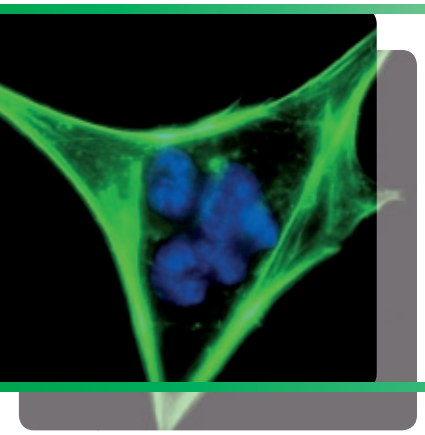


THE FGF FAMILY

The first two fibroblast growth factors (FGFs), acidic FGF (FGF-1) and basic FGF (FGF-2) were originally identified as growth factors for fibroblasts. However, FGFs are now recognized as polypeptide growth factors with diverse biological activities and expression profiles. Today the human FGF family consists of 22 members (FGF-1 to 14 and FGF-16 to 23) and these family members are further divided into six subfamilies (Figure 1). The FGF-11 subfamily is generally not considered to be a member of the FGF family [for a recent review see A. Beenken & M. Mohammadi; Nat. Rev. Drug Discov. **8,** 235 (2009)]. All FGFs, except those of the FGF-1 and FGF-9 subfamily, have signal peptides. The FGF-9 subfamily is nonetheless secreted through the traditional endoplasmic reticulum (ER) – Golgi secretory pathway, whereas the FGF-1 subfamily is secreted independently.

The various FGFs have been reported to regulate complex biological processes such as embryonic development, angiogenesis, wound healing, nerve regeneration, chronic inflammation and cancer. These processes require spatial and temporal integration of several cell responses, including cell survival, proliferation, migration and invasion, and cell differentiation. All these responses or functions are induced or modulated by the interaction of FGFs with tyrosine kinase FGF receptors (FGFRs). There exist four FGFRs (FGFR-1 to 4) which consist of three extracellular immunoglobulin domains (D1-D3), a single transmembrane domain and a cytoplasmic tyrosine kinase domain. Unlike other growth factors, FGFs act in concert with heparin or heparan sulfate proteoglycan (HSPG) to activate FGFRs. The binding of FGF and HSPG to the extracellular ligand domain of FGFR induces receptor dimerization, activation and autophosphorlyation of multiple tyrosine residues in the cytoplasmic domain of the receptor molecule. A variety of signaling proteins are phosphorylated in response to FGF stimulation including Shc, phospholipase Cγ, Gab1 and FRS2α. In addition the interaction of FGFs with these receptors also mediates FGFR cell trafficking. In fact, most FGFs are imported or exported in and out of cells and are translocated to the cell nucleus complexed with their receptors. Internalization and nuclear translocation of receptors results in specific signaling pathways that appear to be different from those elicited at the cell surface. Thus, most FGFs act on cells through autocrine, paracrine and endocrine effects that are modulated by both receptor activation and trafficking. Future application of the FGFs in renal disease, glucose and phosphate homeostasis, stem cell research, angiogenesis, tissue repair and bioengineering are under investigation.

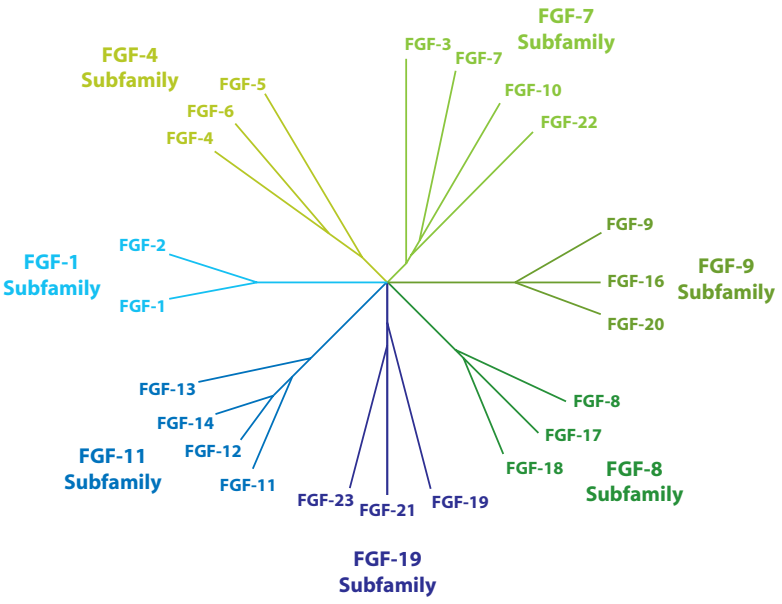


FIGURE: The human FGF Gene Family.

