Regulation of Hypertension and Inflammation in Vascular Aging

2012. 4. 20.

김재룡
영남대학교 의과대학
생화학·분자생물학교실, 노인성혈관질환연구센터
1. Vascular changes with age
2. Hypertension & vascular aging
3. Inflammation in vascular aging
4. Role of PATZ1 in vascular aging
Thomas Sydenham (1624-1689)
A man is only as old as his arteries.

Sir William Osler
The principles and practice of medicine, 1898
Longevity is a vascular question.
Risk factors of cardiovascular disease

- Systolic BP
- Blood glucose
- Cholesterol
- Smoking
- Age
Function of central artery

- Conduit
- Cushion

O’Rourke and Hashimoto, JACC 2007:50:1-13
In extreme old age, the arteries themselves, the grand instruments of circulation, by the continual apposition of earth, become hard, and, as it were, bony, till, having lost the power of contracting themselves, they can no longer propel the blood, even through the largest channels; in consequence of which, death naturally ensues.
Arterial stiffness with age (PWV)

Carotid-femoral PWV

Boutouyrie et al, Art Res 2009:3:3
Arterial stiffness with age (Al)

Sakuragi and Abhayaratna, Int J Cardiol 2009
Arterial stiffness with age (FMD)

Flow mediated dilation

Intima-medial thickness of arterial wall

Size of arterial lumen with age

Central arterial lumen

## Vascular calcification

<table>
<thead>
<tr>
<th></th>
<th>Intimal Calcification</th>
<th>Medial Calcification</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Calcification pattern</strong></td>
<td>Atherosclerotic</td>
<td>Arteriosclerosis or Mönckeberg's sclerosis</td>
</tr>
<tr>
<td><strong>Schematic appearance</strong></td>
<td>![Intimal Calcification Image]</td>
<td>![Medial Calcification Image]</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td>Dyslipidemia, hypercholesterolemia, age, hypertension, diabetes, smoking</td>
<td>Aging, diabetes, renal failure, osteoporosis, hypertension</td>
</tr>
<tr>
<td><strong>Molecular mechanisms</strong></td>
<td>Lipid accumulation, foam cell accumulation, inflammatory cell infiltration, inflammation, oxidative stress, apoptosis</td>
<td>Transdifferentiation of endothelial cells or VSMCs into bone-like cells (osteoblast-chondrocyte and osteoclast-like cells); altered calcium, phosphate and Vitamin D metabolism; loss of calcification inhibitors (matrix Gla protein, pyrophosphate, fetuin)</td>
</tr>
<tr>
<td><strong>Consequences</strong></td>
<td>Plaque formation; luminal stenosis; plaque calcification; altered plaque stability</td>
<td>Arterial stiffening, increased pulse pressure, elevated pulse wave velocity</td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td>Ischemia, infarction</td>
<td>Systolic hypertension, left ventricular hypertrophy</td>
</tr>
</tbody>
</table>

*Kovacic et al, Circulation 2011;123:1900*
Calcification paradox
Multiple causes of arterial stiffness with age

Intima:
- ↑ Collagen, AGE’s, Mφ, Leukocytes, I-CAM, Calcification, MMPs, TGF-β, VSMCs

Media:
- ↑ VSMCs, Collagen, Amyloid β protein, MMPs, AGEs, Calcification, ↓ Elastin

Endothelium:
- Endothelial dysfunction, Increased permeability

Adventitia:
- ↑ Collagen, Fibroblasts

Extrinsic factors:
- NaCl, Lipids, Angiotensin, Sympathetic neurohormones, Shear stress, Increased luminal diameter

Circulation 2011;123:1900
Aging cardiovascular continuum

O’Rourke et al, Vascular Medicine 2010;15:461
CV atherosclerotic continuum

- Dzau et al
- Myocardial infarction
- Neurohormonal activation
- Coronary thrombosis
- Myocardial ischaemia
- CAD
- Atherosclerosis
- LVH

CV aging continuum

- Sudden cardiac death
- Myocardial ischaemia
- Impaired myocardial supply/demand
- LV Hypertrophy
- Isolated systolic hypertension
- Increased aortic impedance
- Increased & early reflection
- Aortic stiffening, dilatation
- Fracture of aortic elastic lamellae
- "pulse wave encephalopathy"
- "pulse wave nephropathy"

Remodelling

- Ventricular enlargement
- Microvascular disease thrombosis, haemorrhage
- Increased aortic impedance
- Increased & early reflection

