## Deregulation of tumor angiogenesis and blockade of tumor growth in $PPAR\beta$ deficient mice

Sabine Müller-Brüsselbach, Martin Kömhoff, Markus Rieck, Wolfgang Meissner, Kerstin Kaddatz, Jürgen Adamkiewicz, Boris Keil, Klaus J. Klose, Roland Moll, Andrew D. Burdick, Jeffrey M. Peters and Rolf Müller

Supplemental Table I

**Table S1:** Microarray analysis of genes differentially expressed at in *Pparb*<sup>-/-</sup> versus *Pparb*<sup>+/+</sup> cells from matrigel plugs. Data have been deposited with the ArrayExpress Database (www.ebi.ac.uk/arrayexpress; accession number E-MEXP-983). Genes with potential functions in cell cycle control, signal transduction, protein modification or transcription are highlighted.

**A:** Genes expressed at **lower levels in Pparb**<sup>-/-</sup> versus **Pparb**<sup>+/+</sup> cells. The first column shows the signal ratio obtained for for **Pparb**<sup>+/+</sup> releative to **Pparb**<sup>-/-</sup> cells.

wt/null	Gene name	Symbol	Function
18.5	TIP30 / CC3 / HIV-1 TAT-interacting protein	Htatip2	Transcription factor, NADPH-binding
17.9	Clone ID: H3095E04	?	?
5.6	Enolase 1-alpha (non-neuron)	Eno1	Glycolytic enzyme
2.4	Proprotein convertase subtilisin/kexin type 5	Pcsk5	Processing of integrin-alpha subunits
2.3	SCY1-like 2 / CVAK104	Scyl2	Phosphorylation of adaptin in plasma membrane adapter AP2
2.3	Nidogen 1	Nid1	Basement membrane glycoprotein
2.2	Solute carrier family 40, member 1	Slc40a1	Iron transport
2.2	Lysyl oxidase-like 2	LoxI2	Cross-linking of collagen and elastin
2.2	Ubiquitin carboxy-terminal hydrolase L1	Uchl1	Cleavage of C-terminal adducts of ubiquitin to monomers
2.1	Pleiomorphic adenoma gene-like 1	Plagi1	Transcription factor; inhibitor of cell proliferation
2.1	Peptidyl arginine deiminase type IV	Padi4	Transcriptional regulation through histone H3 deimination
2.1	Ankyrin repeat and SOCS box-containing protein 4	Asb4	Suppressor of cytokine signaling through inhibition of JAK kinases
2.1	Cysteine dioxygenase 1, cytosolic	Cdo1	Cystein metabolism
2.1	*Fatty acid binding protein 4, adipocyte	Fabp4	Lipid metabolism
2.1	SUMO/sentrin specific peptidase 6	Senp6	Processing of SUMO1 and other ubiquitin-like molecules
2.1	DCP2 decapping enzyme homolog	Dcp2	mRNA decapping prior to degradation
2.0	Transcription elong. factor A (SII), 3 / TFIIS	Tcea3	Transcriptional elongation by RNA polymerase II
2.0	*Acyl-CoA dehydrogenase, long-chain	Acadl	Lipid metabolism
2.0	*Stearoyl-Coenzyme A desaturase 1	Scd1	Lipid metabolism
2.0	Lipocalin 2	Lcn2	Iron transport; modulator of inflammation
1.9	Secreted phosphoprotein / Osteopontin	Spp1	p53-induced cytokine; tumor suppressor; role in wound healing
1.9	Amine oxidase (flavin containing) domain 2	Aof2	Transcriptional regulation through histone H3 Lys4 demethylation

1.9	WNT1 inducible signaling pathway protein 1	Wisp1	Connective tissue growth factor
1.9	HIF prolyl hydroxylase / PHD3 / HIFPH3	Egln3	Negative regulator of hypoxia (HIF)-induced transcription
1.9	*Thrombospondin receptor / Fatty acid translocase	Cd36	Receptor for oxididized LDL, thrombospondins and collagen
1.9	Galactosidase, beta 1	Glb1	Lysosomal enzyme; senescence marker
1.9	Heme oxygenase (decycling) 1	Hmox1	Heme catabolism
1.9	Sorbin and SH3 domain containing 1	Sorbs1	Stimulation of adipocytes by insulin; adaptor at insulin receptor
1.9	Proteasome activator subunit 4	Psme4	Activation of proteasomal hydrolysis of peptides
1.8	Growth factor, erv-like / Augmenter of liver regener.	Gfer	Growth factor
1.8	Insulin-like growth factor binding protein 3	lgfbp3	Modulator of IGF activity; inhibitor of cell proliferation
2.7	Heparan sulfate 6-O-sulfotransferase 2	Hs6st2	Synthesis of heparan sulfates
1.8	Myosin, light polypeptide 9, regulatory	Myl9	Smooth muscle cell contraction
1.8	GalNAc transferase 10	Galnt10	Synthesis of mucin-type oligosaccharides
1.7	Thrombospondin-2	Thbs2	Inhibitor of EC proliferation and modulator of angiogenesis
1.7	O-acyltransferase domain containing 5	Grcc3f	Lipid metabolism
1.7	Ferritin light chain 1	Ftl	Iron storage
1.7	A disintegrin and metallopeptidase domain 8	Adam8	Role in cell adhesion
1.7	Cyclin-dependent kinase inhibitor 1C (p57)	Cdkn1c	Cell cycle inhibitor

<sup>\*</sup>known PPAR target genes: Fabp4 (Targett-Adams et al., 2005), Acadl (Harano et al., 2006), Scd1 (Miller and Ntambi, 1996), Cd36 (Tontonoz et al., 1998).

