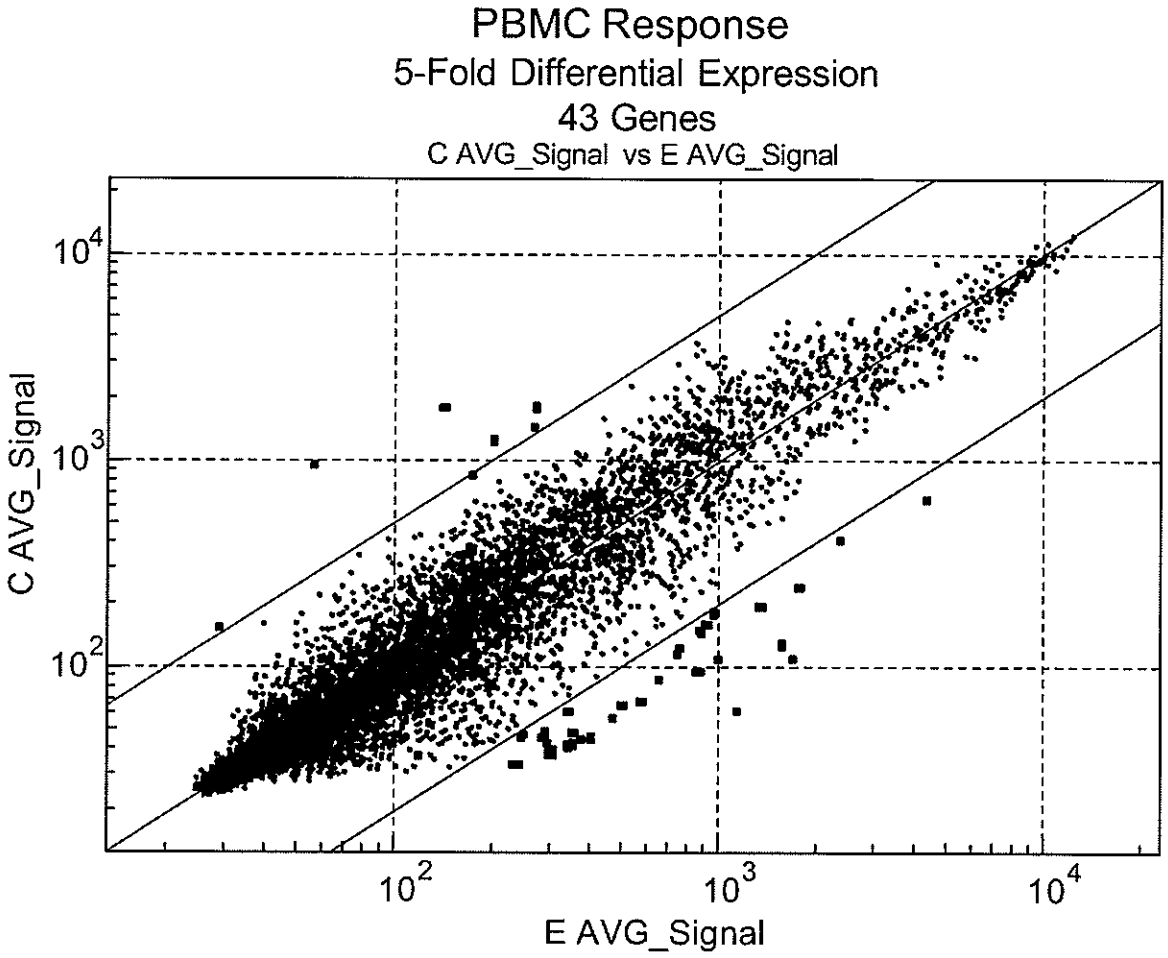

PBMC Response
5-Fold Differential Expression
43 Genes
C AVG_Signal vs E AVG_Signal
C AVG_Signal
E AVG_Signal
10^2
10^3
10^4

