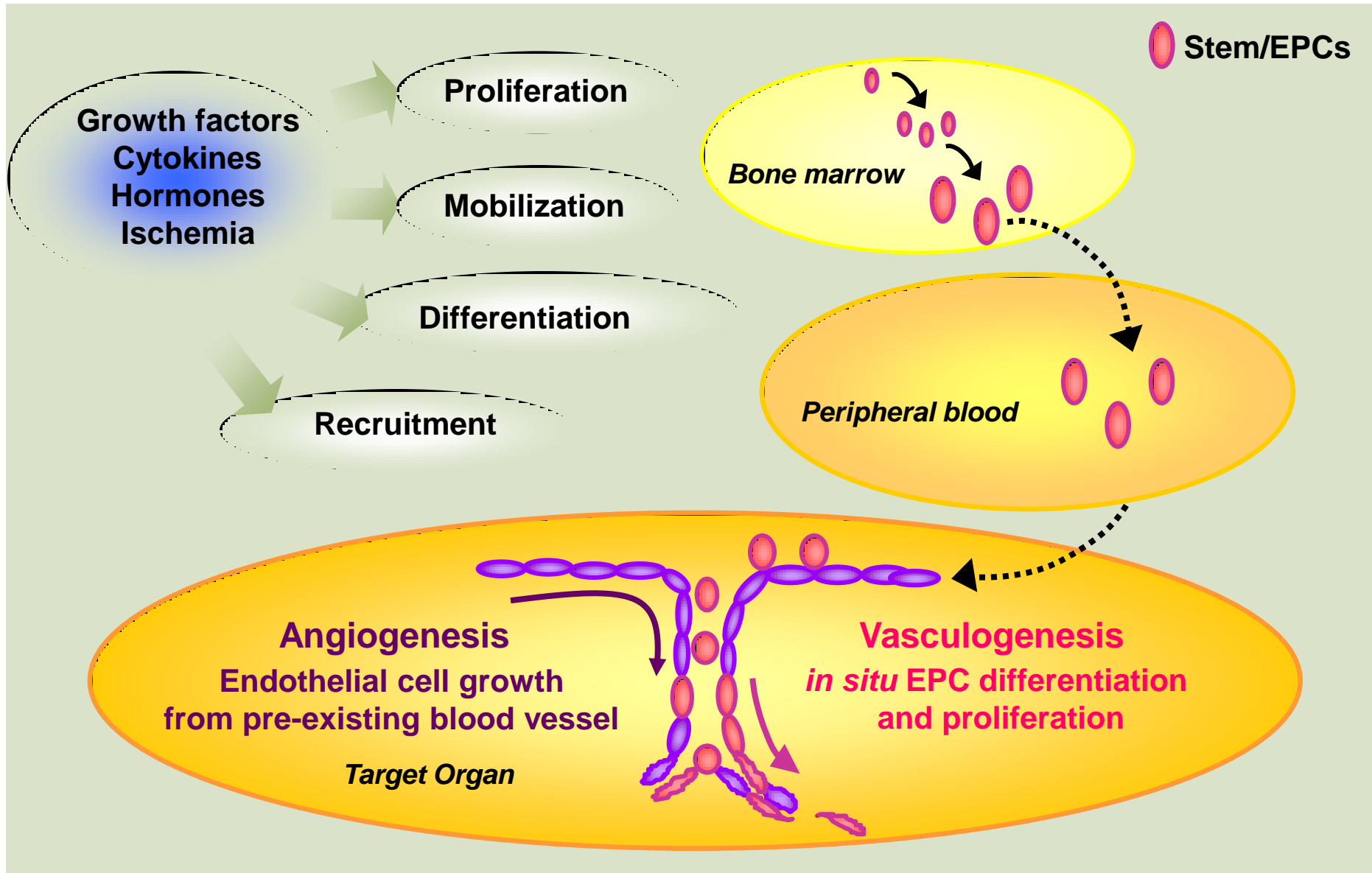


**Amniotic mesenchymal stem cells have robust
angiogenic properties and are effective
in treating wound and ischemic hindlimb**

Sung-Whan Kim Ph.D

**Department of Cardiology and Regional Clinical Trial Center
Dong-A University Hospital**

Neovascularization in Adult Mammals



(Asahara, Science 1997, Circ Res 1999)