*Adapted from: The Fgf families in humans, mice, and zebrafish: their evolutional processes and roles in development, metabolism, and disease: N. Itoh; Biol. Pharm. Bull. **30,** 1819 (2007)*

Selected Review Articles

LIT: Cellular signaling by fibroblast growth factor receptors: V. P. Eswarakumar, et al.; Cytokine Growth Factor Rev. **16,** 139 (2005) ▪ Fibroblast growth factor/fibroblast growth factor receptor system in angiogenesis: M. Presta, et al.; Cytokine Growth Factor Rev. **16,** 159 (2005) ▪ Fibroblast growth factor signaling in tumorigenesis: R. Grose & C. Dickson; Cytokine Growth Factor Rev. **16,** 179 (2005) ▪ Mechanisms underlying differential responses to FGF signaling: L. Dailey, et al.; Cytokine Growth Factor Rev. **16,** 233 (2005) ▪ The Fgf families in humans, mice, and zebrafish: their evolutional processes and roles in development, metabolism, and disease: N. Itoh; Biol. Pharm. Bull. **30,** 1819 (2007) ▪ Fibroblast growth factor regulation of neovascularization: M. Murakami & M. Simons; Curr. Opin. Hematol. **15,** 215 (2008) ▪ FGF signaling: its role in bone development and human skeleton diseases: N. Su, et al.; Front. Biosci. **13,** 2842 (2008) ▪ The FGF family: biology, pathophysiology and therapy: A. Beenken & M. Mohammadi; Nat. Rev. Drug Discov. **8,** 235 (2009)

The FGF-19 Subfamily

Fibroblast growth factors (FGFs) are humoral factors with diverse biological functions. While most FGFs work as local factors regulating cell growth and differentiation, the FGF-19 subfamily members FGF-19 (the human ortholog of mouse FGF-15), FGF-21 and FGF-23 work as systemic factors (Figure 2). βKlotho has been identified as co-factor/co-receptor required for FGF-19 and FGF-21 signaling whereas Klotho is essential for FGF-23 signaling. It has been proposed that the tissue-specific expression of FGF receptor (FGFR) subtypes together with the limited expression of the co-factors/co-receptors βKlotho and Klotho determine the tissue specific metabolic activities of the FGF-19 subfamily members. For a recent review see H. Kurosu & M. Kuro-o; Mol. Cell Endocrinol. **299,** 72 (2009).

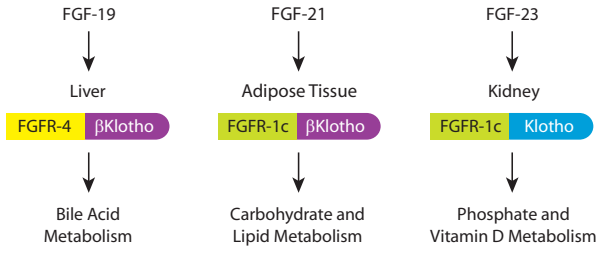


FIGURE: Mode of actions of FGF-19 subfamily members.
FGF-19 subfamily members require Klotho or βKlotho in addition to canonical FGFRs for their actions. Representative target tissues and FGFRs are indicated.
Adapted from: Actions and mode of actions of FGF19 subfamily members: S. Fukumoto; Endocr. J. **55,** 23 (2008)

FGF-19

FGF-19 (human), (rec.) (His-tag)

ALX-201-420-C010 10 µg
ALX-201-420-C050 50 µg

Produced in HEK 293 cells. The original signal peptide and the mature peptide of human FGF-19 (aa 1-216) are fused at the C-terminus to a His-tag.

FGF-19 (human), mAb (FG98-6) NEW

ALX-804-750-C050 50 µg
ALX-804-750-C100 100 µg

CLONE: FG98-6. **ISOTYPE:** Mouse IgG2. **IMMUNOGEN:** Recombinant human FGF-19. **SPECIFICITY:** Recognizes human FGF-19. **APPLICATION:** ELISA, WB.

