The urokinase receptor (uPAR) in vascular ageing: regulatory mechanisms and clinical perspectives

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Vascular smooth muscle cells (VSMC)-the main arterial wall cell population

Vascular aging

Differentiation/proliferation

Senescence/polyploidy

Atherosclerosis/restenosis

Aim of the study: To clarify the role of uPAR in vascular aging

uPAR regulates VSMC differentiation via myocardin

tPA induces internalization of uPAR and its translocation to the cell nucleus

In the nucleus uPAR interacts with myocardin - the main cofactor of SRF transcription factor regulating the expression of smooth muscle genes

Interaction with uPAR leads to proteasomal degradation of myocardin

Degradation of myocardin results in decreased expression of smooth muscle genes

uPAR is involved in regulation of VSMC senescence

Expression of uPAR in VSMC increases with age

Downregulation of uPAR expression (uPARsi) decreases age – associated senescence of VSMC

uPAR-dependent decrease of VSMC senescence is mediated by retinoblastoma protein and p53

Downregulation of uPAR expression decreases polyplidisation of senescent VSMC

uPAR modulates response to vascular injury

Vascular remodeling after injury is diminished in uPAR−/−mice in vivo model

Injury-induced VSMC de-differentiation in uPAR−/−mice is decreased

SEM image of microstructured organically modified ceramics (ORMOCER) substrate

VSMC cultivation on microstructured red substrate leads to cells re-differentiation and prevents nuclear translocation of uPAR

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