Stem cells for the treatment of various ischemic organs

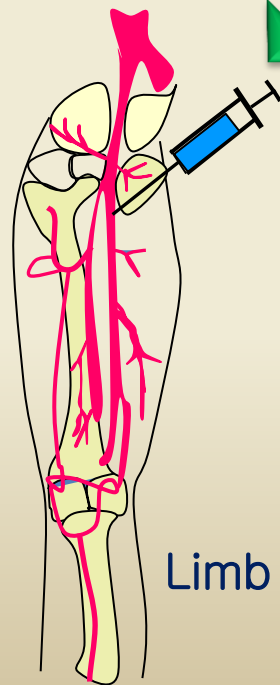
Stem or progenitor cells



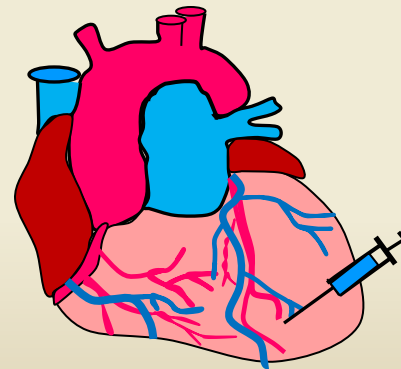
Cell therapy



Ischemic organ

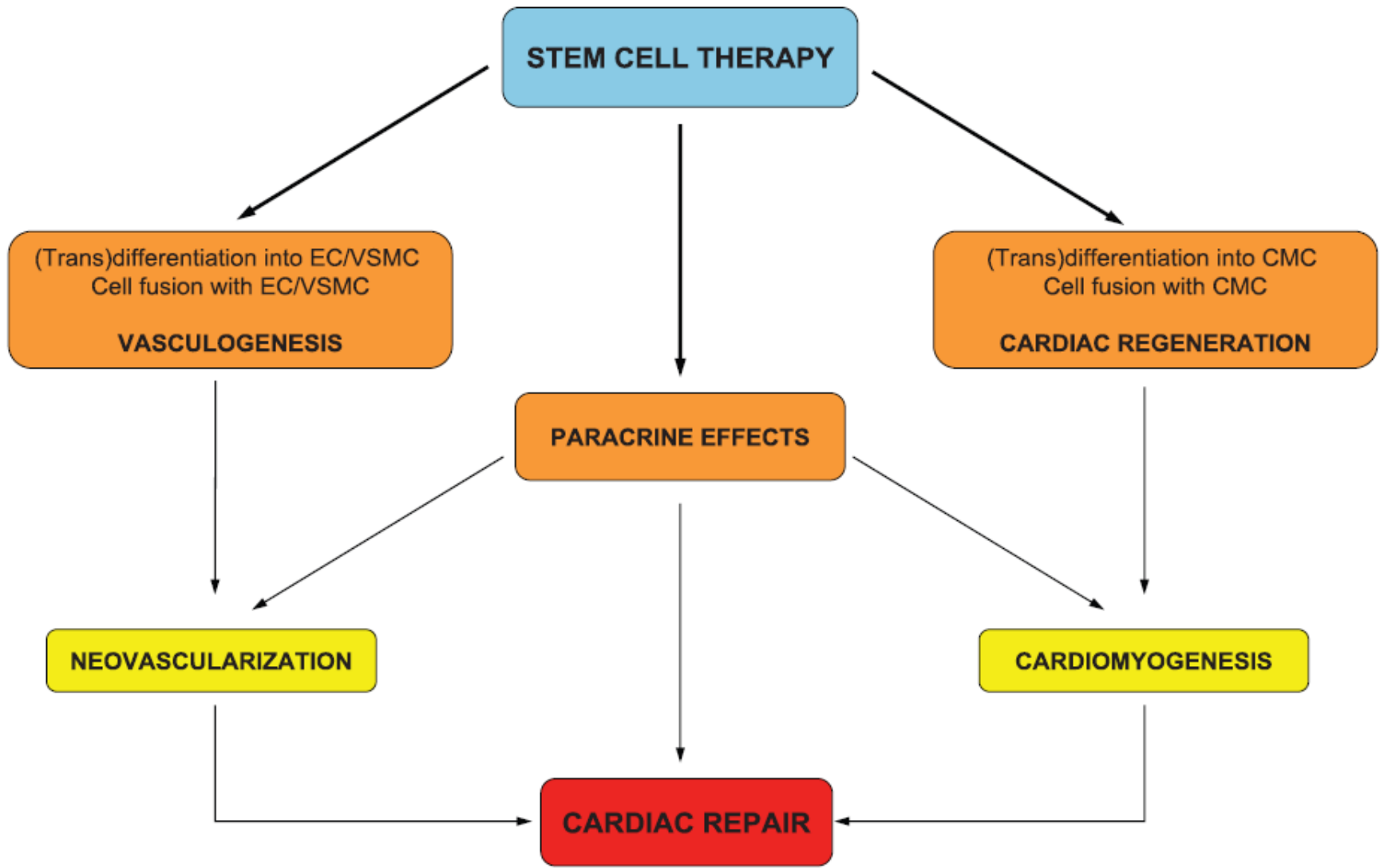


Limb



Myocardium

Mechanisms of stem cells action in cardiac repair

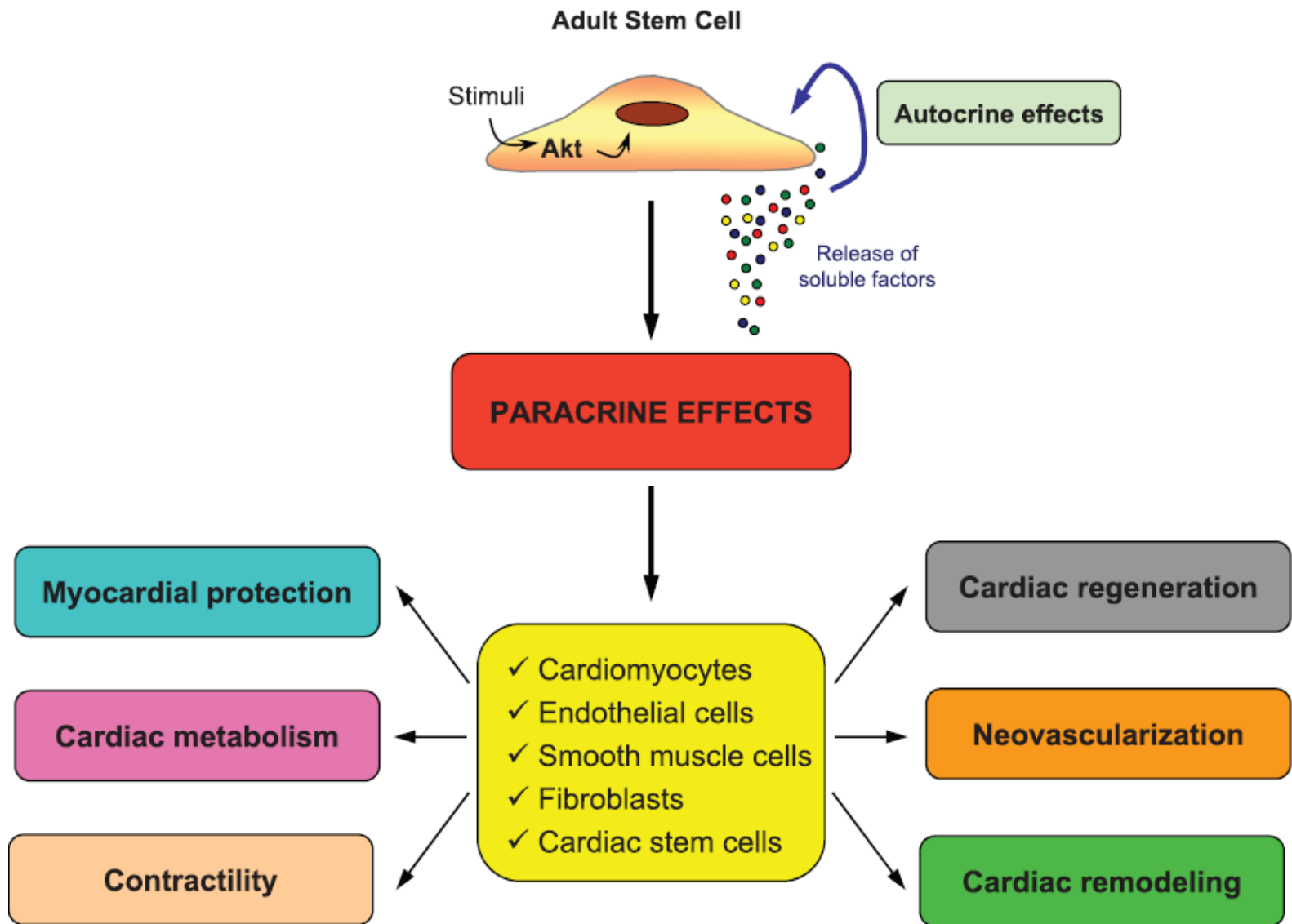


Ongoing Issue with adult stem cells

- Severe controversy exists regarding the **transdifferentiation of BM-derived cells or MSCs** : does **vasculogenesis** really occur in vivo?

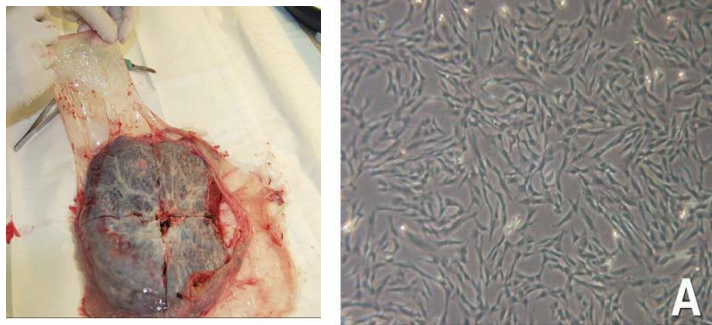
Ziegelhoff *et al.* Circ 2004
Phinney *et al.* Stem cells 2007

Mechanisms of adult stem cells action in cardiac repair



Amniotic mesenchymal stem cells

- Fetal tissue-derived stem cells?
- Amniotic membrane is a high throughput source for multipotent MSCs



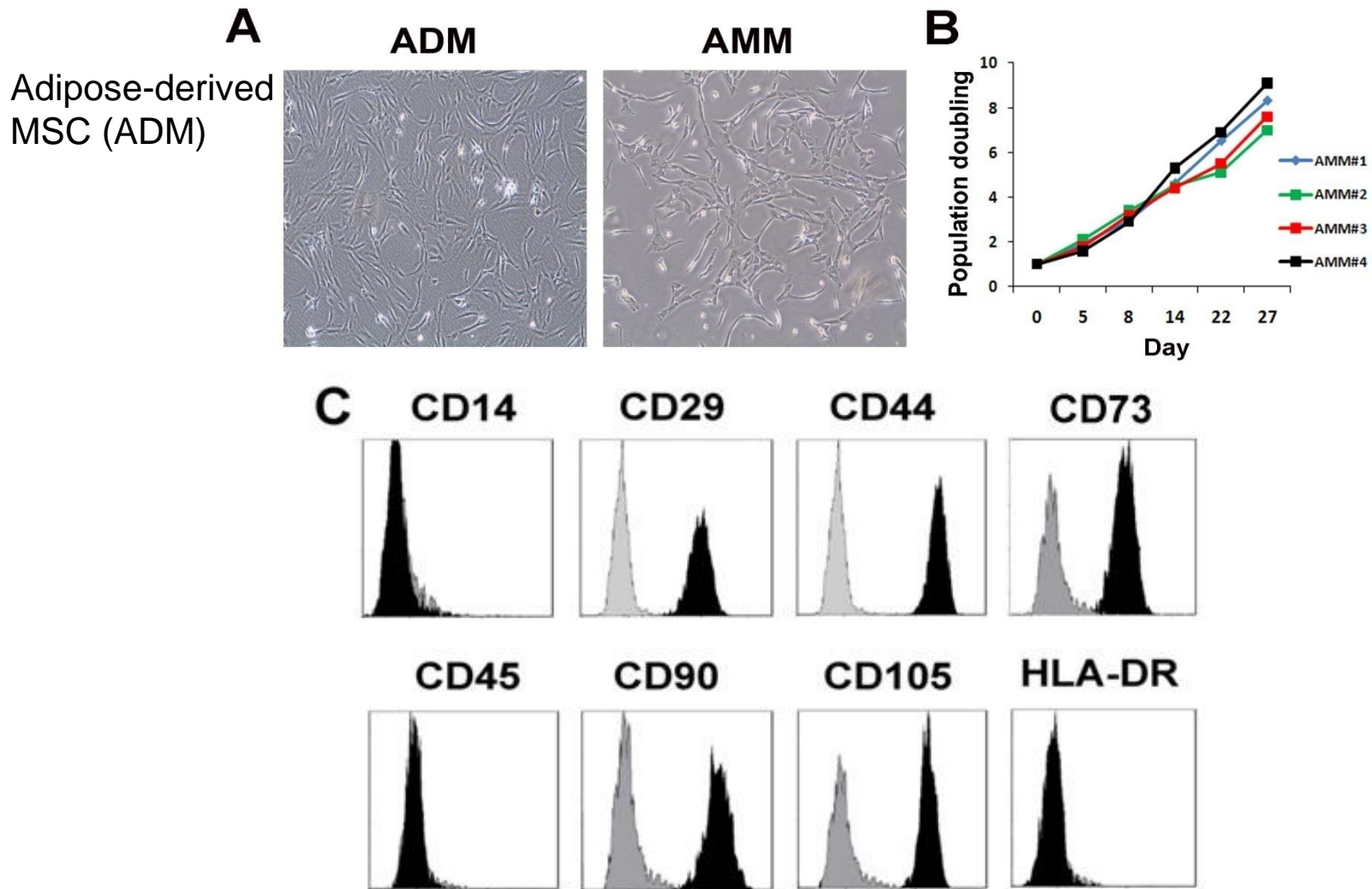
Zhang et al. Exp Hematol 2004
Yen et al. Stem cells 2005
Alviano et al. BMC dev 2007

- We hypothesized that amniotic MSCs (AMMs) possess high angio-vasculogenic potential?

