

Angiopoietin-like Proteins

[ANGPTLs]

highlight

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International Version

CONTENTS	
Introduction	1, 4
MFAP4	1
Product Overview	2-3
ANGPTL7	4
Latest Insights	4

Introduction

Seven proteins have been identified to contain a coiled-coil domain and a fibrinogen-like domain similar to those found in angiopoietins [1-8], and are therefore designated angiopoietin-like proteins (ANGPTLs, or angiopoietin-related proteins) 1-7 (Figure). Although none of these proteins bind the angiopoietin receptors, most members show angiogenic effects on the vasculature. More recently, ANGPTL-family members have been found to be regulators of metabolism.

The N-terminal coiled-coil domains of ANGPTL3 and ANGPTL4 are crucial for the inhibition of LPL by transforming LPL from an active dimer into catalytically inactive monomers [18, 19]. The expression of ANGPTL4 is induced by fasting [13, 20]. The effect of ANGPTL6 (angiopoietin-related growth factor (AGF)) on metabolism has been revealed by studying ANGPTL6-deficient mice [21]. Surviving mice developed marked obesity, lipid metabolic disorders, and insulin resistance accompanied by reduced energy expenditure [21]. In contrast, transgenic ANGPTL6-mice are lean and more insulin-sensitive despite their normal energy intake and serum leptin levels [21].

Metabolism

At least three ANGPTLs show pronounced effects on energy metabolism. The importance of ANGPTL3 for lipid metabolism was first indicated by the genetic analysis of a mutant strain of obese mice with low plasma lipid levels [9]. Administration of recombinant ANGPTL3 (angiopoietin-5) to ANGPTL3-deficient mice as well as wild type mice increased the plasma levels of non-esterified fatty acid (NEFA), triacylglycerol (TG) and cholesterol [9]. ANGPTL3 decreases very-low-density-lipoprotein (VLDL)-TG clearance by inhibiting lipoprotein lipase (LPL) [10], but has also been shown to activate lipolysis upon direct binding to adipocytes [11]. Like ANGPTL3, ANGPTL4 (hepatic fibrinogen/angiopoietin-related protein (HFARP)) [6]; peroxisome proliferator-activated receptor γ angiopoietin-related gene (PGAR) [12]; fasting-induced adipose factor (FIAF) [13]) has been found to inhibit lipoprotein lipase (LPL) and decrease plasma trigly-

Angiogenesis

ANGPTL3 stimulates adhesion and migration of endothelial cells as well induces blood vessel formation [7]. ANGPTL4 showed a proangiogenic response in chicken chorioallantoic membrane assays [8], protects endothelial cells from apoptosis [6], and inhibits VEGF-induced vascular leakiness and neoangiogenesis [4]. Another recent study demonstrated the potential of ANGPTL4 to prevent metastasis by inhibiting vascular activity as well as tumor cell motility and invasiveness [22]. ANGPTL6 promotes angiogenesis [5, 23]. Initially, ANGPTL1 and ANGPTL2 have been reported to exhibit significant but weak endothelial cell-sprouting activities *in vitro* [2, 3]. Later,

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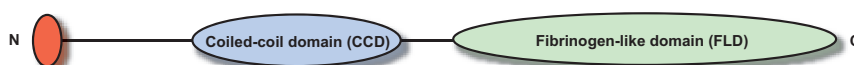


FIGURE: Structure of angiopoietin-like proteins, consisting of a signal sequence (red), a coiled-coil (CCD) and fibrinogen-like (FLD) domain.

NEW

Product Highlight

MFAP4

Ex vivo expansion of hematopoietic stem cells

ANGPTL2, ANGPTL3, ANGPTL5 and ANGPTL7 have recently been shown to stimulate the *ex vivo* expansion of hematopoietic stem cells. The same report showed that the microfibril-associated glycoprotein 4 (MFAP4), which exhibits sequence similarity to ANGPTLs, also possesses such *ex vivo* expansion activity.

lit: Angiopoietin-like proteins stimulate *ex vivo* expansion of hematopoietic stem cells: C. C. Zhang, et al.; Nat. Med. 12, 240 (2006)

MFAP4 (human) (rec.)

