

**Effect of Mesenchymal Stem Cells on TNF- α and IL-10
expression in Atherosclerotic lesion**

Experimental study in Sprague Dawley Rats



Thesis

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by:

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**BIOMEDICAL SCIENCE
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A thesis

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DECLARATION

I hereby declare that this thesis is my own work and has not been submitted in any form for another degree or diploma at any university or other institution of tertiary education, there are no elements belonging Plagiarism forth in Decree No. 17 of 2010. Information derived from the published or unpublished work of others has been acknowledged in the text and a list of reference is given.

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List of abbreviations

(MSCs)	Mesenchymal Stem Cells
(SD)	Sprague Dawley Rats
(N)	Number
(R)	Randomization
(SD)	standard diet
(AD)	atherogenic diet
(LDL)	low density lipoprotein
(HDL)	High density lipoprotein
(TNF-)	tumor necrosis factor
(IL-10)	Interleukin 10
(MCP-1)	monocyte chemotactic protein-1
(TGF- β)	transforming growth factor- β
(PDGF)	platelet-derived growth factor
(VCAM-1)	Vascular cell adhesion molecule-1
(IFN- γ)	Interferon gamma
(G-CSF)	Granulocyte colony-stimulating factor
(PGE2)	Prostaglandin E2
(WHO)	World Health Organization

ABSTRACT

Background: Atherosclerosis is one of the leading causes of cardiovascular mortality and morbidity in the world. Mesenchymal stem cells (MSCs) may be able to ameliorate atherosclerosis through increasing of IL-10 and reducing of TNF- α expression. However, the effect of MSCs on atherosclerotic vessel has never been reported.

Objective: To investigate the effect of MSCs administration on TNF- α and IL-10 expression and on atherosclerotic lesion of abdominal aorta.

Method: Sprague Dawley Rats were divided into negative control group (fed a normal diet, n=6), positive control group (fed a high fat diet, n=6) and MSCs treatment group (fed a high fat diet and treated single dose of 5×10^6 MSCs, n=8). Atherosclerotic appearance in abdominal aorta wall was stained by hematoxylin and eosin, while IL-10 and TNF- α protein expression were observed by immunohistochemistry.

Results: Atherosclerotic appearance in the MSCs treated group was significantly lower than in that of untreated group ($p=0.007$). TNF- α expression in macrophage was significantly higher in the MSCs treated group than that of untreated group ($p=0.047$), while expression of IL-10 in tunica media and endothelial cells were not significant.

Conclusion: MSCs have a potential effect in ameliorating atherosclerotic lesion in SD rats mediated in part by reducing of TNF- α expression in macrophage of abdominal aorta, but not mediated by IL-10 expression.

Keywords: Mesenchymal stem cells, atherosclerosis, Sprague Dawley rats, TNF- α , IL-10.

Abstrak

Latar belakang: Aterosklerosis adalah salah satu penyebab utama mortalitas dan morbiditas di dunia. Sel punca mesenkimal (MSC) mungkin dapat memperbaiki aterosklerosis melalui peningkatan ekspresi IL-10 dan penurunan ekspresi TNF- α . Bagaimanapun juga, efek MSC pada pembuluh darah aterosklerosis belum dilaporkan.

Tujuan: Untuk menginvestigasi efek pemberian MSC terhadap ekspresi TNF- α dan IL-10 pada lesi aterosklerosis aorta abdominal.

Metode: Tikus Sprague Dawley dibagi menjadi kelompok kontrol negatif (diberi makan diet normal, n=6), kelompok kontrol positif (diberi makan diet tinggi lemak, n=6) dan kelompok pengobatan MSC (diberi makan diet tinggi lemak dan diterapi dengan dosis tunggal MSC 5×10^6 , n=8). Penampakan aterosklerosis pada aorta abdominal diwarnai dengan hematoksilin dan eosin, sedangkan ekspresi protein IL-10 dan TNF- α diobservasi melalui immunositokimia.

Hasil: Penampakan aterosklerosis pada kelompok yang diterapi MSC secara signifikan lebih rendah dibanding kelompok yang tidakditerapi aterosklerosis ($p=0.007$). Ekspresi TNF- α pada makrofag secara signifikan lebih tinggi pada kelompok yang diterapi MSC dibanding kelompok yang tidak diterapi ($p=0.047$), sedangkan ekspresi IL-10 di tunika media dan sel endotel tidak signifikan.

Kesimpulan: MSC mempunyai efek potensial dalam memperbaiki lesi aterosklerosis pada tikus SD dengan dimediasi oleh penurunan ekspresi TNF- α oleh makrofag di aorta abdominal, tapi tidak dimediasi melalui ekspresi IL-10.

Kata kunci: Sel punca mesenkimal, aterosklerosis, tikus Sprague Dawley, TNF- α , IL-10