Study Aim

To investigate the angio-vasculogenic property of human amniotic mesenchymal stem cells (AMMs)

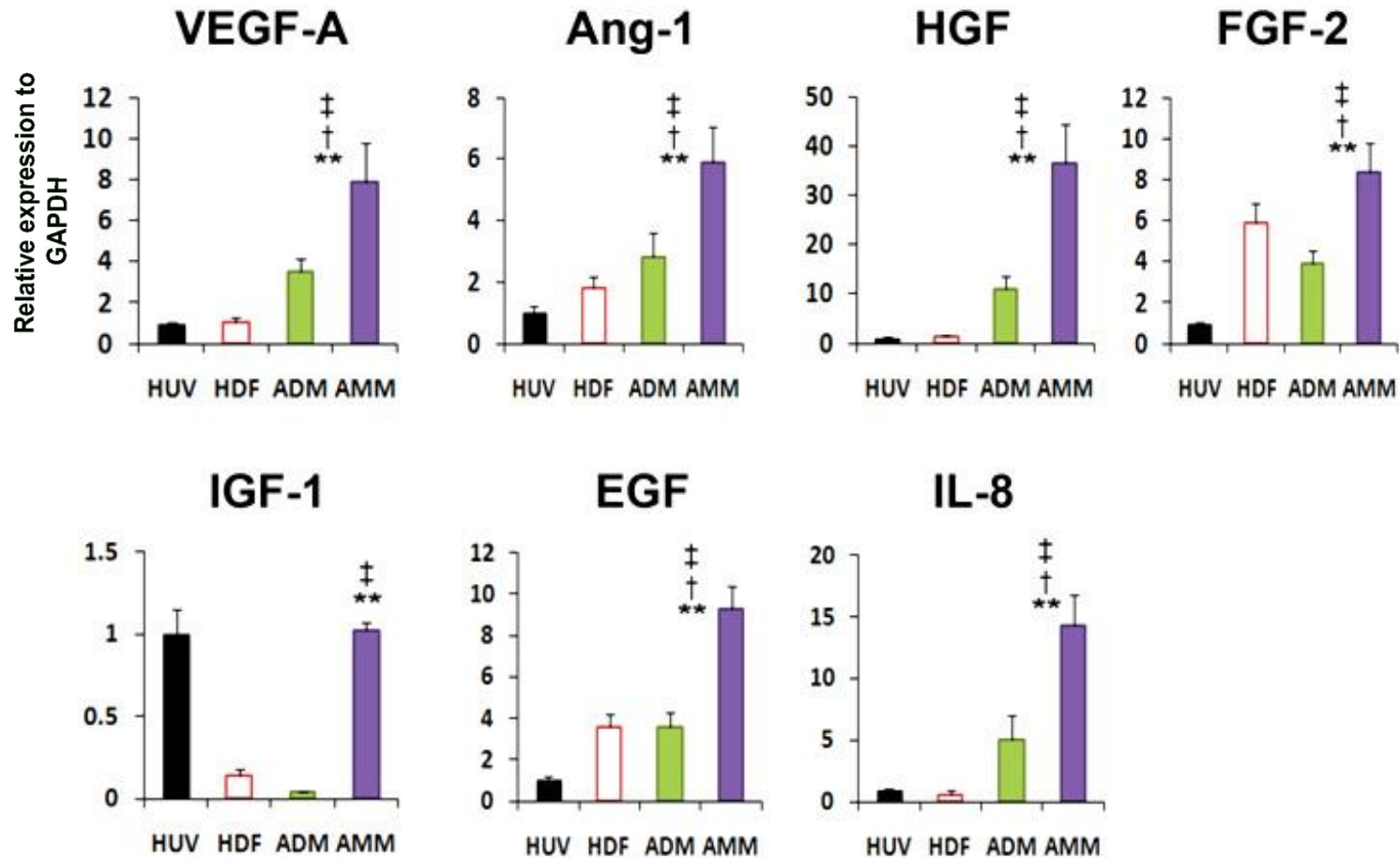
AMM cells express MSC specific markers



Gray: isotype control

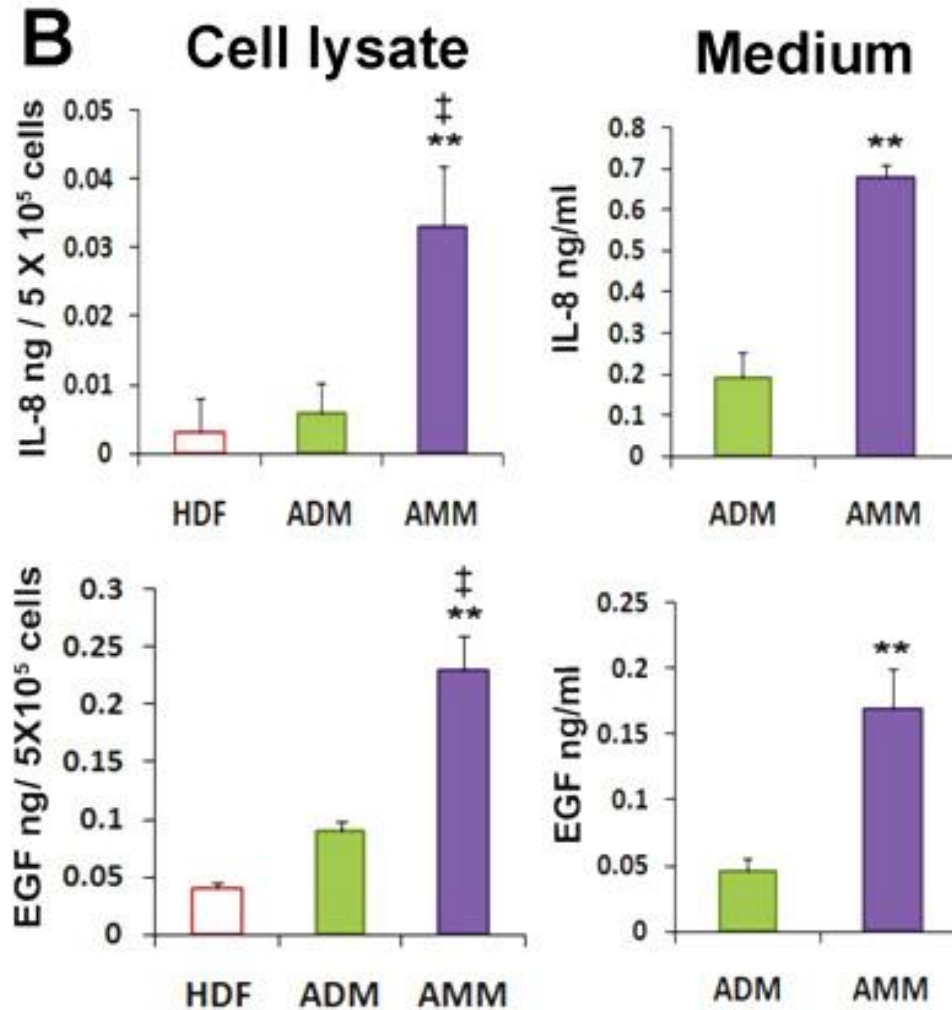
AMMs significantly express angiogenic genes

(qRT-PCR)



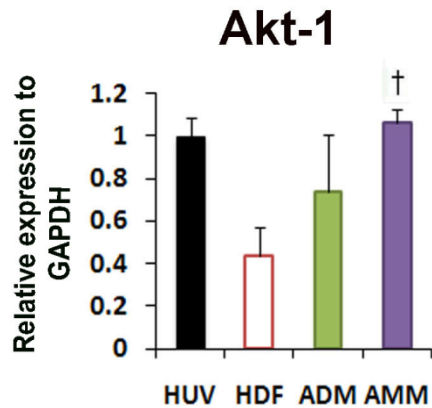
HUVEC (HUV), Human dermal fibroblast (HDF), Human Adipo MSC (ADM)

AMMs significantly secrete angiogenic protein (ELISA)



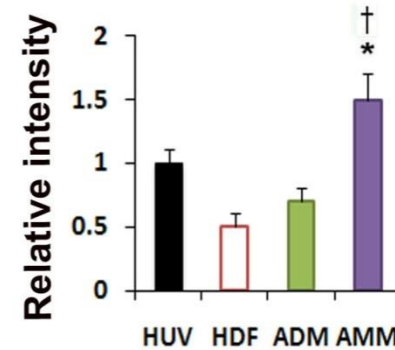
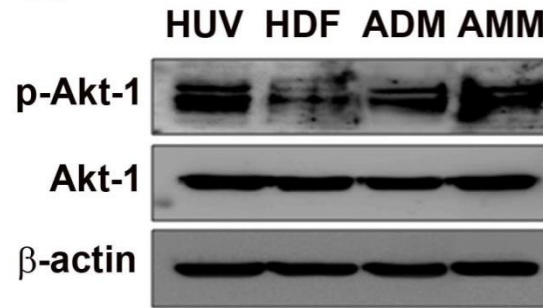
AMMs exhibit higher anti-apoptotic property