[Microfibril-associated Glycoprotein 4 (human) (rec.)]

ALX-201-381-C010 10 μ g

ALX-201-381-C050 50 μ g

Produced in HEK 293 cells. Mature human MFAP4 (microfibril-associated glycoprotein 4) (aa 1-255) is fused at the C-terminus to a FLAG[®]-tag.

Angiopoietin-like Proteins [ANGPTLs] – Products

Proteins

Prod. Name	Source/Host	Prod. No.	Size
ANGPTL1 (Fibrinogen-like Domain) (human) (rec.)	Produced in HEK293 cells. Fibrinogen-like domain of human ANGPTL1 (aa 197-491) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-387-C010 ALX-201-387-C050	10 µg 50 µg
ANGPTL2 (Coiled-coil Domain) (human) (rec.)	Produced in HEK293 cells. Coiled-coil domain of human ANGPTL2 (aa 23-248) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-396-C010 ALX-201-396-C050	10 µg 50 µg
ANGPTL2 (Fibrinogen-like Domain) (human) (rec.)	Produced in HEK293 cells. Fibrinogen-like domain of human ANGPTL2 (aa 245-493) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-392-C010 ALX-201-392-C050	10 µg 50 µg
ANGPTL3 (human) (rec.)	Produced in HEK293 cells. Human ANGPTL3 (aa 1-460) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-359-C010 ALX-201-359-C050	10 µg 50 µg
ANGPTL3 (Coiled-coil Domain) (human) (rec.)	Produced in HEK293 cells. Coiled-coil domain of human ANGPTL3 (aa 1-222) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-378-C010 ALX-201-378-C050	10 µg 50 µg
ANGPTL3 (Fibrinogen-like Domain) (human) (rec.)	Produced in HEK293 cells. Fibrinogen-like domain of human ANGPTL3 (aa 224-460) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-380-C010 ALX-201-380-C050	10 µg 50 µg
ANGPTL3 (mouse) (rec.)	Produced in HEK293 cells. Mature human ANGPTL3 (aa 17-455) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-391-C010 ALX-201-391-C050	10 µg 50 µg
ANGPTL4 (human) (rec.)	Produced in HEK293 cells. Mature human ANGPTL4 (aa 26-406) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-338-C010 ALX-201-338-C050	10 µg 50 µg
ANGPTL4 (Coiled-coil Domain) (human) (rec.)	Produced in HEK293 cells. Signal peptide and coiled-coil domain of human ANGPTL4 (aa 1-161) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-373-C010 ALX-201-373-C050	10 µg 50 µg
ANGPTL4 (Fibrinogen-like Domain) (human) (rec.)	Produced in HEK293 cells. Fibrinogen-like domain of human ANGPTL4 (aa 166-406) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-379-C010 ALX-201-379-C050	10 µg 50 µg
ANGPTL4 (mouse) (rec.)	Produced in COS-7 cells. Mouse ANGPTL4 (aa 1-410) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-384-C010 ALX-201-384-C050	10 µg 50 µg
ANGPTL5 (Coiled-coil Domain) (human) (rec.)	Produced in HEK293 cells. Signal peptide and coiled-coil domain of human ANGPTL5 (aa 1-130) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-385-C010 ALX-201-385-C050	10 µg 50 µg
ANGPTL5 (Fibrinogen-like Domain) (human) (rec.)	Produced in HEK293 cells. Fibrinogen-like domain of human ANGPTL5 (aa 146-388) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-393-C010 ALX-201-393-C050	10 µg 50 µg
ANGPTL6 (human) (rec.)	Produced in HEK293 cells. Mature human ANGPTL6 (aa 21-470) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-337-C010 ALX-201-337-C050	10 µg 50 µg
ANGPTL6 (Fibrinogen-like Domain) (human) (rec.)	Produced in HEK293 cells. Fibrinogen-like domain of human ANGPTL6 (aa 231-470) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-394-C010 ALX-201-394-C050	10 µg 50 µg
ANGPTL7 (human) (rec.)	Produced in HEK293 cells. human ANGPTL7 (aa 1-346) is fused at the C-terminus to a FLAG [®] -tag.	ALX-201-368-C010 ALX-201-368-C050	10 µg 50 µg
ANGPTL7 (Fibrinogen-like Domain) (human) (rec.)	Produced in HEK293 cells. Fibrinogen-like domain of human ANGPTL6 (aa 126-346) is fused at the N-terminus to a FLAG [®] -tag.	ALX-201-395-C010 ALX-201-395-C050	10 µg 50 µg

