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## Targeting glycolysis in endothelial cells to prevent intraplaque neovascularization and atherogenesis in mice

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intraplaque neovascularization and atherogenesis in mice

**Paola Perrotta**



Targeting glycolysis in endothelial cells to prevent  
intraplaque neovascularization and atherogenesis in mice

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de graad van Doctor aan de Universiteit Leiden,  
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door

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geboren op 11 September 1986

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“Science knows no country, because knowledge belongs to humanity, and is the torch which illuminates the world”.

Louis Pasteur

**Cover Image:** Microscopic image of a vein graft with intraplaque neovessels

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**Abbreviations:**

AA: aortic arch

ApoE: apolipoprotein E

ATP: adenosine triphosphate

CA: carotid artery

CD31: cluster of differentiation 31

CPT1: carnitine palmitoyltransferase 1A

CHD: coronary heart disease

DCM : dichloromethane

DMSO: dimethylsulfoxide

EC: endothelial cell

EF: ejection fraction

ECM : extracellular matrix

FAO: fatty acid oxidation

FAS : fatty acid synthesis

Fbn: fibrillin

FDG: fluorodeoxyglucose

FGF: fibroblast growth factor receptor

FS: fractional shortening

F-1,6-P<sub>2</sub> : fructose -2,6-bisphosphate

F-6-P: fructose-6-phosphate

GAPDH: Glyceraldehyde-3-Phosphate Dehydrogenase

GLUT: Glucose transporter

HAEC: human aortic endothelial cell

HDL: high-density lipoprotein

HE: haematoxylin-eosin

HIF: hypoxian inducible factor

HK: Hexokinase

HMG-CoA: 3-hydroxy-3-methylglutaryl-coenzyme A

HUVEC: Human umbilical vein endothelial cell

ICAM-1: intercellular cell adhesion molecule

iDISCO: immunolabeling-enabled 3D Imaging of Solvent Cleared Organs

IL: interleukin  
iNOS: inducible nitric oxide synthase  
IP/PI: intra-plaque  
IVRT: isovolumic relaxation time  
i.p.: intraperitoneal  
i.v.: intravenous  
KLF2: Kruppel Like Factor 2  
 $\alpha$ -KG:  $\alpha$ -ketoglutaric acid  
LDH: lactate dehydrogenase  
LDL: low-density lipoprotein  
LDLR: LDL receptor  
LV: left ventricular  
LVID: left ventricular internal diameter  
MI: myocardial infarction  
MMP: matrix metalloproteinase  
NADH: nicotinamide adenine dinucleotide  
OOA: oxalacetate  
Ox: oxidized  
PAD: peripheral arterial disease  
PDGF: platelet-derived growth factor  
PET: positron emission tomography  
PFK-1: 6-phosphofructo-1 -kinase  
PFKFB3: 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 3  
PF: platelet factor  
PFPE: paraformaldehyde fixed paraffin embedded  
PGI: phosphoglucose isomerase  
Plgf: placenta growth factor  
PCSK9: Proprotein convertase subtilisin/kexin type 9  
PGK: phosphoglycerate kinase  
SMC: smooth muscle cell  
TCFA : thin cap fibroatheroma  
TGF- $\beta$ : transforming growth factor- $\beta$   
TIA: transient ischaemic attack

TNF- $\alpha$ : Tumor necrosis factor alfa

VCAM-1 : vascular cell adhesion molecule-1

VEGF: vascular endothelial growth factor

VEGFR : VEGF receptor

vWF: von Willebrand factor

WD : western-type diet

WT: wild type

3PO: 3-(3-pyridinyl)-1-(4-pyridinyl)-2-propen-1-one

3D: three dimensional