(qRT-PCR)



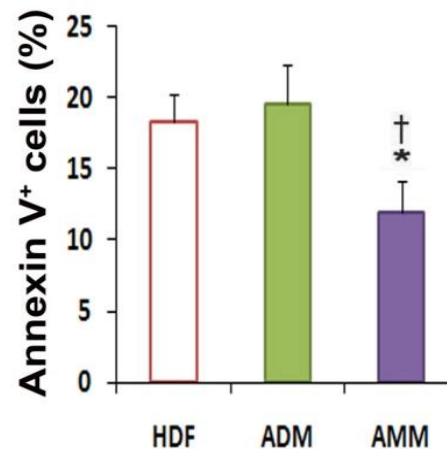
(Western)

B



(Apoptosis assay)

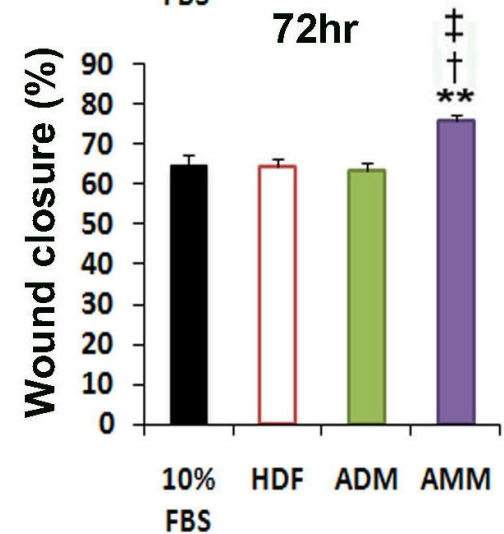
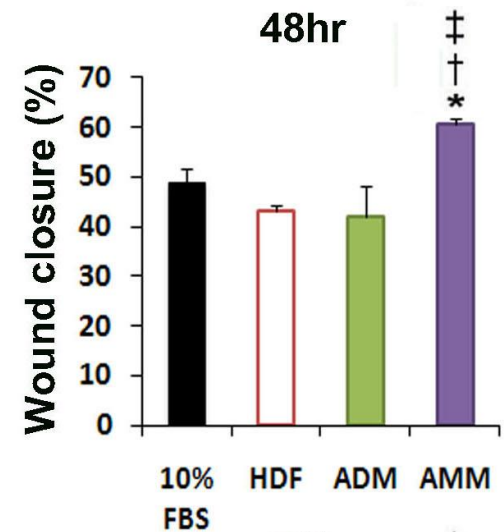
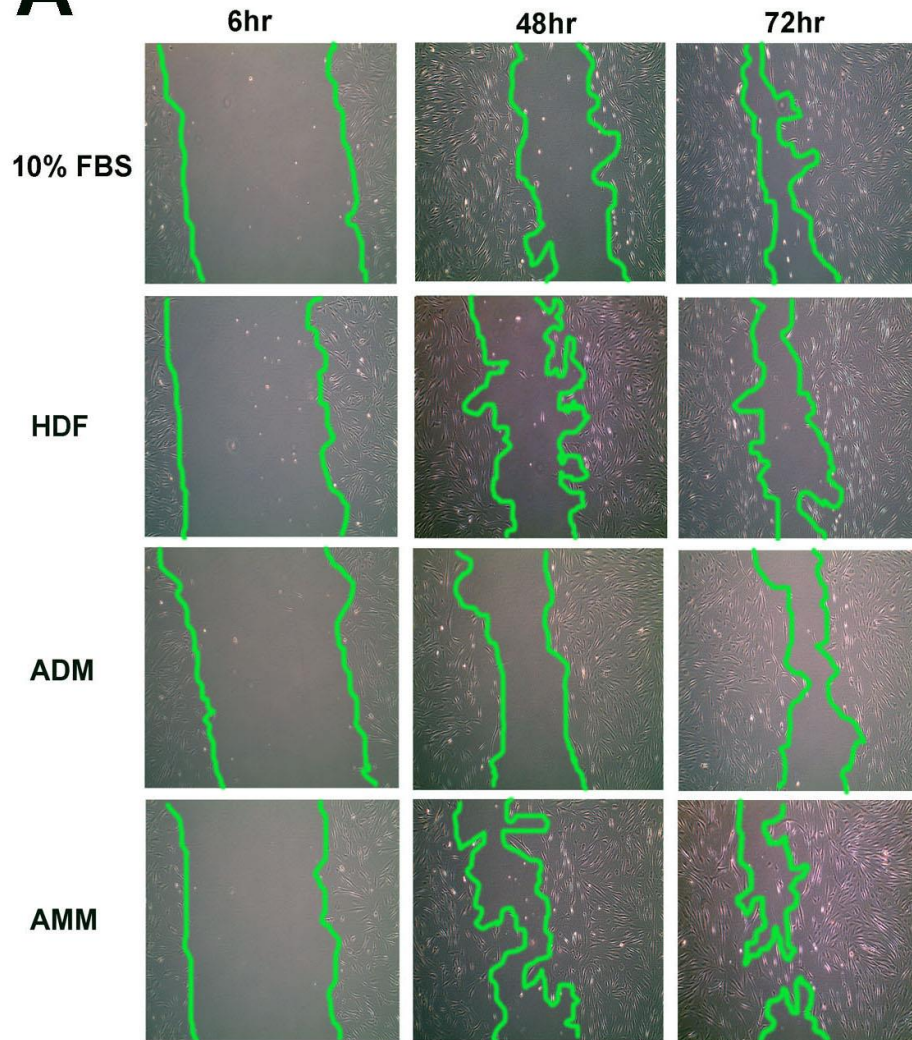
C



AMMs-CM significantly affect cell migration

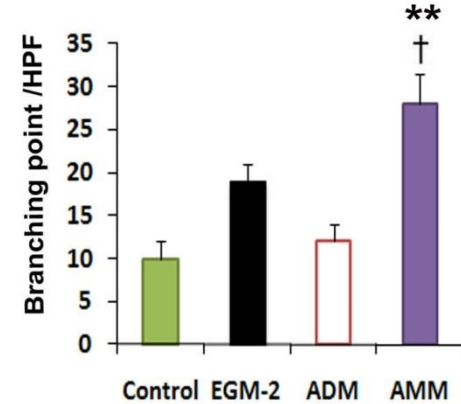
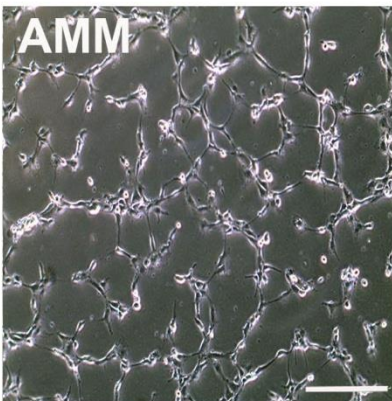
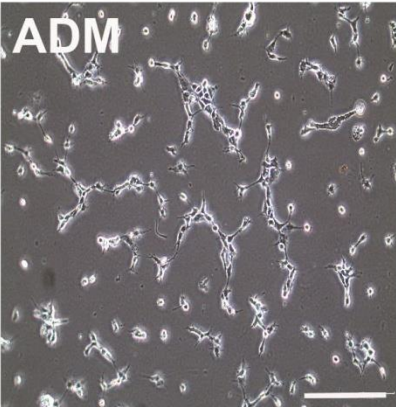
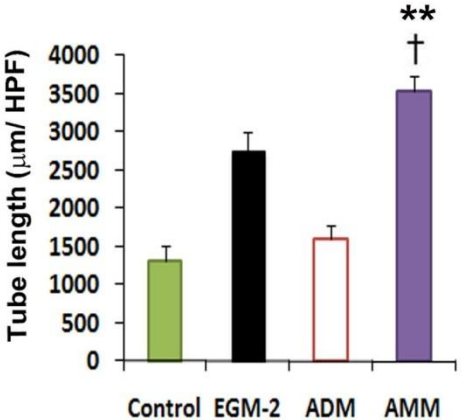
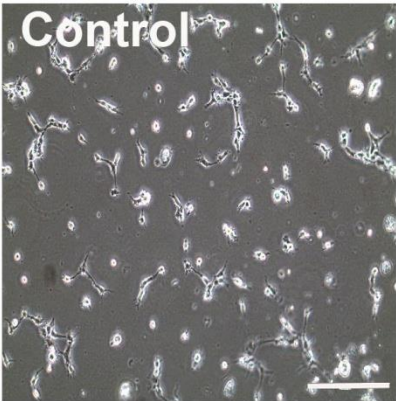
A