## **B:** Genes expressed at **higher levels in** *Pparb*<sup>-/-</sup> versus *Pparb*<sup>+/+</sup> cells. The first column shows the signal ratio obtained for *Pparb*<sup>-/-</sup> releative to *Pparb*<sup>+/+</sup> cells.

null/wt	Gene name	Symbol	Function
3.7	Laminin B1 subunit 1	Lamb1-1	Major component of the basal lamina
3.1	Erythroid differentiation regulator 1	Erdr1	unknown
3.0	DEAD-H box 6 / Oncogene RCK	Ddx6	RNA helicase, putative activator of cell proliferation
3.0	WD repeat and FYVE domain containing 3	Wdfy3	β-N-acetylglucosaminylglycopeptide β-1,4-galactosyltransferase activity
2.8	Coatomer protein complex, subunit zeta 1	Copz1	Protein transporter activity, intracellular protein transport
2.4	R3H domain 1 (binds single-stranded nucleic acids)	R3hdm	Single-stranded nucleic acid binding protein
2.4	Myocyte enhancer factor 2C	Mef2c	Myogenic basic helix-loop-helix transcription factor

2.3	MAD homolog 9 / SMAD9	Smad9	Signal transduction from BMP type 1 receptor
2.3	Gene regulated by estrogen in breast cancer protein	Greb1	Hormone-regulated inducer of cell proliferation
2.3	Growth differentiation factor 3	Gdf3	TGF-beta type ligand associated with undifferentiated cells
2.2	Solute carrier family 38, member 1	Slc38a1	Amino acid transporter
2.1	Oxidative-stress responsive 1	Oxsr1	Protein kinase
2.1	O-linked acetylglucosamine transferase	Ogt	Protein glycosylation
2.0	Carboxypeptidase E	Сре	Processing of prohormone intermediates
2.0	Calmodulin-like 4	Calml4	Calcium ion binding
1.9	G protein-coupled receptor 178 ?? Dynein light chain	Tctex1	Major microtubular motor protein
1.9	Apolipoprotein B editing complex 1	Apobec1	Switching of apoB-100 to apoB-48 mRNA
1.8	SH3-domain GRB2-like 3 / Endophilin A3	Sh3gl3	Protein interactions (Mta1)
1.8	ATPase, Ca++ transporting, plasma membrane 1	Atp2b1	ATPase activity, coupled to transmembrane movement of calcium ions
1.8	FXYD domain-containing ion transport regulator 6	Fxyd6	Ion channel activity
1.8	Copine family member IX	Cpne9	Calcium-dependent binding of phospholipids
1.8	SAM and SH3 domain containing 1	Sash1	Putative adapter and scaffold protein 1
1.7	Carboxypeptidase A3, mast cell	Cpa3	Carboxypeptidase A activity, metallopeptidase activity
1.7	Transcription factor 12	Tcf12	Regulation of polymerase II transcription, interacts with Th1
1.7	Deubiquitinating enzyme 2a	Dub2a	Ubiquitin-specific protease activity
1.7	Leucine-rich repeats & immunoglobulin-like domains 1	Lrig1	Transferase activity

## References

- Harano, Y., Yasui, K., Toyama, T., Nakajima, T., Mitsuyoshi, H., Mimani, M., Hirasawa, T., Itoh, Y. and Okanoue, T. (2006) Fenofibrate, a peroxisome proliferator-activated receptor alpha agonist, reduces hepatic steatosis and lipid peroxidation in fatty liver Shionogi mice with hereditary fatty liver. *Liver Int*, **26**, 613-620.
- Miller, C.W. and Ntambi, J.M. (1996) Peroxisome proliferators induce mouse liver stearoyl-CoA desaturase 1 gene expression. Proc Natl Acad Sci U S A, 93, 9443-9448.
- Targett-Adams, P., McElwee, M.J., Ehrenborg, E., Gustafsson, M.C., Palmer, C.N. and McLauchlan, J. (2005) A PPAR response element regulates transcription of the gene for human adipose differentiation-related protein. *Biochim Biophys Acta*, **1728**, 95-104.
- Tontonoz, P., Nagy, L., Alvarez, J.G., Thomazy, V.A. and Evans, R.M. (1998) PPARgamma promotes monocyte/macrophage differentiation and uptake of oxidized LDL. *Cell*, **93**, 241-252.