MAbs

Prod. Name	Isotype	Specificity	Immunogen	Application	Prod. No.	Size
MAb to ANGPTL3 (human) Clone: Kairos-37	Mouse IgG1	Recognizes human ANGPTL3. Does not cross-react with other ANGPTL family proteins.	Recombinant human ANGPTL3.	ELISA, WB	ALX-804-724-C050 ALX-804-724-C100	50 µg 100 µg
MAb to ANGPTL3 (human) Clone: 1D10	Mouse IgG1	Recognizes human ANGPTL3. Detects bands of ~64kDa (full-length) and ~36kDa (cleaved ANGPTL3) by Western blot.	Recombinant human ANGPTL3 (aa 243-460).	ELISA, WB	ALX-804-635-R050 ALX-804-635-R100	50 µl 100 µl
<p>lit: Angiopoietin-like protein 3 mediates hypertriglyceridemia induced by the liver X receptor. T. Inaba, et al.; J. Biol. Chem. 278, 21344 (2003) ▪ Protein region important for regulation of lipid metabolism in angiopoietin-like 3 (ANGPTL3); ANGPTL3 is cleaved and activated in vivo: M. Ono, et al.; J. Biol. Chem. 278, 41/804 (2003)</p>						
MAb to ANGPTL4 (Fibrinogen-like Domain) (human) Clone: Kairos-1	Mouse IgG1	Recognizes the fibrinogen-like domain (FLD) of human ANGPTL4. Does not cross-react with other ANGPTL family proteins.	Recombinant human ANGPTL4.	ELISA, IHC (PS), WB	ALX-804-723-C050 ALX-804-723-C100	50 µg 100 µg
MAb to ANGPTL6 (human) Clone: Kairos-60	Mouse IgM	Recognizes human ANGPTL6. Does not cross-react with other ANGPTL family proteins.	Recombinant human ANGPTL6.	ELISA, WB	ALX-804-725-C050 ALX-804-725-C100	50 µg 100 µg