Fibroblast



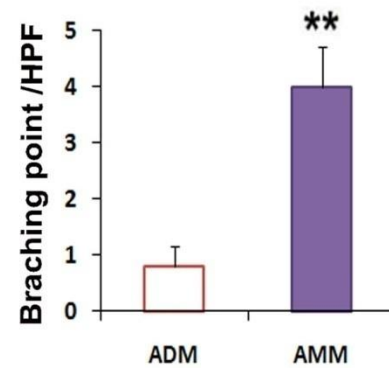
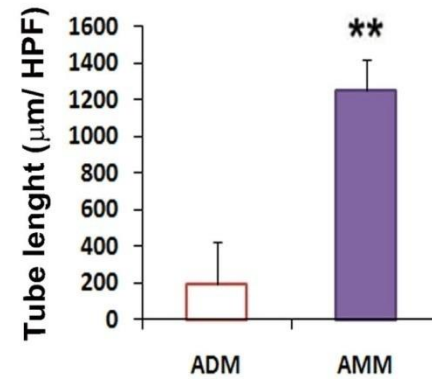
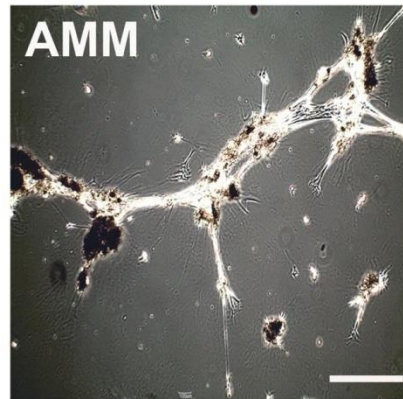
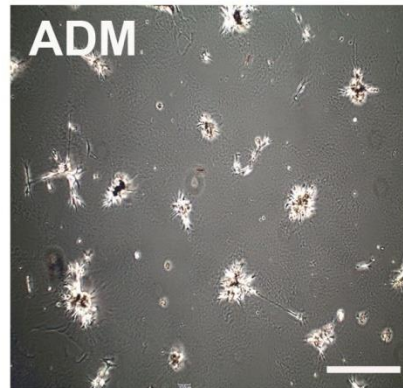
AMMs-CM significantly induced Matrigel tube

A



AMMs highly formed Matrigel tube

B



AMMs formed vascular-like structure *in vitro*

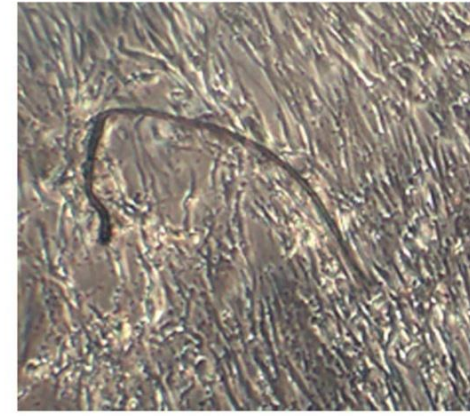
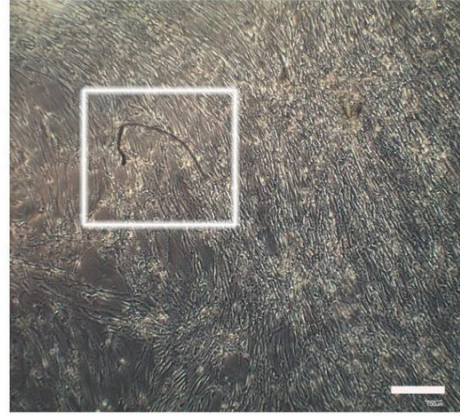
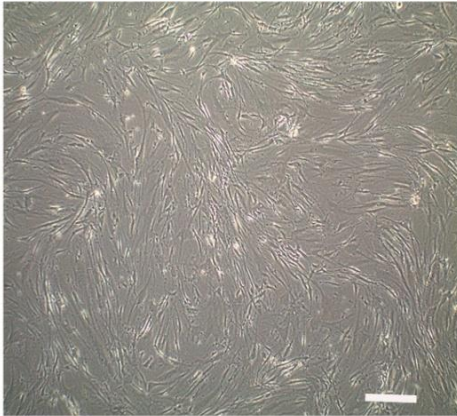
(Endothelial cell differentiation)

A

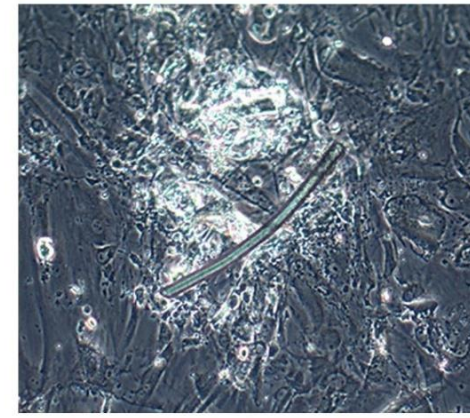
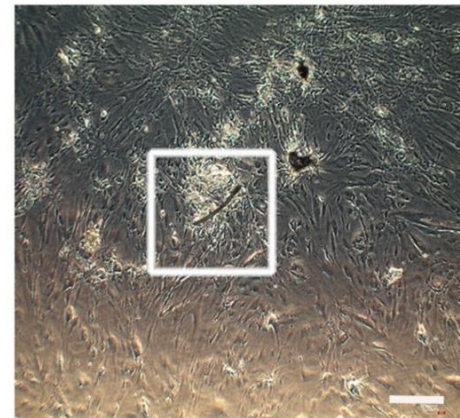
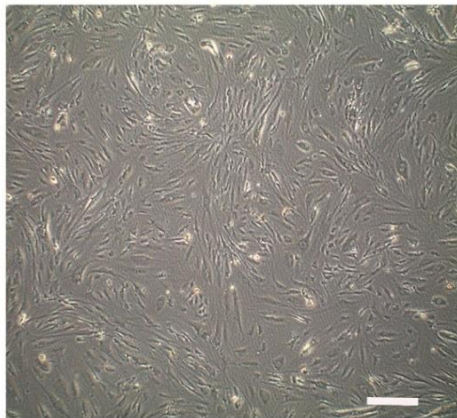
D0

D10

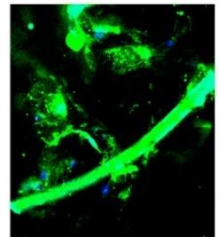
ADM



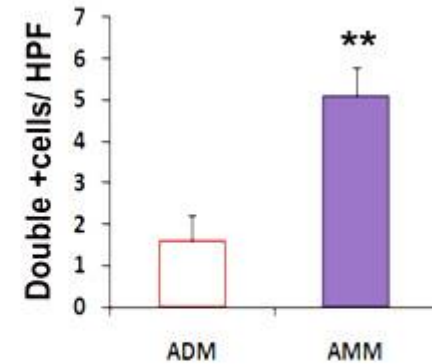
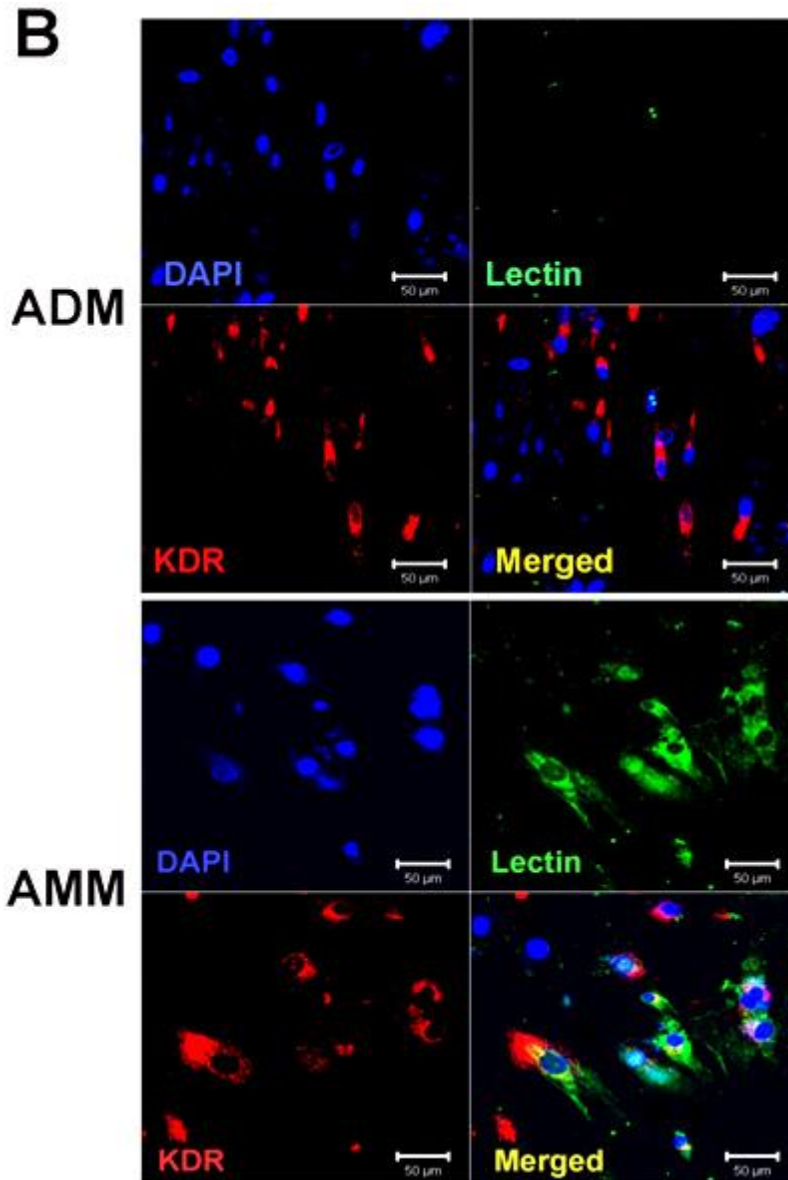
AMM



