

رویکردی جدید در درمان بیماری دیابت خودایمن وابسته به انسولین با استفاده از سلول‌های دندریتیک تیمار شده با اینترلوکین ۱۰ (IL-10)

*

چکیده

مقدمه:

T

(DCs)

T

IL-4 GM-CSF

LPS IL-10

روش‌ها:

T

IL-10

MHC class II

یافته‌ها:

(P < /)

) LPS

T

IL-10

(P < /)

IFN- γ

IL-10

IL-10

نتیجه‌گیری:

IL-10

واژگان کلیدی:

* نشانی:

moazzeni@dr.com :

تاریخ دریافت مقاله: ۸۴/۷/۲۴

تاریخ پذیرش مقاله: ۸۵/۴/۲۰

مقدمه

(IL-10)

IL-12 IL-10 β T

Th2 IL-10 T

IL-10 T []

T [] T

T [] A []

IL-10 IL-10 []

IL-10 (DC)

IDDM [] T

روش‌ها

C57BL/6 T

(LPS)

% RPMI (Gibco) CpG DNA TNF-α

μg/ml (Gibco) U/ml FBS (Gibco) CD40 CD40 IFN-γ

(Sigma) (Gibco)

mrTNF-α (Bender mrIL-4(R&D) mrGM-CSF(R&D)

mrIL-10 (Bender Med) Med) T

antiCD11c(PE-conjugated) IL-12

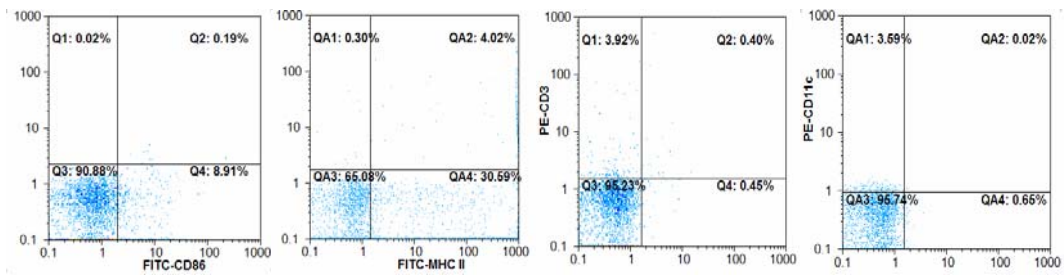
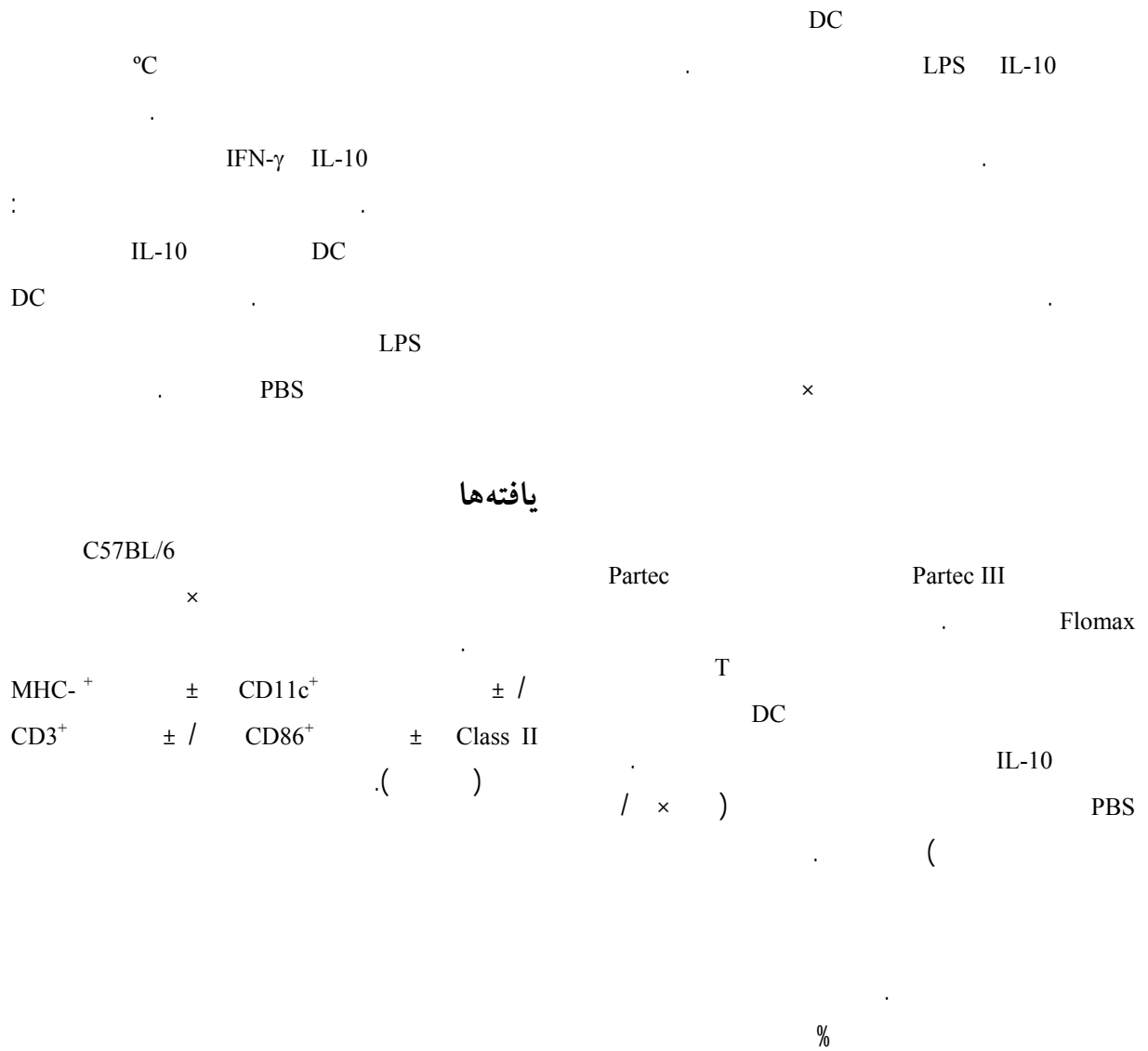
anti CD11b(FITC-conjugated) Th2 Th1