Figure 4

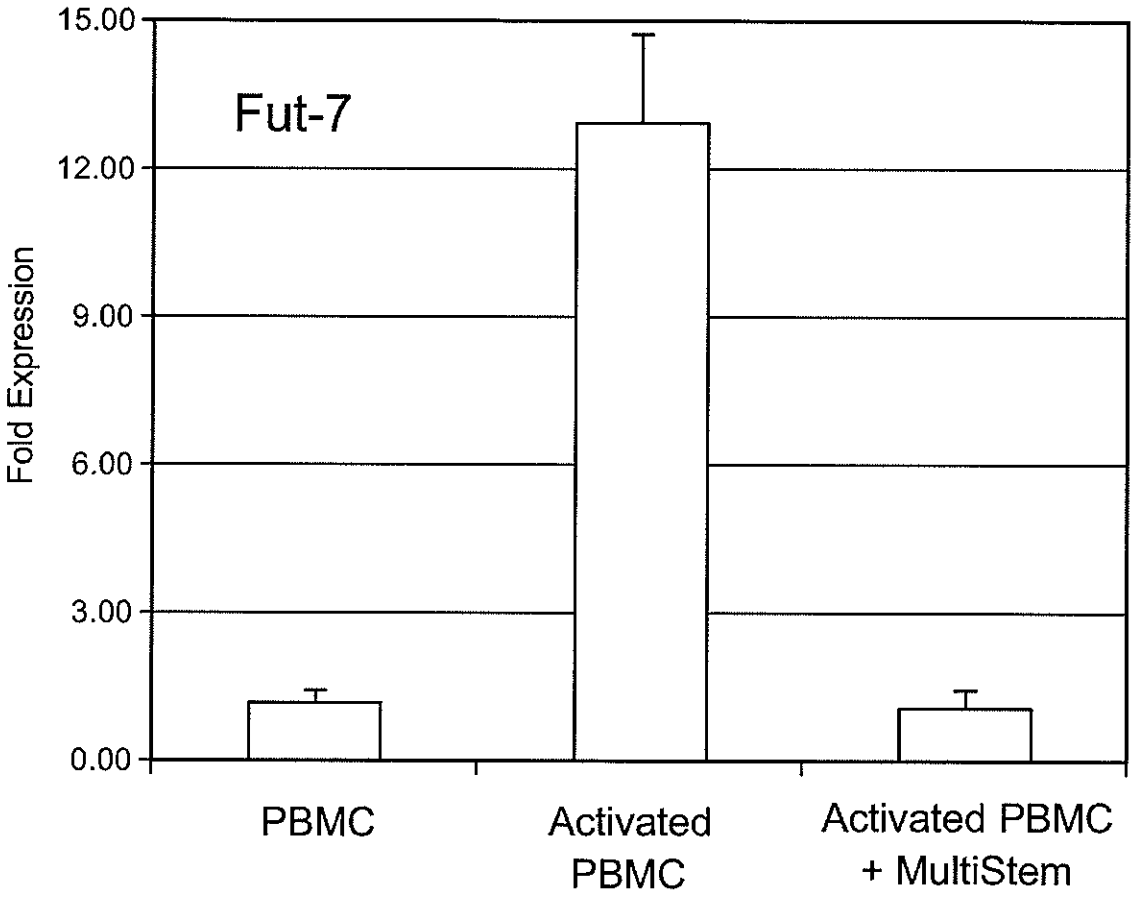

Fut-7
15.00
12.00
9.00
6.00
3.00
0.00
Fold Expression
PBMC
Activated PBMC
Activated PBMC + MultiStem