CD146
DAPI



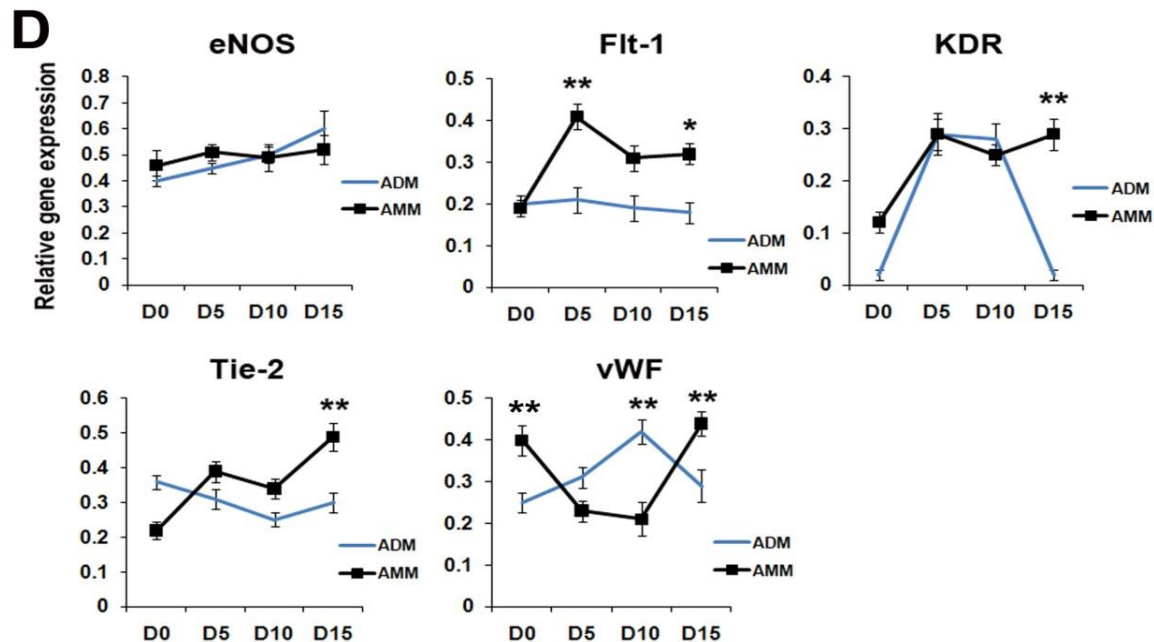
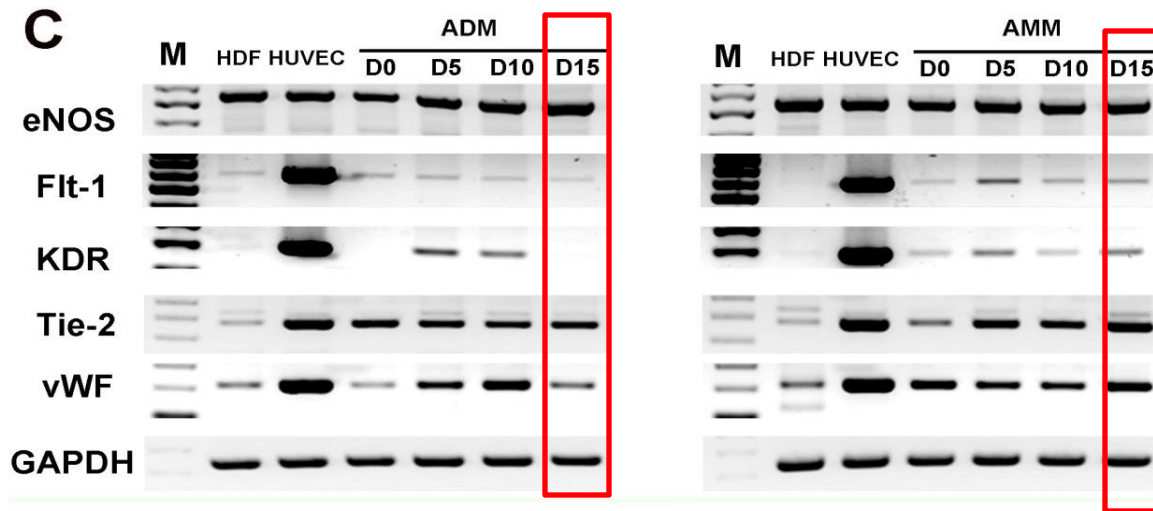
AMMs highly express endothelial protein *in vitro*



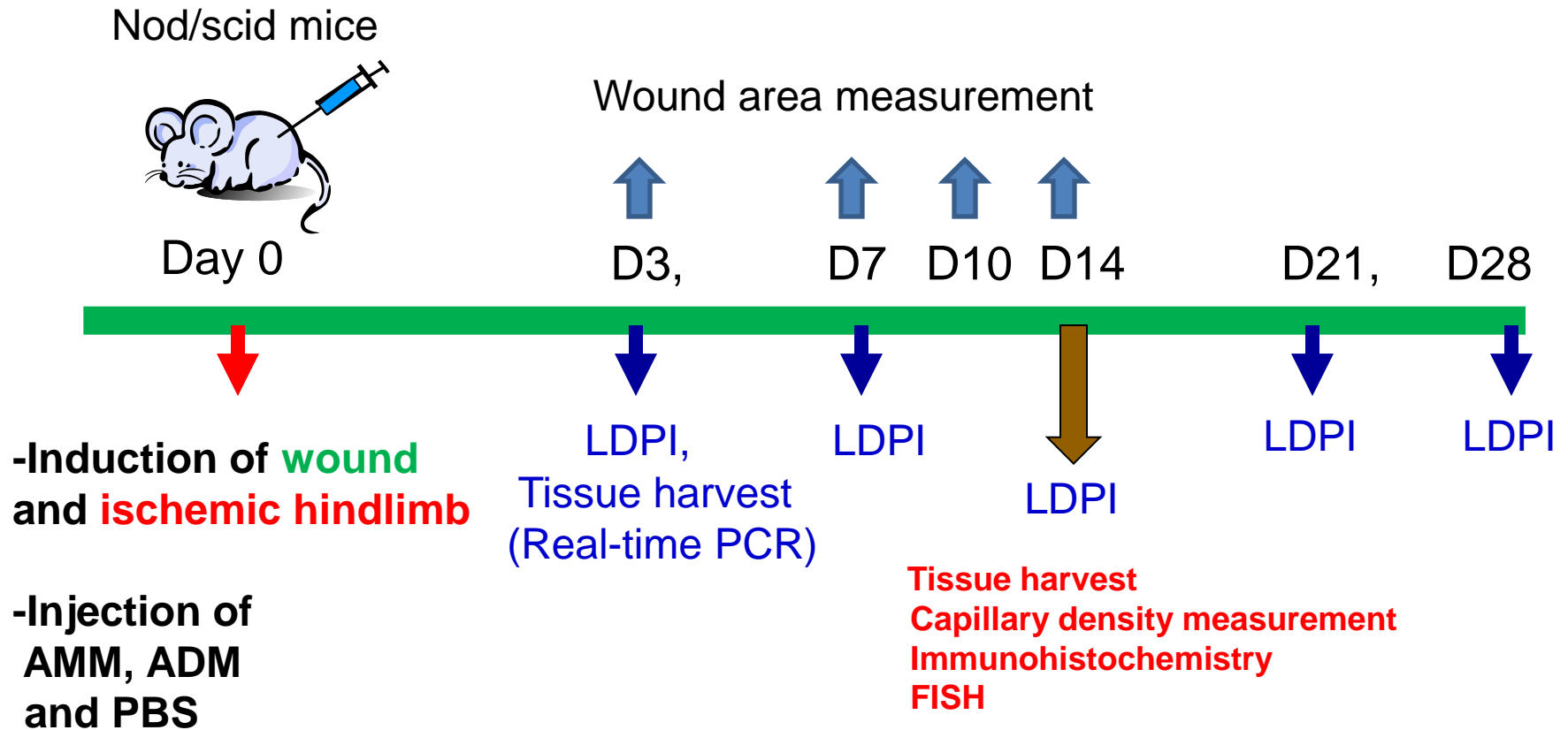
Endothelial cell differentiation
At Day 5