anti CD8α(PE-conjugated) []

anti-

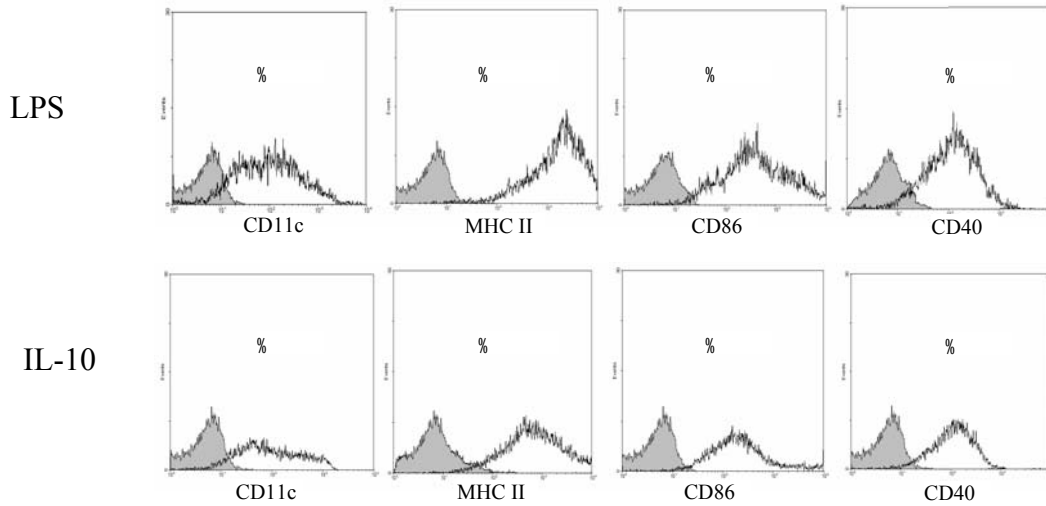
Haase anti CD40(PE- MHC class II I-A^E(FITC-conjugated)
 U/ml [] anti CD86(PE-conjugated) conjugated)
 anti-CD3(PE-
 % T conjugated)
 IL-10 BD Biosciences
 CO₂ %
 () LPS
 DC
 % /
 g
 Polyinosinic-Polycytidylic acid mm PBS
 (poly I/C) cc
 Insulin 2B chain / cc
 peptide B: 9-23(SHLVEALYLVCGERG)
 µg/ml (Flush out)
 g
 DCs)
 T × ()
 DC DC RPMI
 (DC2 DC1)
 MHC-II CD11c DCs U/ml cm²
 CD86 rmIL-4 u/ml rmGM-CSF
 IL-10 CD40 % CO₂ °C
 LPS
 CD11b CD8α %
 CD8α
 DC DC
 DC DC
 DC CD11b