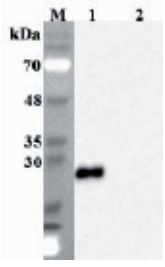


FIGURE: Western blot analysis of human FGF-19 using FGF-19 (human), mAb (FG98-6) (Prod. No. ALX-804-750) at 1:2,000 dilution.
1. FGF-19 (human), (rec.) (His-tag) (Prod. No. ALX-201-420)
2. Recombinant mouse Vaspin-His (negative control)

FGF-19 (human), mAb (FG369-1) NEW

ALX-804-751-C050 50 µg
ALX-804-751-C100 100 µg

CLONE: FG369-1. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Recombinant human FGF-19. **SPECIFICITY:** Recognizes human FGF-19. **APPLICATION:** ELISA, WB.

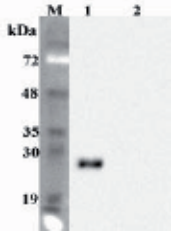


FIGURE: Western blot analysis of human FGF-19 using FGF-19 (human), mAb (FG369-1) (Prod. No. ALX-804-751) at dilution 1:2,000.
1. FGF-19 (human), (rec.) (His-tag) (Prod. No. ALX-201-420)
2. Recombinant mouse Vaspin-His (negative control)

Selected Literature References

LIT: Tissue-specific expression of betaKlotho and fibroblast growth factor (FGF) receptor isoforms determines metabolic activity of FGF19 and FGF21: H. Kurosu, et al.; J. Biol. Chem. **282,** 26687 (2007) ▪ Liver-specific activities of FGF19 require Klotho beta: B. C. Lin, et al.; J. Biol. Chem. **282,** 27277 (2007) ▪ betaKlotho is required for metabolic activity of fibroblast growth factors 21: Y. Ogawa, et al.; PNAS **104,** 7432 (2007) ▪ Actions and mode of actions of FGF19 subfamily members: S. Fukumoto; Endocr. J. **55,** 23 (2008) (Review) ▪ The Klotho gene family as a regulator of endocrine fibroblast growth factors: H. Kurosu & M. Kuro-o; Mol. Cell Endocrinol. **299,** 72 (2009) (Review)

Latest Insight

The FGF Family – FGFR Interaction – A Target For Developing New Therapeutics?

The involvement of FGF signaling in human disease is well documented. Therapeutic approaches using exogenous FGFs, antibodies or small molecules are still relatively new and many avenues of investigation remain open. Recombinant FGF-7 is already in use for the treatment of chemoradiation-induced oral mucositis. Continued efforts to understand the structural biology of FGF-FGFR interactions will play a key part in driving the discovery of new therapies. For the latest review on the current knowledge regarding FGF-FGFR signaling, the biology, pathology and recent developments regarding the pharmalogical applications of each FGF ligand see The FGF family: biology, pathophysiology and therapy: A. Beenken & M. Mohammadi; Nat. Rev. Drug Discov. **8,** 235 (2009).

FGF-21

FGF-21 (human), (rec.)

ALX-201-400-C010 10 µg
ALX-201-400-C050 50 µg

Produced in HEK 293 cells. Mature human FGF-21 (aa 1-209) is fused at the C-terminus to a FLAG®-tag.

FGF-21 (human), (rec.) (His-tag)

ALX-201-407-C010 10 µg
ALX-201-407-C050 50 µg

Produced in HEK 293 cells. Mature human FGF-21 (aa 1-209) is fused at the C-terminus to a His-tag.

FGF-21 (human):Fc (human), (rec.)

ALX-201-404-C010 10 µg
ALX-201-404-C050 50 µg

Produced in HEK 293 cells. Mature human FGF-21 (aa 1-209) is fused at the C-terminus to the Fc portion of human IgG.

FGF-21 (mouse), (rec.)

ALX-201-401-C010 10 µg
ALX-201-401-C050 50 µg

Produced in HEK 293 cells. Mature mouse FGF-21 (aa 1-210) is fused at the C-terminus to a FLAG®-tag.

FGF-21 (mouse), (rec.) (His-tag)

ALX-201-409-C010 10 µg
ALX-201-409-C050 50 µg

Produced in HEK 293 cells. Mature mouse FGF-21 (aa 1-210) is fused at the C-terminus to a His-tag.

FGF-21 (mouse):Fc (human), (rec.)

ALX-201-406-C010 10 µg
ALX-201-406-C050 50 µg

Produced in HEK 293 cells. Mature mouse FGF-21 (aa 1-210) is fused at the C-terminus to the Fc portion of human IgG.

FGF-21 (FG224-7), mAb

ALX-804-736-C100 100 µg

CLONE: FG224-7. **ISOTYPE:** Rat IgG1. **IMMUNOGEN:** Recombinant mouse FGF-21. **SPECIFICITY:** Recognizes human and mouse FGF-21. Detects a band of ~25kDa by Western blot. **APPLICATION:** ELISA, WB.