AMMs highly express endothelial genes *in vitro*

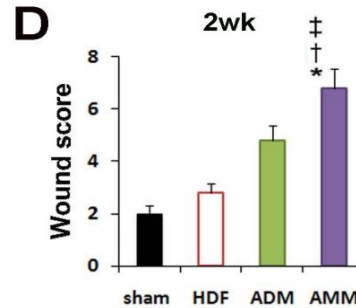
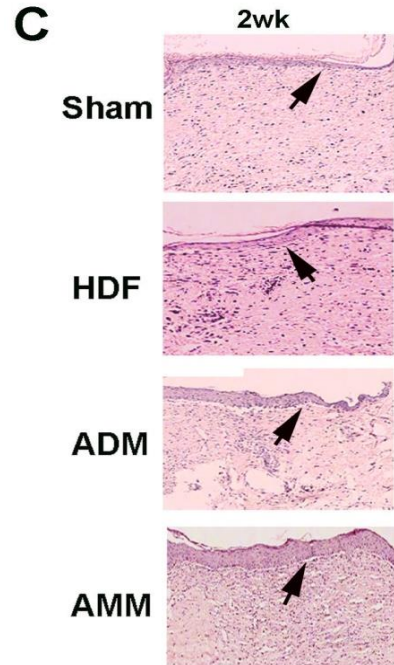
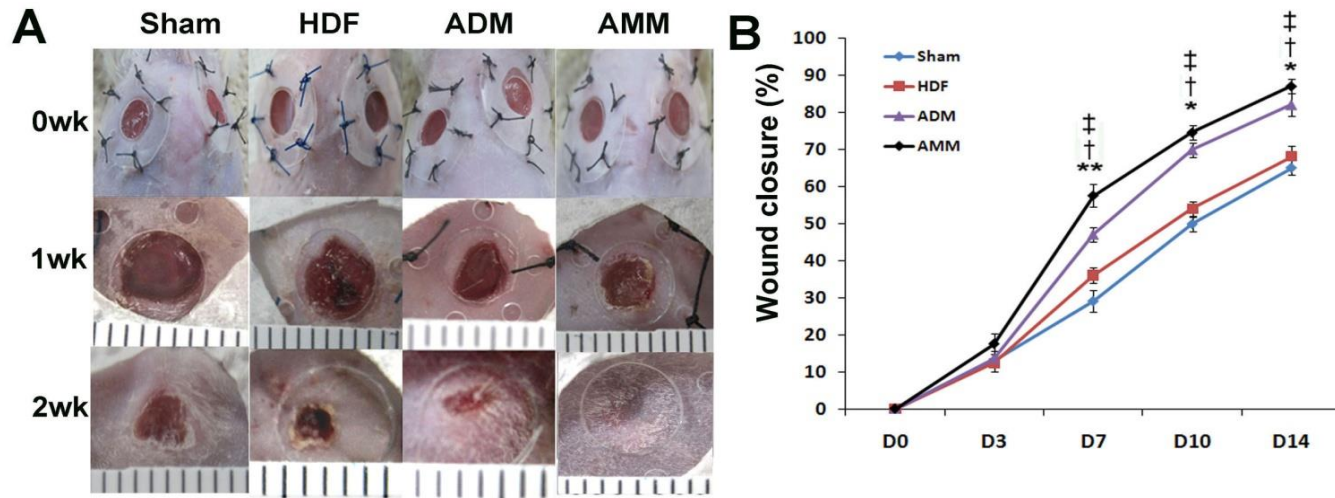
(Endothelial cell differentiation: RT-PCR)



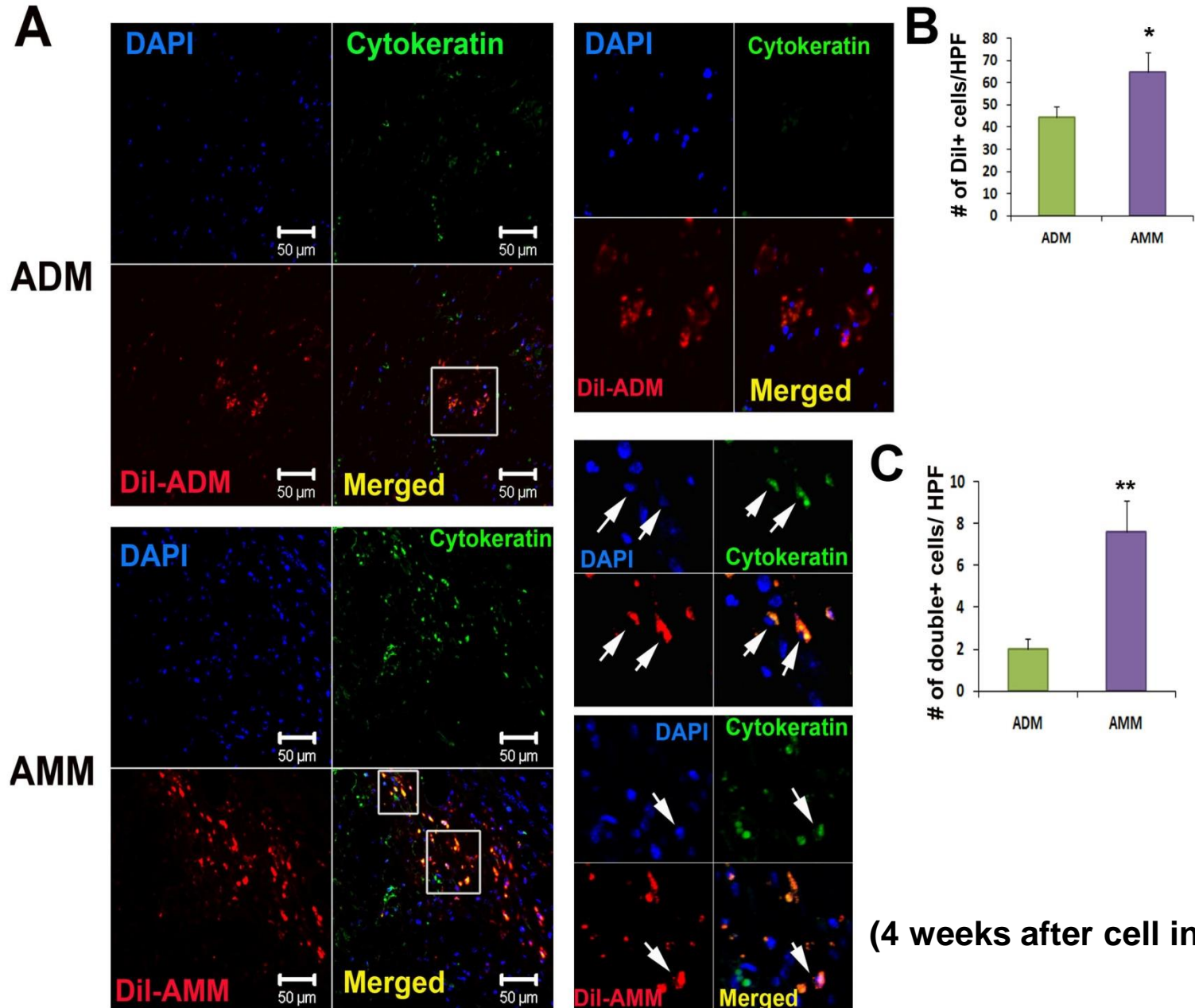
Study design (*in vivo*)