Figure 5

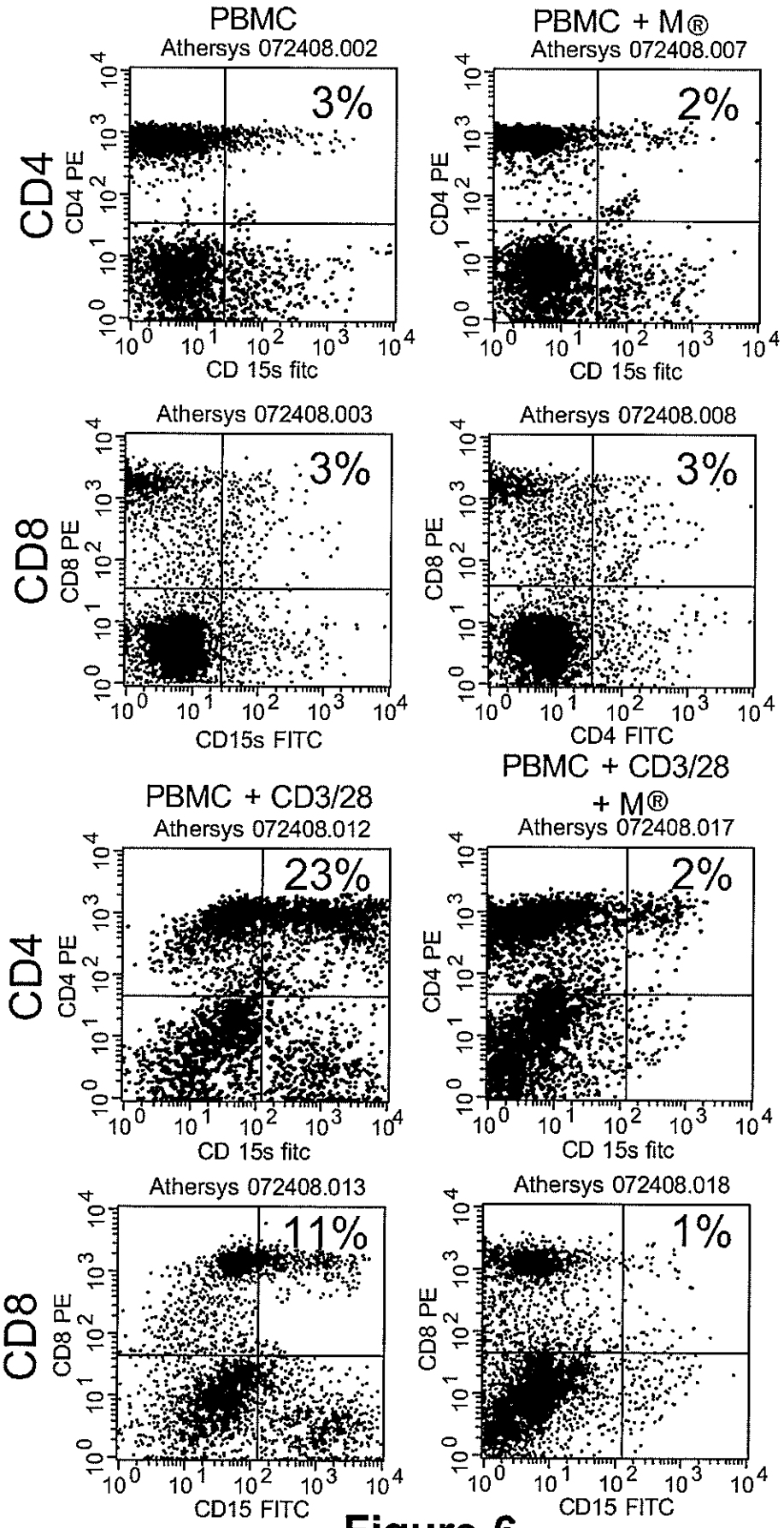

PBMC
Athersys 072408.002
3%
CD4
CD4 PE
CD 15s fitc
PBMC + M®
Athersys 072408.007
2%
CD4 PE
CD 15s fitc
Athersys 072408.003
3%
CD8
CD8 PE
CD15s FITC
Athersys 072408.008
3%
CD8 PE
CD4 FITC
PBMC + CD3/28
Athersys 072408.012
23%
CD4
CD4 PE
CD 15s fitc
PBMC + CD3/28
+ M®
Athersys 072408.017
2%
CD4 PE
CD 15s fitc
Athersys 072408.013
11%
CD8
CD8 PE
CD15 FITC
Athersys 072408.018
1%
CD8 PE
CD15 FITC