Angiopoietin-like Proteins [ANGPTLs] – Products

PABs

Prod. Name	Source/Host	Specificity	Immunogen	Application	Prod. No.	Size
PAb to ANGPTL3 (human)	From rabbit	Recognizes human ANGPTL3. Does not cross-react with human ANGPTL4 or ANGPTL6.	Recombinant human ANGPTL3.	ELISA, WB	ALX-210-448-C100	100 µg
PAb to ANGPTL3 (human)	From rabbit	Recognizes human ANGPTL3. Does not cross-react with other ANGPTL family proteins.	Synthetic peptide corresponding to aa 194-213 (S ¹⁹⁴ QIKEIENQLRRT-SIQEPT ²¹³) of human ANGPTL3.	ELISA, WB	ALX-210-455-C100	100 µg
PAb to ANGPTL3 (Coiled-coil Domain) (human)	From rabbit	Recognizes the coiled-coil domain of human ANGPTL3.	Coiled-coil domain of recombinant human ANGPTL3.	ELISA, WB	ALX-210-463-C100	100 µg
PAb to ANGPTL3 (Fibrinogen-like Domain) (human)	From rabbit	Recognizes the fibrinogen-like domain of human ANGPTL3.	Fibrinogen-like domain of recombinant human ANGPTL3.	ELISA, WB	ALX-210-468-C100	100 µg
PAb to ANGPTL4 (human)	From rabbit	Recognizes human ANGPTL4.	Recombinant human ANGPTL4.	ELISA, WB	ALX-210-439-C100	100 µg
PAb to ANGPTL4 (Coiled-coil Domain) (human)	From rabbit	Recognizes the coiled-coil domain of human ANGPTL4. Weakly cross-reacts with human ANGPTL6. Does not cross-react with other ANGPTL family proteins.	Synthetic peptide corresponding to aa 79-101 (A ⁷⁹ CQG-TEGSTDPLA-PESRVDEP ¹⁰¹) of human ANGPTL4.	ELISA, WB	ALX-210-458-C100	100 µg
PAb to ANGPTL4 (Coiled-coil Domain) (human)	From rabbit	Recognizes the coiled-coil domain of human ANGPTL4. Weakly cross-reacts with human ANGPTL2 (CCD), ANGPTL3 and ANGPTL5 (CCD).	Coiled-coil domain of recombinant human ANGPTL4.	ELISA, WB	ALX-210-470-C100	100 µg
PAb to ANGPTL4 (Fibrinogen-like Domain) (human)	From rabbit	Recognizes the fibrinogen-like domain of human ANGPTL4. Reacts with human ANGPTL6. Does not cross-react with other ANGPTL family proteins.	Fibrinogen-like domain of recombinant human ANGPTL4.	ELISA, WB	ALX-210-469-C100	100 µg
PAb to ANGPTL4 (rat)	From rabbit	Recognizes rat ANGPTL4.	Synthetic peptide corresponding to aa 80-94 (C ⁸⁰ QGPKGKDAPFKDSE ⁹⁴) of mouse ANGPTL4.	WB	ALX-210-360-C100	100 µg
PAb to ANGPTL5 (Coiled-coil Domain) (human)	From rabbit	Recognizes the coiled-coil domain of human ANGPTL4. Reacts with human ANGPTL5 (CCD). Does not cross-react with other ANGPTL family proteins.	Coiled-coil domain of recombinant human ANGPTL5.	ELISA, WB	ALX-210-473-C100	100 µg
PAb to ANGPTL6 (human)	From rabbit	Recognizes human ANGPTL6.	Synthetic peptide corresponding to aa 114-130 (L ¹¹⁴ QHEAGPGAGP-GADLGA ¹³⁰) of human ANGPTL6.	ELISA, WB	ALX-210-430-C100	100 µg
PAb to ANGPTL6 (human)	From rabbit	Recognizes human ANGPTL6.	Recombinant human ANGPTL6.	ELISA, WB	ALX-210-438-C100	100 µg
PAb to ANGPTL7 (human)	From rabbit	Recognizes human ANGPTL7. Weakly cross-reacts with human ANGPTL3 and ANGPTL4. Does not cross-react with ANGPTL1, ANGPTL2 and ANGPTL6.	Recombinant human ANGPTL7.	ELISA, WB	ALX-210-453-C100	100 µg

Introduction

continued

it was reported that ANGPTL1 inhibited VEGF-induced angiogenesis, and it was thus named "Angioarrestin" [24]. Recently, ANGPTL1 and ANGPTL2 have been shown to exhibit antiapoptotic activity [25].

LIT: [1] Angiopoietin-related growth factor (AGF) promotes epidermal proliferation, remodeling, and regeneration: Y. Oike, et al.; *PNAS* **100**, 9494 (2003) • [2] Molecular cloning and characterization of a novel angiopoietin family protein, angiopoietin-3: I. Kim, et al.; *FEBS Lett.* **443**, 353 (1999) • [3] Molecular cloning, expression, and characterization of angiopoietin-related protein. angiopoietin-related protein induces endothelial cell sprouting: I. Kim, et al.; *J. Biol. Chem.* **274**, 26523 (1999) • [4] Inhibition of angiogenesis and vascular leakiness by angiopoietin-related protein 4: Y. Ito, et al.; *Cancer Res.* **63**, 6651 (2003) • [5] Angiopoietin-related growth factor (AGF) promotes angiogenesis: Y. Oike, et al.; *Blood* **103**, 3760 (2004) • [6] Hepatic expression, synthesis and secretion of a novel fibrinogen/angiopoietin-related protein that prevents endothelial-cell apoptosis: I. Kim, et al.; *Biochem. J.* **346** Pt 3, 603 (2000) • [7] ANGPTL3 stimulates endothelial cell adhesion and migration via integrin alpha v beta 3 and induces