Transplantation of AMMs enhance wound healing and re-epithelialisation

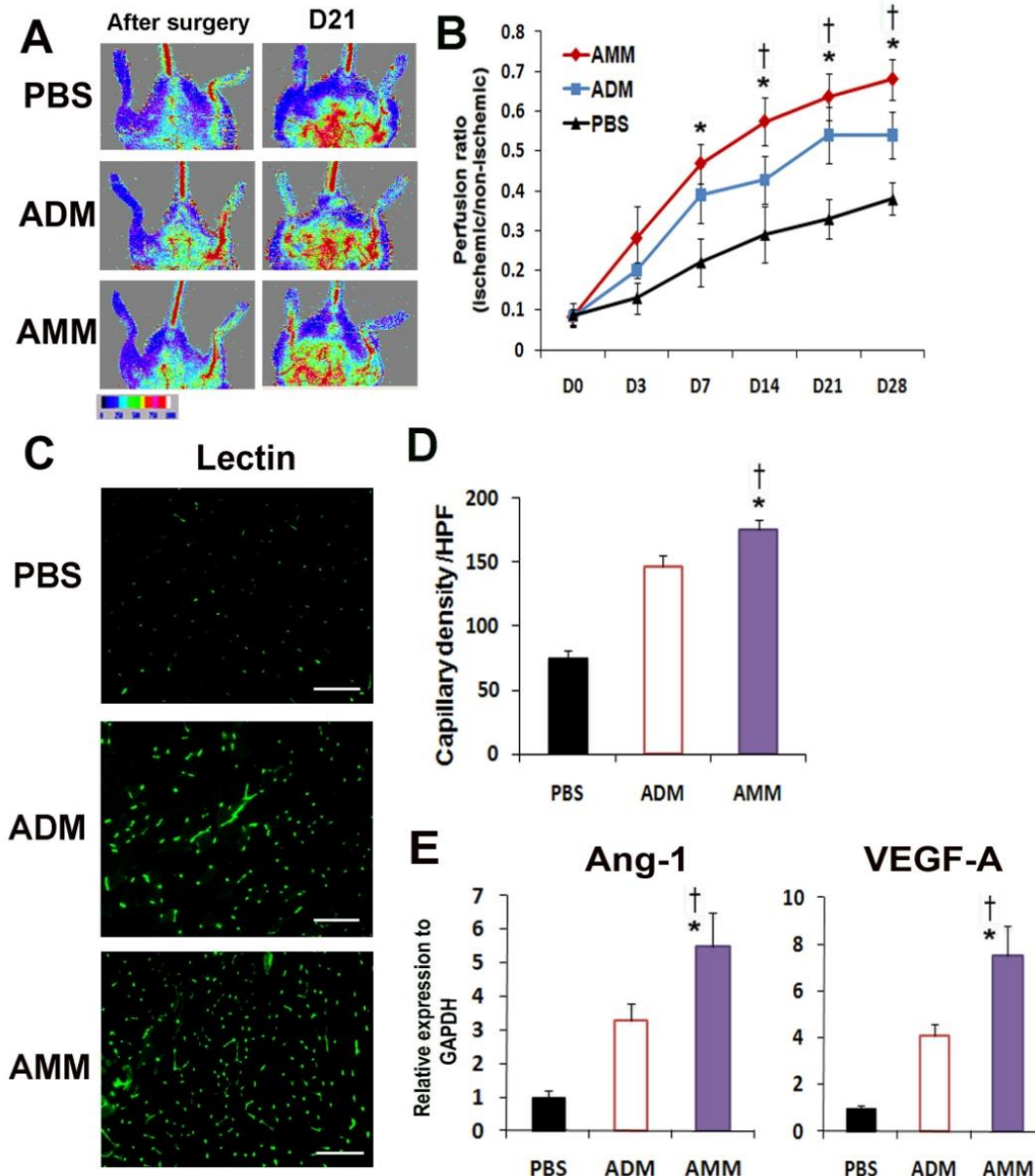


Increased AMM engraftment and differentiation in wound area

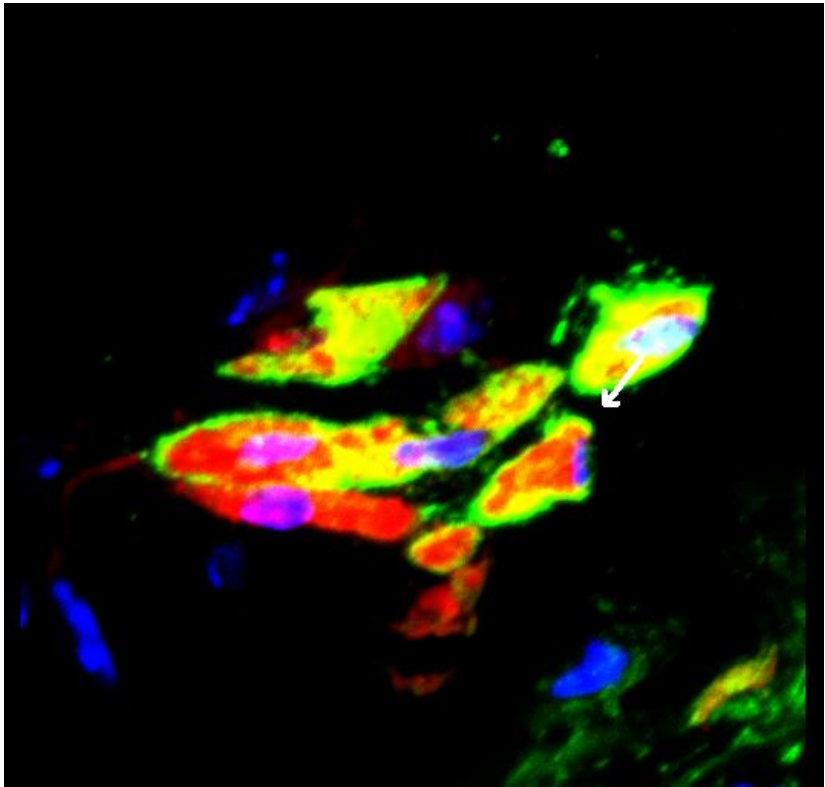
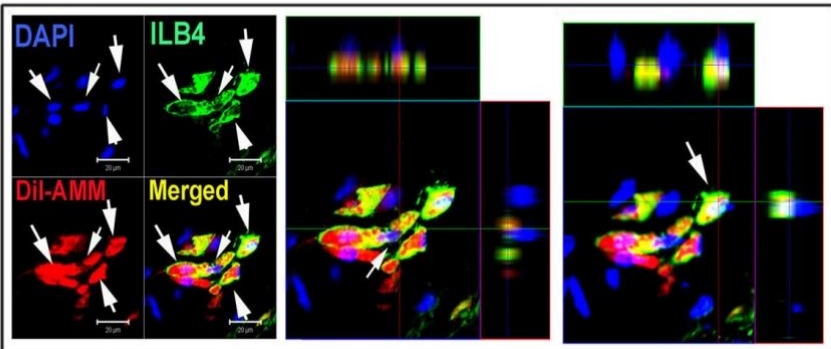
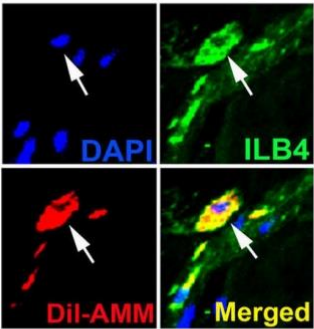
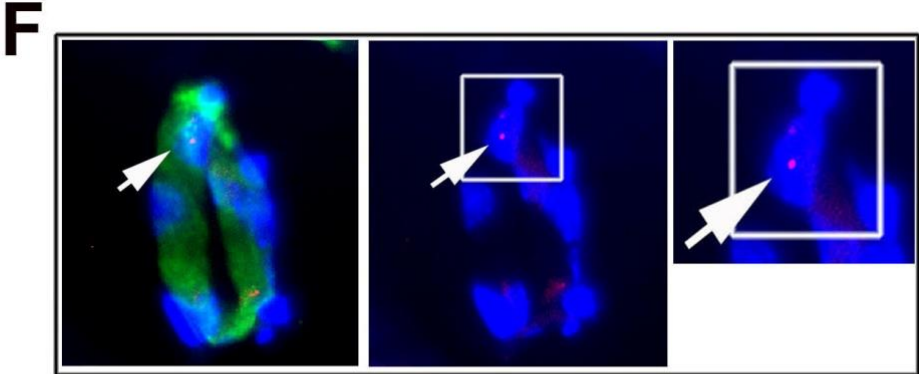
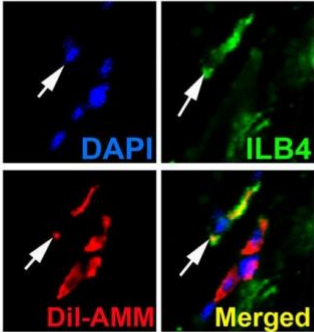
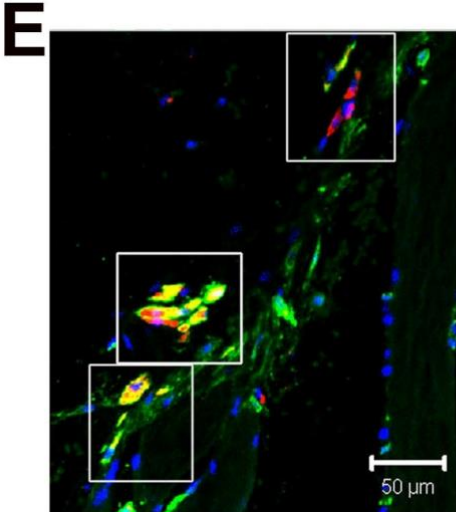


(4 weeks after cell injection)

Favourable therapeutic effects of AMMs in hind limb ischemia



Differentiation of AMM into endothelial cell in ischemic hindlimb



Summary

- **AMMs exhibited high angio-vasculogenic and anti-apoptotic properties.**
- **Transplantation of AMMs show enhanced therapeutic effects in wound and hindlimb ischemia.**

Conclusion

- **These data suggested that AMMs could be used as promising angio-vasculogenic stem cells for treating ischemic cardiovascular diseases.**

Acknowledgement

- **Dong-A Univ. Hospital , Dept. of Cardiology,
Regional Clinical Center**

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Hong-Zhe Zhang, MD

Chae-Eun Kim, MS

Long-Zhe Guo, MD

Thank you!