Figure 6

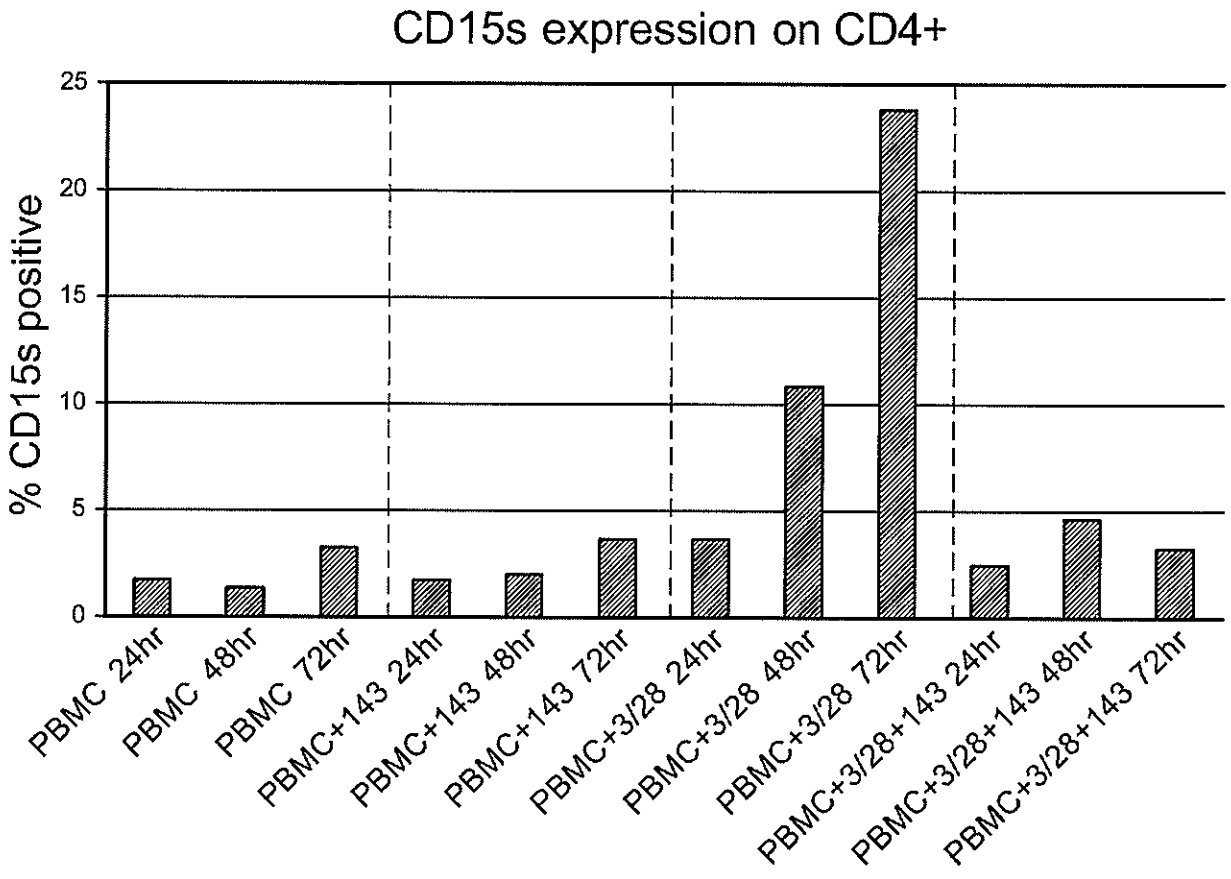
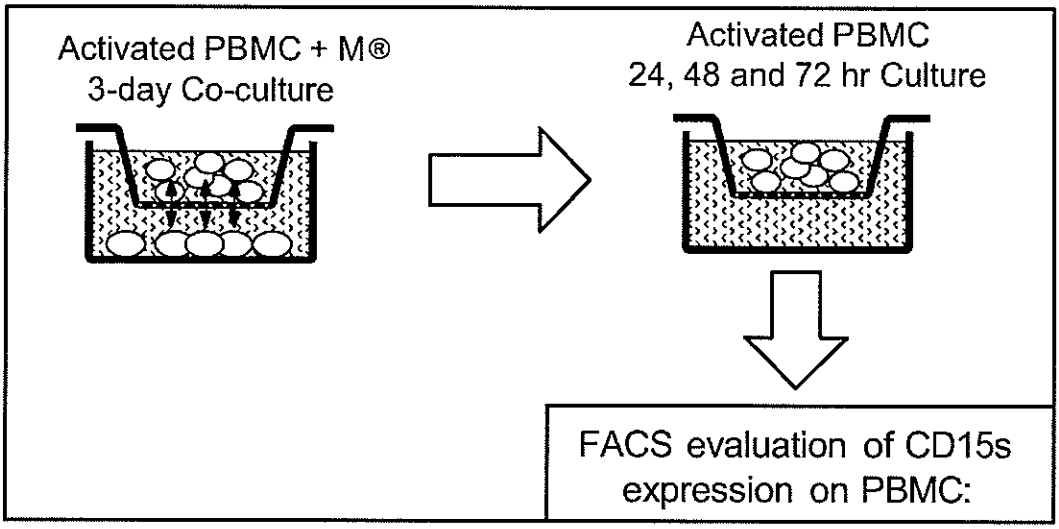

