

Cellular and Molecular Pathophysiology of Idiopathic Pulmonary Arterial Hypertension

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서론

폐동맥 고혈압 (pulmonary hypertension)은 폐동맥의 벽에 여러 가지 변화가 일어나서 발생하는 질환이다. 폐동맥의 벽에 일어나는 변화는 (transmural pressure)가 증가하면, 폐동맥의 벽에 (internal elastic lamina)가 형성되고, (neointima)가 형성된다. 또한, 폐동맥의 벽에 (myofibroblast)가 증가하고, 폐동맥의 벽에 (vasa vasorum)가 형성된다. 폐동맥의 벽에 (neovascularization)가 일어나고, 폐동맥의 벽에 (adventitia)가 형성된다. 폐동맥의 벽에 (thrombosis)가 일어나고, 폐동맥의 벽에 (shear stress)가 증가한다.

1.

2.

2. 내피세포

세포성 변화

1. 평활근세포와 섬유모세포

평활근세포와 섬유모세포는 폐동맥의 벽에 (shear stress)가 증가하면, 폐동맥의 벽에 (plexiform)가 형성된다. 폐동맥의 벽에 (apoptosis)가 일어나고, 폐동맥의 벽에 (TGF- β re-Bax)가 형성된다.

(plexiform)
1,3

(shear stress),

가
(apoptosis) TGF- β re-Bax

3. 염증세포

monocrotaline

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HIV

5.

가

6-

F1 α

8.

9,

(proinflammatory cytokine) IL-1 IL-6가

가 가

RANTES fractalkine

가

6.

(NO synthase)가

가

10.

4. 혈소판과 혈전증

5

3'-5' (cyclic

7. (in situ throm- guanosine 3'-5' monophosphate, cGMP)

bosis) , , cGMP

가

11.

분자학적 기전

(vasoactive intestinal peptide, VIP)

12.

(NO) (prostaglandin I₂) VIP

(ET-1) 가

VIP가

VIP

VIP

12.

(: , ET-1).

2. 엔도셀린-1 (ET-1)

ET-1

1. 프로스타사이클린, 혈관작용펩티드와 일산화질소

가 /

3'-5' ET-1 가 13,

(cyclic adenosine 3'-5' monophosphate, cAMP) ET-1

10~30%²¹⁻²³ 가
 BMPR2
 가

3. 칼륨이온 통로
 (Kv) Kv 1.5
¹⁴, Kv 1.5 Kv 2.1
¹⁵ Kv 가
 Kv
 dexfenfluramine aminorex가 Kv 1.5
 Kv 2.1 가¹⁶ Kv
 가
 (NO)
 cGMP protein kinase G
 BKCA

4. 세로토닌
 가 ,
 amine [5-HT] ¹⁷ (5-hydroxytrypt-
 5-HT
 가 ¹⁸, 5-HT가

5. TGF-β superfamily
 TGF-β superfamily TGF-β 1-3, (bone
 morphogenetic proteins, BMPs), (activin)
^{19,20},
 BMP type-2 (BMPR2)
 (gene coding) (germline
 mutation) 가 60% ,
^{28,29}

10~30%²¹⁻²³ 가
 BMPR2
 가

BMP/TGF-β
 TGF-β , ALK-1 endoglin
 가 (hereditary hemor-
 rhagic telangiectasia) 가
^{24,25}

6. 혈관생성(angiogenesis)과 세포자멸사(apoptosis)
 (vascular endothelial growth factor,
 VEGF) VEGFR-1
 VEGFR-2
 (endothelial-cell-specific-angiogenic mitogen)
 VEGF
 VEGF가
 VEGF
 가 ^{3,26}
 (platelet derived growth factor,
 PDGF), (basic fibroblast growth
 factor, BFGF), (Epidermal growth factor,
 EGF)
 가

7. Proteolysis
 가
 (elastin)가
 (extracellular matrix)
 가
²⁷
 monocrotaline
 (elastase) 가 가
²⁷

결 론

가
가

가
cell-based therapy

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