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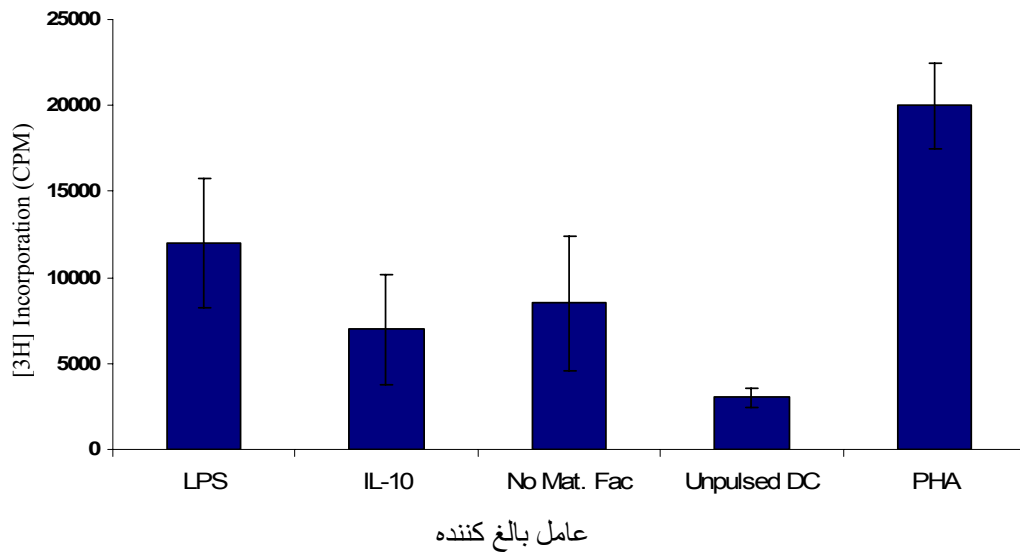


نمودار ۱- نمونه ای از نمودارهای حاصل از آنالیز فلوسیتومتری سلولهای بدست آمده از مغز استخوان

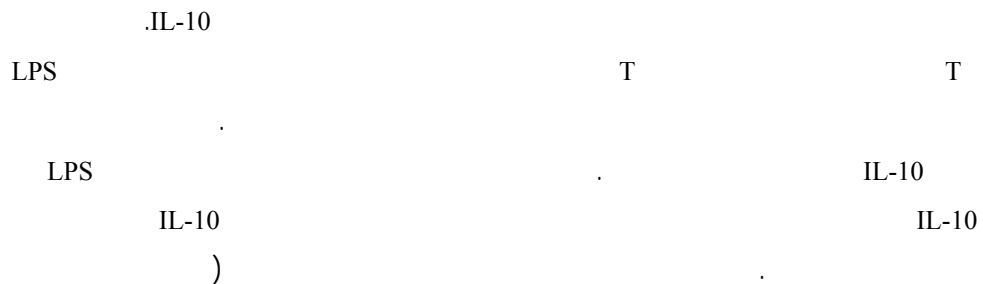
$\% \pm$ MHC ClassII⁺
 $\% \pm$ CD40⁺ $\% \pm$ CD86⁺ CD11c⁺ \pm
 CD86 MHC class II IL-10
 LPS) CD11c⁺
 (P= /)
 .() MHC $\% \pm$
 IL-10 . CD40⁺ $\% \pm$ CD86⁺ $\% \pm$ ClassII⁺
 C11c⁺ CD8 α
 IL-10 LPS (DC2) CD11b
 .()
In vivo IL-10 Th2
 IL-10
In vivo IL-10 LPS
 LPS
 $\% \pm$
 T $\% \pm$
 IL-10 MHC $\% \pm$ LPS
 (SD=) CPM $\% \pm$ CD86⁺ $\% \pm$ ClassII⁺
 LPS MHC ClassII . CD40⁺
 (SD=) CPM
 IL-10 MFI
 IL-10 (P= /)
 T T
 T IL-10 MHC ClassII
 .()
 IL-10
 .() $\% \pm$
 LPS $\% \pm$