CD15s expression on CD4+
% CD15s positive
25
20
15
10
5
0
PBMC 24hr
PBMC 48hr
PBMC 72hr
PBMC+143 24hr
PBMC+143 48hr
PBMC+143 72hr
PBMC+3/28 24hr
PBMC+3/28 48hr
PBMC+3/28 72hr
PBMC+3/28+143 24hr
PBMC+3/28+143 48hr
PBMC+3/28+143 72hr

Figure 7


Activated PBMC + M®
3-day Co-culture
Activated PBMC
24, 48 and 72 hr Culture
FACS evaluation of CD15s
expression on PBMC:

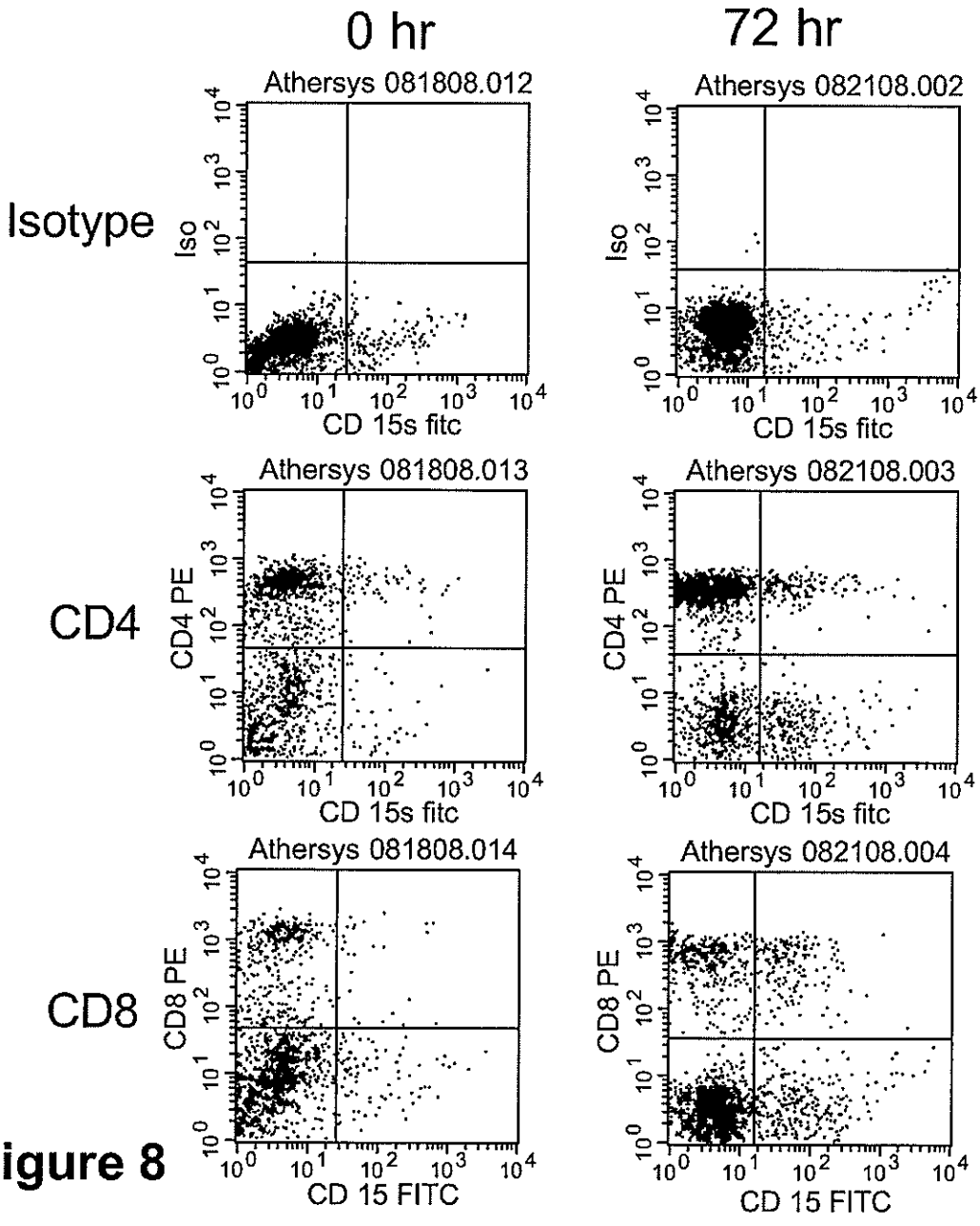

0 hr
72 hr
Isotype
CD4
CD8
Athersys 081808.012
Athersys 082108.002
Athersys 081808.013
Athersys 082108.003
Athersys 081808.014
Athersys 082108.004
Iso
CD4 PE
CD8 PE
CD 15s fitc
CD 15 FITC

