The role of TGF-β and the transcription factor KLF-10 in the function of Early Endothelial Progenitor Cells


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Disclosures

None!
Early proangiogenic cells (EPCs)
EPCs and cardiovascular Risk factors

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Response</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>↓ EPC cytopoiesis</td>
</tr>
<tr>
<td></td>
<td>↓ EPC mobilization (chronic e acute)</td>
</tr>
<tr>
<td></td>
<td>↓ EPC survival</td>
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<tr>
<td></td>
<td>↓ EPC functional activity</td>
</tr>
<tr>
<td>Oestrogens</td>
<td>↑ EPC concentration</td>
</tr>
<tr>
<td>Exercise</td>
<td>↑ EPC concentration</td>
</tr>
</tbody>
</table>

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**CV risk factors**

- Number of CV risk factors
- Framingham CV total risk score
- Optimal flow-mediated dilation
- Smoking
- Hypertension
- Hypercholesterolaemia
- Diabetes mellitus

- ↓ EPC number
- ↓ EPC number
- ↑ CD34/KDR+ number
- ↑ EPC number
- ↑ CD34/KDR+ number
- ↓ EPC number
- ↑ EPC proliferation
- ↓ EPC survival
- ↓ EPC proliferation
- ↓ EPC migratory capacity
- ↓ EPC vasculogenetic property
- ↓ EPC survival
- ↓ EPC proliferation
- ↓ EPC number
EPCs and cardiovascular disorders

The level of circulating CD34+KDR+ endothelial progenitor cells predicts the occurrence of cardiovascular events and death from cardiovascular causes and may help to identify patients at increased cardiovascular risk

Platelets and EPCs

Platelets And EPCs

Recent studies have shown that in the presence of direct interaction with platelets, EPCs improve their functional properties. In vitro exposure to platelets in culture conditions enhances the capacity of EPCs to form colonies, to proliferate and migrate.

KLF-10

• a subclass of the zinc-finger family of transcription factors, participate in various aspects of cellular growth, development, and differentiation.

• KLF-10 targets CACCC element or GC BOX which are present in a large number of growth regulatory gene sequence including TGF-β, PDGF and FGF.
TGF-β and KLF-10 Signal Transduction

In response to TGFβ-1, KLF10 plays an important role in controlling EPC differentiation and function in vitro and in vivo.

KLF10 expression was found to be reduced in EPCs from patients with Peripheral Artery Disease.

AIMs

- **General aim**- to explore the mechanism of enhancement of EPCs function by platelets.
- **Specific aims**-
  to examine the role of TGF-β and its transcription factor KLF-10 in the enhancement of EPCs function by platelets.
Experimental Design

Human EPCs were isolated from donated buffy coats and cultured for 7 days on a traditional fibronectin matrix in one of the following conditions:
1. Alone (control)
2. Co-incubated with platelets
3. Co-incubated with platelets and TGFβRII inhibitor.
EPCs identification
COLONY FORMING UNITS ASSAY (CFU)

EPC

PLT

TGF-βRII inhibitor

Colony per field

n=17

P<0.001
Viability and Endothelial Markers

**MTT**

- **Tie-2**
  - EPC
  - PLT
  - TGFβ

  *p* = 0.012

  *n* = 8

- **VE-cadherin**
  - EPC
  - PLT
  - TGFβRⅡ

  *p* = 0.011

  *p* = 0.008

  *n* = 8
TGF-β LEVELS

TGF-β1

P=0.012

n=8
TGF beta mRNA levels in EPCs

- EPCs
- EPCs & PLT

p<0.05

n=10
KLF-10 mRNA levels in EPCs

![Bar chart showing KLF-10 relative expression levels for EPCs and EPCs & PLT. The chart indicates a significant difference (p<0.001) between the two groups.]

n=10
Improved functional properties

KLF10

TGFβ

EPCs

KLF10

TGFβ

Growth Factors, cytokines and chemokines

PLT
CONCLUSIONS

• TGF-β has a central role in the effect of platelets on EPCs.

• This effect might be modulated by KLF-10.

• Further study is required in order to examine the role of KLF-10 in the enhancement of EPCs function by platelets and to explore its mechanisms of action.
THANKs

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