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Nucleus

Pericyte

ECs

Angiogenesis
Destabilization of pericyte coverage

Pericyte recruitment
Mesenchymal cell differentiation
Mural cell proliferation and migration

Quiescent vessel
Vessel maturation / stability
Maintenance of pericyte coverage

TGFβ-Alk5
Smad2/3
Quiescent vessel

Vessel maturation / stability
Maintenance of pericyte coverage

TGFβ-Alk1
PDGFB-PDGFRβ
VEGFA enhances angiogenic potential

Ang2 - Tie2

VEGF-A
Ang1 - Tie2
Angiogenesis↑↑
Destabilization of pericyte coverage

VEGF and Ang2↑↑↑

VEGFA enhances angiogenic potential

Ang2 - Tie2

ECs

Pericyte recruitment↓
Mesenchymal cell differentiation
Mural cell proliferation and migration

Quiescent vessel
Excessive deposition of basement membrane molecules

Deposition of basement membrane molecules↑↑↑

PDGFRβ inactivation↑

Smad 1/5

Smad 2/3

TGFβ↑↑↑

VEF and Ang2↑↑↑

TGFβ - Alk5

TGFβ - Alk1

PDGFB - PDGFRβ

HB-EGF - EGFR

Ang1 - Tie2
**Hyperglycaemia**
- Polyol pathway
- AGEs

**Hyperinsulinaemia**
- ?

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**Pericyte dysfunction**
- PKC ↑
- ROS ↑ (or disruption)
- VEGF ↑
- Ang2 ↑
- TGFB ↑

**Pericyte phenotypical changes**
- cell size ↑
- contractile filaments ↓
- connexin-43 ↓

**Basement membrane thickening**
- fibronectin
- collagen IV

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**Impaired neovascularization**
- hypoxia induced
- proliferative
- disrupted

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**Pericyte loss**
-acellular capillaries
-capillary dilation
-vascular leakage

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**Pericyte apoptosis**
- NF-κB activation
- PDGFRβ ↓ by PKC, SHP1
- Immune system activation

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**Endothelial dysfunction**

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**Metabolic memory**

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