Figure 8

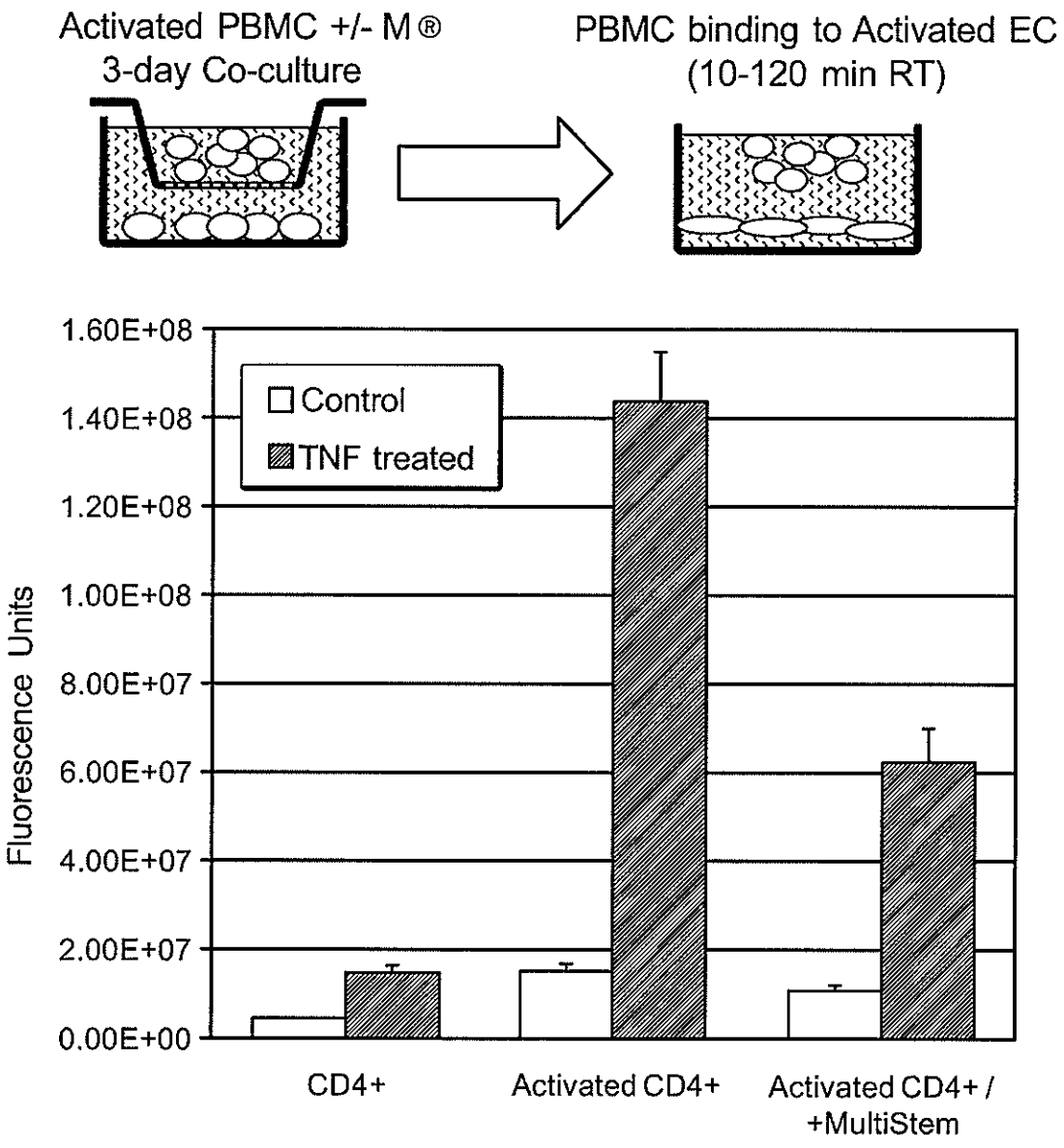
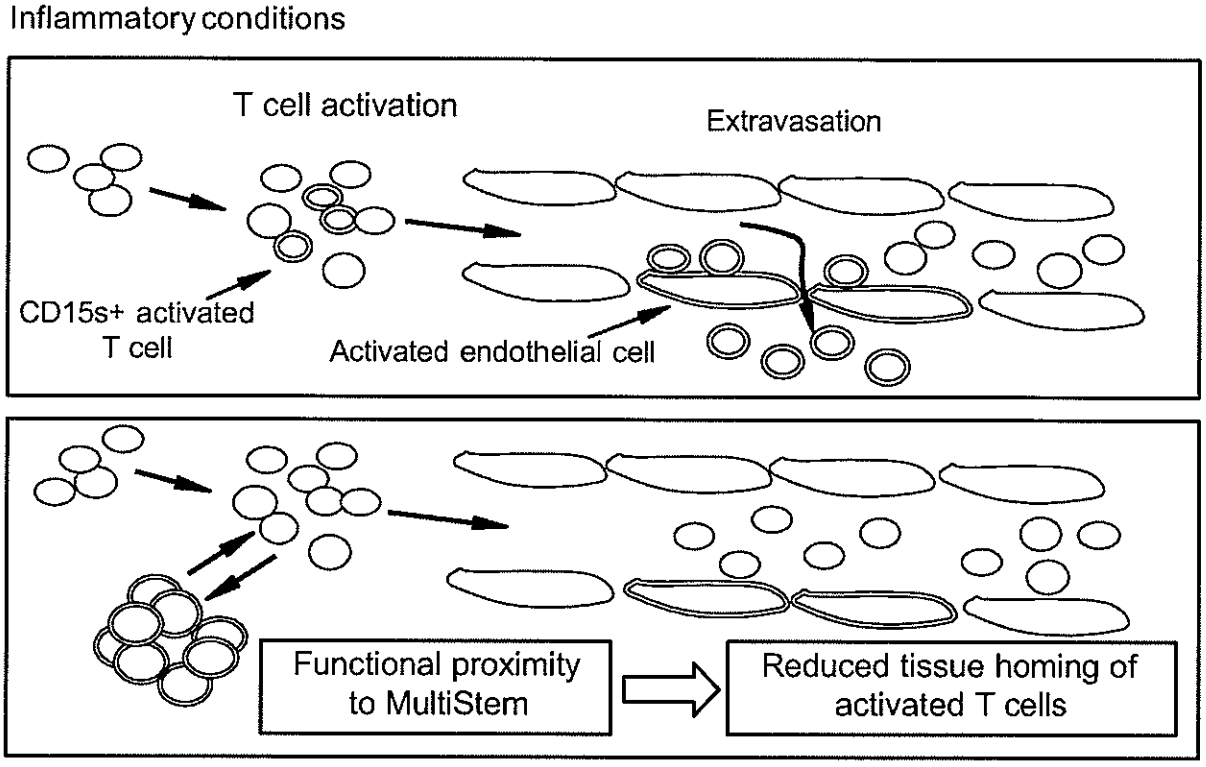

Activated PBMC +/- M®
3-day Co-culture
PBMC binding to Activated EC
(10-120 min RT)
Fluorescence Units
1.60E+08
1.40E+08
1.20E+08
1.00E+08
8.00E+07
6.00E+07
4.00E+07
2.00E+07
0.00E+00
Control
TNF treated
CD4+
Activated CD4+
Activated CD4+ /
+MultiStem

Figure 9



Possible mechanism for prevention of inflammatory conditions by MultiStem through cross-talk with inflammatory cells.