CHF

- End-stage heart disease
- Interaction of the two continua
- End-stage renal disease
- Dementia

Risk factors
- Dyslipidaemia
- Hypertension
- Diabetes
- Smoking
- Obesity (visceral adiposity)

O'Rourke et al, Vascular Medicine 2010;15:461
Cell aging vs Tissue aging
Replicative senescence (Hayflick limit)

- Restricted cell proliferation of normal somatic cells

1928-
Cellular senescence

Tissue aging

Tumor formation
Telomere dysfunction/shortening
DNA damage
Oncogene/tumor suppressor gene activation
Oxidative stress
Inflammation
Chemotherapeutic agents
Telomere dysfunction/shortening
DNA damage
Oncogene/tumor suppressor gene activation
Oxidative stress
Inflammation
DNA scars, Heterochromatin foci
Senescence-associated β-galactosidase
Growth arrest
Senescence-associated secretory phenotype
Resistance to apoptosis
Flatten & enlarged cell morphology
p53/p21
Rb/p16
others
Others
Vascular Cell Senescence
Contribution to Atherosclerosis

Tohru Minamino, Issei Komuro
Mechanisms of age-related arterial changes

Impaired NO/cGMP

↑Apoptosis, Senescence

↑Oxidative stress

↑AGE

↑Inflammation

Mateos-Caceres et al, Int J Hypertension. 2012 150107
Additional mechanisms of age-related arterial changes

- Microparticles
- Telomere shortening
- Stem cells
- Epigenetics

Int J Hypertension. 2012 150107
Dysfunctional telomere & premature aging

**Legend:**
- **+/− Terc or Tert**
- **+/+**
- **+/-**
- **−/-**
- **G**

**Graphical Representation:**
- **Telomeres intact**
  - Post-mitotic tissues
    - No overt degenerative condition
  - Proliferative organs
    - Modest stem-cell dysfunction
  - Near-normal lifespan
- **Telomere loss and end fusions**
  - Post-mitotic tissues
    - Cardiomyopathy
    - Insulin resistance
  - Proliferative organs
    - Stem-cell dysfunction
    - Organ atrophy
    - Diminished stress response
    - Modest increase in cancer
  - Markedly decreased lifespan

**References:**
NATURE 2010;464 doi:10.1038/nature08982
Telomere length during human aging

- Telomere shortening with age: a surrogate marker for aging and cell senescence

Physiol Rev 88:557, 2008
Mice Deficient in Telomerase Activity Develop Hypertension Because of an Excess of Endothelin Production

Gema Pérez-Rivero, MS*; María P. Ruiz-Torres, PhD*; Juan V. Rivas-Elena, MS; Mirjana Jerkic, PhD; María L. Díez-Marques, PhD; José M. Lopez-Novoa, PhD; María A. Blasco, PhD; Diego Rodríguez-Puyol, MD

*(Circulation. 2006;114:309-317.)*
Telomere length, risk of coronary heart disease, and statin treatment in the West of Scotland Primary Prevention Study: a nested case-control study

Scott W Brouilette, Jasbir S Moore, Alex D McMahon, John R Thompson, Ian Ford, James Shepherd, Chris J Packard, Nilesh J Samani; for the West of Scotland Coronary Prevention Study Group

Lancet 2007;369:107
Short Telomeres and Prognosis of Hypertension in a Chinese Population

Zhiwei Yang, Xin Huang, Hong Jiang, Yanrong Zhang, Hongxia Liu, Chuan Qin, Gilbert M. Eisner, Pedro Jose, Lenhard Rudolph, Zhenyu Ju

(Hypertension. 2009;53:639-645.)
Telomere shortening in Framingham heart study

- Hypertension (Aging Cell 2007;5:14-21)
- Premature myocardial infarction (ATVB 2003;23:842)
- Renin-angiotensin-aldosterone systems (Circulation 2008;117:1138)
- Chronic heart failure (JACC 2007; 49:1459-1464)
- Intima-media thickening: no significance (ATVB 2008;28:1165)
Elizabeth Blackburn gave the first lecture at the 2011 Lindau meeting, describing her Nobel prizewinning work on telomeres. These chromosomal caps are known to play a role in cancer and are implicated in ageing — but their full biological utility remains a mystery.
### Changes of Inflammatory Parameters during Aging Process