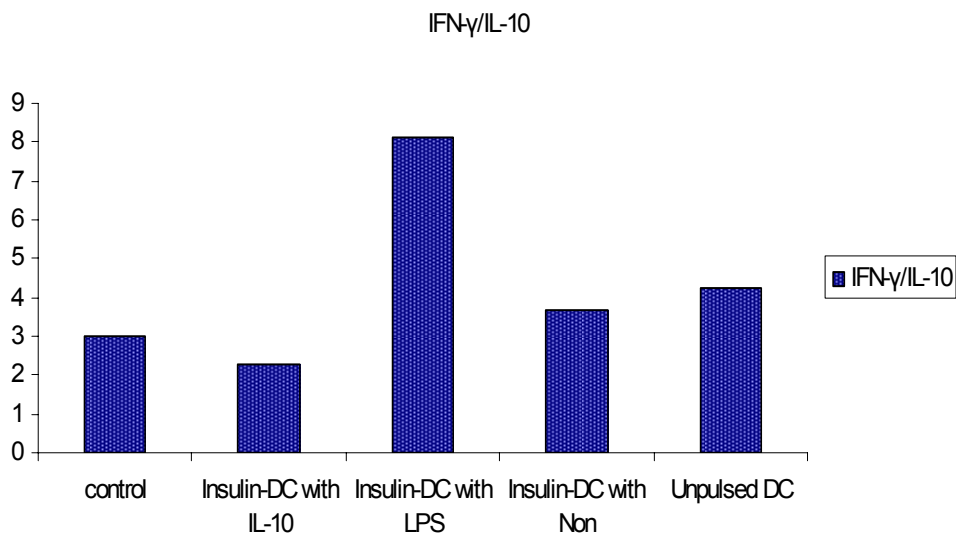
نمودار ۲- میزان بروز هر یک از شاخص‌های بلوغ بر روی سلول‌های دندریتیک بعد از اضافه نمودن عوامل بلوغ. نمودارهای خاکستری مربوط به ایزوتیپ کنترل هر یک از شاخص‌ها بر روی سلول‌های مورد مطالعه می‌باشد.



نمودار ۳- میزان تکثیر سلول‌های T در مواجهه با آنتی‌ژن در آزمون سنجش تکثیر سلول‌های T در گروه‌های مختلف سلول‌های دندریتیک تیمار شده با IL-10 و LPS گروه No Mat . Fac مربوط به سلول‌های دندریتیک است که هیچ عامل بالغ کننده‌ای دریافت نکرده‌اند و unpulsed DC مربوط به گروهی است که با پپتید انسولین بارگذاری نشده‌اند.



IL- Th2 (P < /) IFN-γ/IL-10 (P < /)
 .() LPS
 IFN-γ/IL-10



نمودار ۴- نسبت ساینوکین‌های IFNγ/IL10 تولید شده توسط لنفوسیت‌های T در گروه‌های مورد مطالعه تزریق شده توسط سلول‌های دندریتیکی که به صورت‌های متفاوتی تیمار شده اند.

بحث
 GM-CSF + IL-3 + IL- DC
 .[] Th2 T 4 DC T
 DC T DC T
 T IL-10 β₂
 Th2 CD58 CD50, CD54, CD2, β₁
 CD40L IL-12P70 T .[]
 Kalinski.[]
 IL-12 IL-12 IL-1, IL-6
 .[] Th2 Th1 .[]
 IL-10 IFN-γ, PGE₂
 Th2 Th1
 DC
 GM-CSF + IL-3 + IFN-γ
 IL-10 DC IL-12
 IFN-γ
 Th1 T
 IL-10 .[]
 [] NK

[] Dhodapkar
 IL-10 DC
 T_{reg} *In vivo*
 IL-10 []
 T_{reg} T_{reg}
 DC [] T_{reg}
 NOD IL-10
 (CD25⁺CD4⁺) T_{reg} [] IL-10
 [] IL-10
 CD4⁺T
 T *Ex vivo* []
 DC [] Steinbrink
 T_{reg} GM-CSF IL-4
 IL-10
 DC
 DC CD8⁺T
 Papaccio IL-10
 HCG
 Th2
 NOD IL-10
 [] B7-1/-2 MHCII
 IL-10 (ICAM-1)
 DC IL-10 []
 Th2 T
 IL-1, IL-6, IL-8, TNF- α
 [] GM-CSF
 BB NOD
 DC
 IL-10 IL-10
 IL-10 [] Th2
In vitro DC
 []

مآخذ

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