Figure 10

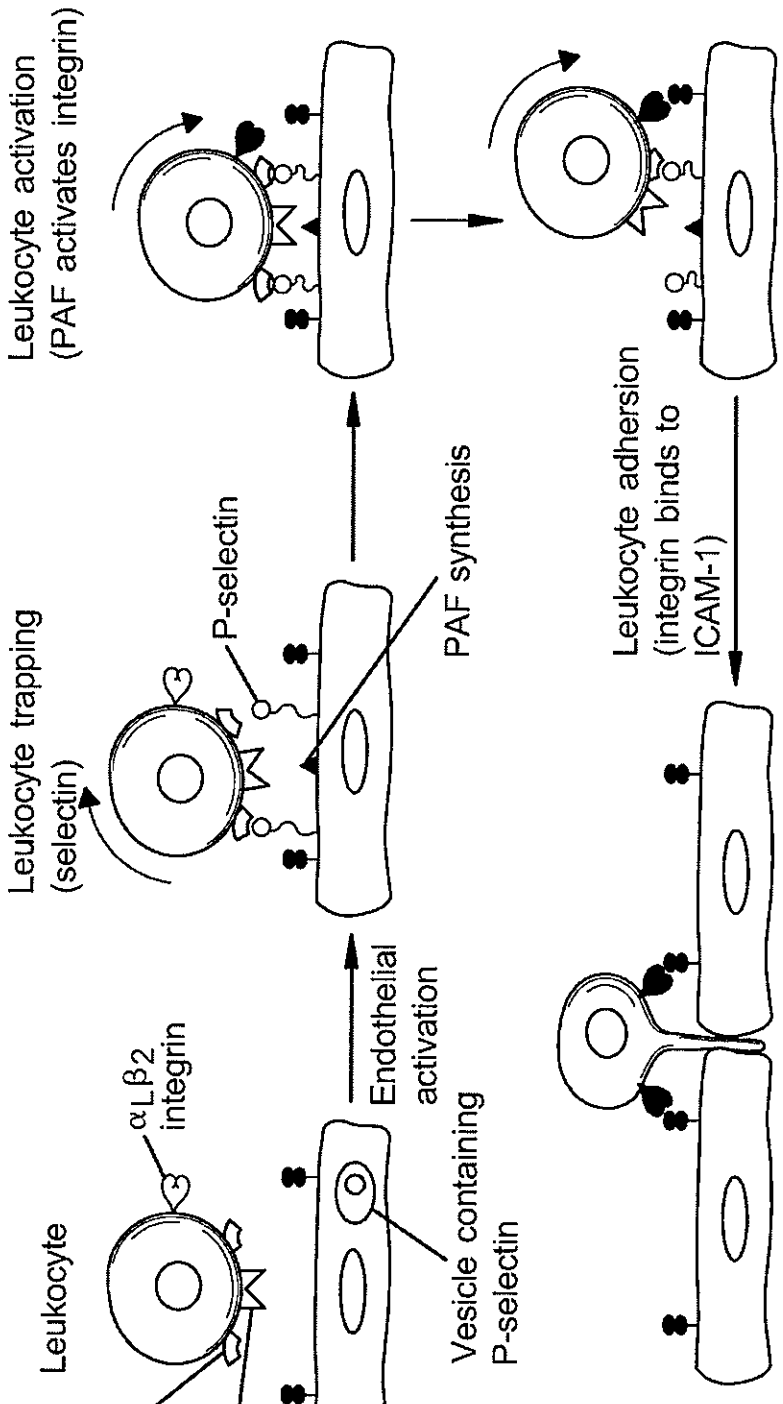

Leukocyte activation
(PAF activates integrin)
Leukocyte trapping
(selectin)
P-selectin
PAF synthesis
Leukocyte adhersion
(integrin binds to
ICAM-1)
Endothelial
activation
Leukocyte
$\alpha_L\beta_2$
integrin
Selectin
ligand (specific
carbohydrate)
PAF receptor
ICAM-1
Endothelial
cell
Vesicle containing
P-selectin
Extravasation

Figure 11