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Inflammation</th>
<th>Aging</th>
<th>Calorie restriction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Redox state</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROS/RNS</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Catalase, Superoxide dismutase</td>
<td>↓</td>
<td>↓</td>
<td>R</td>
</tr>
<tr>
<td>GSH peroxidase, GSH/GSSG</td>
<td>↓</td>
<td>↓</td>
<td>R</td>
</tr>
<tr>
<td><strong>Proinflammatory enzymes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inducible NO Synthase</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Heme oxygenase-1</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Cyclooxygenase-2</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Xanthine Oxidase</td>
<td>↑</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td><strong>Proinflammatory cytokines</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL-1β</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>IL-6</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>TNF-α</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td><strong>Adhesion molecules</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-selectin</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>P-selectin</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>VCAM-1</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>ICAM-1</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td><strong>NF-κB activation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NF-κB DNA binding activity</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>NIK/IKK activation</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Phosphorylation of IκBα</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Degradation of IκB in cytoplasm</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Nuclear translocation of p65 and p50</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>NF-κB-dependent gene expression</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
<tr>
<td>Active MAPKs (ERK, JNK, p38 MAPK)</td>
<td>↑</td>
<td>↑</td>
<td>R</td>
</tr>
</tbody>
</table>

*Chung et al, Microsc Res Tech. 59:264, 2002*
Angiotensin II system

Wang et al, Hypertension 2007:50:219
Angiotensin II Induces Premature Senescence of Vascular Smooth Muscle Cells and Accelerates the Development of Atherosclerosis via a p21-Dependent Pathway

Takeshige Kunieda, MD, PhD*; Tohru Minamino, MD, PhD*; Jun-ichiro Nishi, MD; Kaoru Tateno, MD, PhD; Tomomi Oyama, MD, PhD; Taro Katsuno; Hideyuki Miyauchi, MD, PhD; Masayuki Orimo, MD; Sho Okada, MD; Masayuki Takamura, MD, PhD; Toshio Nagai, MD, PhD; Shuichi Kaneko, MD, PhD; Issei Komuro, MD, PhD

(Circulation. 2006;114:953-960.)
Endothelial Cell-Specific NF-κB Inhibition Protects Mice from Atherosclerosis

Cell Metabolism 2008;8:372

Ralph Gareus,1,5,7 Elena Kotsaki,2,5 Sofia Xanthoulea,3 Ingeborg van der Made,3 Marion J.J. Gijbels,3,4 Rozina Kardakaris,1 Apostolos Polykratis,1 George Kollias,2 Menno P.J. de Winther,3,6 and Manolis Pasparakis1,6,*
Senescence-Messaging Secretome (SMS) or Senescence-associated secretory phenotypes

Exploration of replicative senescence-associated genes in human dermal fibroblasts by cDNA microarray technology

In Kyung Yoon\textsuperscript{a}, Hyun Kyoung Kim\textsuperscript{a}, Yu Kyoung Kim\textsuperscript{a}, In-Hwan Song\textsuperscript{b}, Wankee Kim\textsuperscript{c}, Seongyong Kim\textsuperscript{a}, Suk-Hwan Baek\textsuperscript{a}, Jung Hye Kim\textsuperscript{a}, Jae-Ryong Kim\textsuperscript{a,*}
Inflammatory molecules in EC senescence


IGFBP3, IGFBP5

IFN-γ, α
(Mech Ageing Dev, 2008)

PLA2

PGE2
(Biogerontology, 2011)

p53

9 생약추출물, epifriedelanol
(JKSABC, 2010: Plant Med, 2010)
IGFBP-5 immunohistochemical staining in normal and atherosclerotic arteries.

0/30

6/25 (24%)

28/31 (90%)

# Intervention Tools of Vascular Aging

<table>
<thead>
<tr>
<th>Tools</th>
<th>Class</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life style changes</td>
<td>Calorie restriction</td>
<td>Obesity-related drugs, Smoking-cessation drugs, Antihypertensive drugs, Lipid-lowering drugs, Antidiabetic drugs, Antiplatelet agents</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dietary changes (low-salt diet, moderate alcohol consumption, garlic powder, (\alpha)-linoleic acid, dark chocolate, fish oil, etc)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Modifiable CV risk factors and classic drug targets</td>
<td></td>
</tr>
<tr>
<td>Pharmacol. treatments</td>
<td>Current alternatives to classic drugs, under evaluation</td>
<td>Sex hormones (estrogen) Advanced-glycation end product breakers Selective treatments for osteoporosis Farnesyltransferase inhibitors mTOR inhibitors (rapamycin)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Future alternatives to classic drugs</td>
<td>Telomerase activators Sirt1 activators (resveratrol)</td>
</tr>
</tbody>
</table>
POZ/BTB and AT-hook-containing zinc finger protein (PATZ1)