blood vessel formation in vivo: G. Camenisch, et al.; *J. Biol. Chem.* **277**, 17281 (2002) • [8] Angiopoietin-like 4 is a proangiogenic factor produced during ischemia and in conventional renal cell carcinoma: S. Le Jan, et al.; *Am. J. Pathol.* **162**, 1521 (2003) • [9] Angpt3 regulates lipid metabolism in mice: R. Koishi, et al.; *Nat. Genet.* **30**, 151 (2002) • [10] ANGPTL3 decreases very low density lipoprotein triglyceride clearance by inhibition of lipoprotein lipase: T. Shimizugawa, et al.; *J. Biol. Chem.* **277**, 33742 (2002) • [11] Angiopoietin-like protein 3, a hepatic secretory factor, activates lipolysis in adipocytes: M. Shimamura, et al.; *BBRC* **301**, 604 (2003) • [12] Peroxisome proliferator-activated receptor gamma target gene encoding a novel angiopoietin-related protein associated with adipose differentiation: J. C. Yoon, et al.; *Mol. Cell. Biol.* **20**, 5343 (2000) • [13] Characterization of the fasting-induced adipose factor FIAF, a novel peroxisome proliferator-activated receptor target gene: S. Kersten, et al.; *J. Biol. Chem.* **275**, 28488 (2000) • [14] Angiopoietin-like protein 4 is a potent hyperlipidemia-inducing factor in mice and inhibitor of lipoprotein lipase: K. Yoshida, et al.; *J. Lipid Res.* **43**, 1770 (2002) • [15] Transgenic angiopoietin-like (angptl)4 overexpression and targeted disruption of angptl4 and angptl3: regulation of triglyceride metabolism: A. Koster, et al.; *Endocrinology* **146**, 4943 (2005) • [16] Angiopoietin-like protein 4 decreases blood glucose and improves glucose tolerance but induces hyperlipidemia and hepatic steatosis in mice: A. Xu, et al.; *PNAS* **102**,

6086 (2005) • [17] Lipid-lowering effects of anti-angiopoietin-like 4 antibody recapitulate the lipid phenotype found in angiopoietin-like 4 knockout mice: U. Desai, et al.; *PNAS* **104**, 11766 (2007) • [18] Protein region important for regulation of lipid metabolism in angiopoietin-like 3 (ANGPTL3): ANGPTL3 is cleaved and activated in vivo: M. Ono, et al.; *J. Biol. Chem.* **278**, 41804 (2003) • [19] Angiopoietin-like protein 4 converts lipoprotein lipase to inactive monomers and modulates lipase activity in adipose tissue: V. Sukonina, et al.; *PNAS* **103**, 17450 (2006) • [20] Food restriction regulates adipose-specific cytokines in pituitary gland but not in hypothalamus: G. Wiesner, et al.; *J. Endocrinol.* **180**, R1 (2004) • [21] Angiopoietin-related growth factor antagonizes obesity and insulin resistance: Y. Oike, et al.; *Nat. Med.* **11**, 400 (2005) • [22] Angiopoietin-like 4 prevents metastasis through inhibition of vascular permeability and tumor cell motility and invasiveness: A. Galaup, et al.; *PNAS* **103**, 18721 (2006) • [23] Angiopoietin-related growth factor (AGF) supports adhesion, spreading, and migration of keratinocytes, fibroblasts, and endothelial cells through interaction with RGD-binding integrins: Y. Zhang, et al.; *BBRC* **347**, 100 (2006) • [24] Angioarrestin: an antiangiogenic protein with tumor-inhibiting properties: M. Dhanabal, et al.; *Cancer Res.* **62**, 3834 (2002) • [25] Cooperative interaction of Angiopoietin-like proteins 1 and 2 in zebrafish vascular development: Y. Kubota, et al.; *PNAS* **102**, 13502 (2005)

