

AGE - RAGE

POLYOL
SORBITOL
PATHWAY

**HYPERGLYCEMIA
GLUCOTOXICITY**

DAG

Ang II

ROS

**PKC beta II isoform
PKC**

ROS

ROS

TGF-beta
CCN2:

Connective tissue growth factor

PAI-1

Impaired
fibrinolysis

CAMs
ICAM
inflammation

Signal Pathways

Kinases

Lipases

Prostanoids

VEGF
PKC

ET-1

eNOS Dec
Procontractive

Gene Expression

NF kappa B

ANP, cFOS

Inflammation

Collagen
Fn

Basement Membrane

**^ Permeability
Angiogenesis
Cell Turnover**