Cho JH et al, Cell Death Diff  2012

A

B

PATZ1
GAPDH

Y  O

Y  O

PATZ1
pATM
pRb
p53
p21
GAPDH
• Zinc finger protein 278 (ZNF278), MAZ-related factor, or zinc finger sarcoma gene (ZSG)
• A putative transcription regulator with 7 C₂H₂ type zinc fingers
• Important for normal male gametogenesis and testicular tumor
• 60 proteins in human genome
### Putative roles of POZ-ZF proteins

<table>
<thead>
<tr>
<th>Protein name</th>
<th>Repressor, activator or both?</th>
<th>Putative function(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLZF</td>
<td>Repressor</td>
<td>Limb development; gene regulation in APL</td>
</tr>
<tr>
<td>Bcl-6</td>
<td>Repressor</td>
<td>Plasma cell fate; germinal center formation; germ cell apoptosis; gene regulation in B cell lymphoma</td>
</tr>
<tr>
<td>FAZF</td>
<td>Repressor</td>
<td>T cell proliferation; cytokine production; hematopoietic stem cell proliferation</td>
</tr>
<tr>
<td>MIZ-1</td>
<td>Both</td>
<td>Gastrulation; cell cycle progression; regulator of Myc-mediated gene regulation</td>
</tr>
<tr>
<td>HIC-1</td>
<td>Repressor</td>
<td>Tumor suppressor; craniofacial development; DNA damage responses; inhibition of Wnt signaling</td>
</tr>
<tr>
<td>ZBTB7</td>
<td>Repressor</td>
<td>Proto-oncogene; regulator of oncogenesis; stimulator of HIV1 Tat activity</td>
</tr>
<tr>
<td>Kaiso</td>
<td>Both</td>
<td>Gastrulation; canonical and noncanonical Wnt signaling; regulator of synapse formation</td>
</tr>
<tr>
<td>BAZF</td>
<td>Repressor</td>
<td>Activation of naïve T cells</td>
</tr>
<tr>
<td>APM-1</td>
<td>Repressor</td>
<td>Possible tumor suppressor; cell growth inhibition; downregulated in cervical carcinoma cell lines</td>
</tr>
<tr>
<td>Nac-1</td>
<td>Repressor</td>
<td>Neuronal apoptosis; behavioral sensitization to cocaine; regulation of p53 levels? (Figure 2)</td>
</tr>
<tr>
<td>ZBTB38</td>
<td>Repressor</td>
<td>Expression in late postmitotic neurons; function unknown</td>
</tr>
<tr>
<td>ZBTB4</td>
<td>Repressor</td>
<td>Ubiquitous expression; function unknown</td>
</tr>
</tbody>
</table>
Effects of PATZ1 knockdown on EC senescence

Cho JH et al, Cell Death Diff  2012

A

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Y</th>
<th>NC</th>
<th>2</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PATZ1</strong></td>
<td>siPATZ1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GAPDH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B

Y

O

NC

siPATZ1
Effects of PATZ1 knockdown on EC senescence

Cho JH et al, Cell Death Diff 2012

Effects of PATZ1 knockdown on EC senescence
Effects of PATZ1 knockdown on EC senescence

Cho JH et al, Cell Death Diff 2012

**Fig. 2**

<table>
<thead>
<tr>
<th></th>
<th>4 days</th>
<th>6 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>siPATZ1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PATZ1</td>
<td>1.0</td>
<td>0.35</td>
</tr>
<tr>
<td>pATM</td>
<td>1.0</td>
<td>2.68</td>
</tr>
<tr>
<td>pRb</td>
<td>1.0</td>
<td>0.43</td>
</tr>
<tr>
<td>p53</td>
<td>1.0</td>
<td>1.30</td>
</tr>
<tr>
<td>p21</td>
<td>1.0</td>
<td>1.35</td>
</tr>
<tr>
<td>GAPDH</td>
<td>1.0</td>
<td>1.35</td>
</tr>
</tbody>
</table>

[Image of Western blots and fluorescence images showing DAPI and p-H2AX staining]
Effects of PATZ1 knockdown on EC senescence