ANGPTL7

Human ANGPTL7 is produced as a secreted glycoprotein with a molecular mass of 45 kDa in SDS-PAGE analysis. Human mRNA is expressed in neural tissues, keratoconus cornea, trabecular meshwork, melanotic melanoma and uterus endometrial cancer, while mouse *Angptl7* mRNA is expressed in four-cell embryos, synovial fibroblasts, thymus, uterus and testis. ANGPTL7 reduces tumor growth and aberrant blood vessel formation by inducing massive fibrosis in a mouse xenograft model [1]. It was reported that addition of ANGPTL7 results in a further increase in hematopoietic stem cells (HSC) activities. This suggests that ANGPTL7 may activate signal transduction pathways that cannot be activated by stem cell factors, thrombopoietin, insulin-like growth factor 2 (IGF-2)

or fibroblast growth factor 1 (FGF-1) [2]. Human ANGPTL7, characterized as potent target gene of WNT/ β -catenin signalling pathway, is a pharmacogenomics target in the fields of oncology and regenerative medicine [3].

LIT: [1] The angiopoietin-like factor cornea-derived transcript 6 is a putative morphogen for human cornea: R. Peek, et al.; *J. Biol. Chem.* **277**, 686 (2002) • [2] Angiopoietin-like proteins stimulate ex vivo expansion of hematopoietic stem cells: C. C. Zhang, et al.; *Nat. Med.* **12**, 240 (2006) • [3] Comparative integrinomics on Angiopoietin family members: Y. Katoh & M. Katoh; *Int. J. Mol. Med.* **17**, 1145 (2006)

NEW ANGPTL7 (human) (rec.)

ALX-201-368-C010 10 μ g
ALX-201-368-C050 50 μ g

Produced in HEK 293 cells. Human ANGPTL7 (angiopoietin-like protein 7) (aa 1-346) is fused at the C-terminus to a FLAG[®]-tag.

NEW ANGPTL7 (Fibrinogen-like Domain) (human) (rec.)

ALX-201-395-C010 10 μ g
ALX-201-395-C050 50 μ g

Produced in HEK 293 cells. Mature human ANGPTL7 (angiopoietin-like protein 7) (aa 126-346) is fused at the N-terminus to a FLAG[®]-tag.

NEW PAb to ANGPTL7 (human)

ALX-210-453-C100 100 μ g

From rabbit. **IMMUNOGEN:** Recombinant human ANGPTL7 (angiopoietin-like protein 7). **SPECIFICITY:** Recognizes human ANGPTL7. Weakly cross-reacts with human ANGPTL3 and ANGPTL4. Does not cross-react with ANGPTL1, ANGPTL2 and ANGPTL6. **APPLICATION:** ELISA, WB.

Latest Insight

Human ANGPTL4 Variant reduces triglycerides and increase HDL

A recent analysis of the ANGPTL4 gene in a multiethnic population showed, that individuals carrying a ANGPTL4 variant called E40K had significantly lower triglyceride levels and higher high-density lipoprotein cholesterol levels.

LIT: Population-based resequencing of ANGPTL4 uncovers variations that reduce triglycerides and increase HDL: S. Romeo, et al.; *Nat. Genet.* **39**, 513 (2007)

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Latest Insight

The PC-ANGPTL3-EL-HDL pathway controls the HDL metabolism and cholesterol homeostasis

W. Jin, et al. showed recently that hepatic proprotein convertase (PC) reduces endothelial lipase (EL) function through direct inactivating cleavage of EL as well as through activating cleavage of angiopoietin-like protein 3 (ANGPTL3), an endogenous inhibitor of EL.

LIT: Hepatic Proprotein Convertases Modulate HDL Metabolism: W. Jin, et al.; *Cell Metab.* **6**, 129 (2007)

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