Cho JH et al, Cell Death Diff 2012

**Fig. 2**

**H**

- **Y**
  - PATZ1 knockdown
  - Cell morphology
- **O**
- **NC**
- **siPATZ1**

**I**

- **PARP1**
  - Protein expression levels
- **Caspase 3**
- **GAPDH**

**Annexin-V staining (fold)**

- **NC**
- **siPATZ1**
- **Etoposide**

*Significant difference*
Effects of PATZ1 up-regulation on EC senescence

Cho JH et al, Cell Death Diff 2012
Effects of PATZ1 up-regulation on EC senescence

Cho JH et al, Cell Death Diff 2012
Effects of PATZ1 up-regulation on EC senescence

Cho JH et al, Cell Death Diff 2012

E

Cell population(%) vs G1/G0, S, G2/M

F

4 days 6 days

<table>
<thead>
<tr>
<th>Protein</th>
<th>V</th>
<th>PATZ1</th>
</tr>
</thead>
<tbody>
<tr>
<td>PATZ1</td>
<td>1.0</td>
<td>1.71</td>
</tr>
<tr>
<td>pRb</td>
<td>1.0</td>
<td>1.29</td>
</tr>
<tr>
<td>pATM</td>
<td>1.0</td>
<td>0.41</td>
</tr>
<tr>
<td>p53</td>
<td>1.0</td>
<td>0.63</td>
</tr>
<tr>
<td>p21</td>
<td>1.0</td>
<td>0.57</td>
</tr>
<tr>
<td>GAPDH</td>
<td>1.0</td>
<td>0.57</td>
</tr>
</tbody>
</table>

* Y: control, O: PATZ1

** V: control, V: PATZ1
p53 or p16 in PATZ1-mediated EC senescence

Cho JH et al, Cell Death Diff 2012

**Figure 4**

A

**RT-PCR**

<table>
<thead>
<tr>
<th></th>
<th>Y</th>
<th>O</th>
<th>p16sh</th>
<th>p53sh</th>
</tr>
</thead>
<tbody>
<tr>
<td>p53</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAPDH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**WB**

<table>
<thead>
<tr>
<th></th>
<th>Y</th>
<th>O</th>
<th>p53sh</th>
<th>p16sh</th>
</tr>
</thead>
<tbody>
<tr>
<td>p53</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p21</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p16</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PATZ1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAPDH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**B**

![Graph showing cell number over time](image)
**p53 or p16 in PATZ1-mediated EC senescence**

**Table C**

<table>
<thead>
<tr>
<th></th>
<th>p53sh</th>
<th>p53sh+siPATZ1</th>
<th>p16sh</th>
<th>p16sh+siPATZ1</th>
</tr>
</thead>
<tbody>
<tr>
<td>NC</td>
<td>1.0</td>
<td>0.55</td>
<td>1.0</td>
<td>0.47</td>
</tr>
<tr>
<td>siPATZ1</td>
<td>1.0</td>
<td>1.13</td>
<td>1.0</td>
<td>1.65</td>
</tr>
<tr>
<td>pRb</td>
<td>1.0</td>
<td>1.3</td>
<td>1.0</td>
<td>0.23</td>
</tr>
<tr>
<td>p53</td>
<td>1.0</td>
<td>0.7</td>
<td>1.0</td>
<td>1.94</td>
</tr>
<tr>
<td>GAPDH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure D**

Cho JH et al, Cell Death Diff 2012

*p53 or p16 in PATZ1-mediated EC senescence*
ROS involvement in PATZ1-mediated EC senescence

Cho JH et al, Cell Death Diff  2012
ROS involvement in PATZ1-mediated EC senescence

Cho JH et al, Cell Death Diff 2012
PATZ1 level in atherosclerotic tissues

Cho JH et al, Cell Death Diff 2012
PATZ1 level in young and old arteries

Young

CD34

PATZ1

CD34+PATZ1

Old

50 µm

50 µm
PATZ1 down-regulation accelerated EC senescence.

PATZ1 up-regulation reversed senescence phenotypes in ECs.

p53 knockdown inhibited PATZ1-mediated EC senescence.

PATZ1 immunoreactivity was decreased in endothelial cells of atherosclerotic tissues in LDLR-/- mice and old human arteries.
Acknowledgements

- Hallym University: Yong Sun Kim MD, PhD
- Yeungnam University, AVDRC
  - Suk-Hwan Baek PhD
  - ChuHee Lee PhD
  - Hwa-Young Kim PhD
  - Kwang-Seok Kim PhD
  - Jung Hee Cho MS
  - Hyo Hyun Yang
- Genomictree Inc.: Sung Hwan Ahn PhD
- Busan National University
  - Hae Young Chung PhD
감사합니다!
20세 젊은 혈관을 80세까지..