FGF-21 (human), mAb (FG204-3) NEW

ALX-804-752-C050 50 µg
ALX-804-752-C100 100 µg

CLONE: FG204-3. **ISOTYPE:** Mouse IgG2. **IMMUNOGEN:** Recombinant human FGF-21. **SPECIFICITY:** Recognizes human FGF-21. Does not cross-react with mouse FGF-21. **APPLICATION:** ELISA, WB.

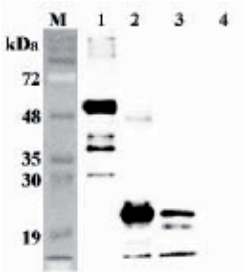


FIGURE: Western blot analysis of human FGF-21 using FGF-21 (human), mAb (FG204-3) (Prod. No. ALX-804-752) at 1:2,000 dilution.

1. FGF-21 (human):Fc (human), (rec.) (Prod. No. ALX-201-404)
2. FGF-21 (human), (rec.) (Prod. No. ALX-201-400)
3. FGF-21 (human), (rec.) (His-tag) (Prod. No. ALX-201-407)
4. Jagged-1 (human):Fc (human), (rec.) (Prod. No. ALX-201-390) (negative control)

FGF-21 (human), mAb (FG348-1)

ALX-804-753-C05050 µg
ALX-804-753-C100 100 µg

CLONE: FG348-1. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Recombinant human FGF-21. **SPECIFICITY:** Recognizes human FGF-21. Does not cross-react with mouse FGF-21. **APPLICATION:** ELISA, WB.

FGF-21, pAb NEW

ALX-210-478-C100 100 µg

From rabbit. **IMMUNOGEN:** Recombinant human FGF-21. **SPECIFICITY:** Recognizes human and mouse FGF-21. **APPLICATION:** ELISA, WB.

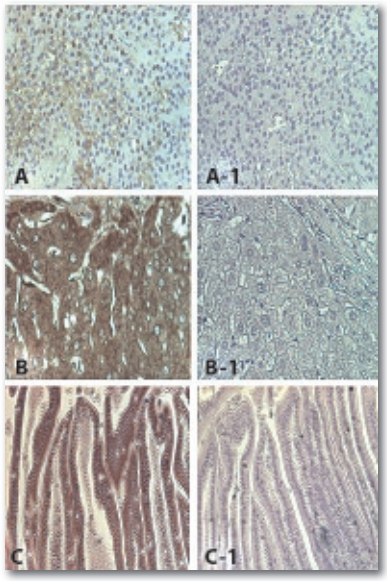


FIGURE: Immunoperoxidase staining of FGF-21 in formalin-fixed, paraffin-embedded human tissue using FGF-21, pAb (Prod. No. ALX-210-478) at 1:5,000 dilution (A, B, C) or preimmune rabbit serum at dilution 1:500 (A-1, B-1, C-1) as negative control.

A, A-1: Parathyroid (200x magnification)

B, B-1: Liver (200x magnification)

C, C-1: Small intestine (100x magnification)

FGF-21 (mouse), pAb

ALX-210-480-C100 100 µg

From rabbit. **IMMUNOGEN:** Recombinant mouse FGF-21. **SPECIFICITY:** Recognizes mouse FGF-21. Weak cross-reactivity with human FGF-21. **APPLICATION:** ELISA, WB.

FGF-23

FGF-23 (human), (rec.) (His-tag)

ALX-201-423-C010 10 µg
ALX-201-423-C050 50 µg

Produced in HEK 293 cells. The original signal peptide and the mature peptide of human FGF-23 (aa 1-251) are fused at the C-terminus to a His-tag.

FGF-23 (human):Fc (human), (rec.)

ALX-201-418-C010 10 µg
ALX-201-418-C050 50 µg

Produced in HEK 293 cells. The original signal peptide and the mature peptide of human FGF-23 (aa 1-251) are fused at the C-terminus to the Fc portion of human IgG.

FGF-23 (R179Q Mutant) (human), (rec.) (His-tag)

ALX-201-435-C010 10 µg

Produced in HEK 293 cells. The original signal peptide and the mature peptide of human FGF-23 (aa 1-251) are fused at the C-terminus to a His-tag. The R179Q mutant is resistant to degradation by the endopeptidase PHEX.

FGF-23 (mouse):Fc (human), (rec.)

ALX-201-437-C010 10 µg
ALX-201-437-C050 50 µg

Produced in HEK 293 cells. The original signal peptide and the mature peptide of mouse FGF-23 (aa 1-251) are fused at the C-terminus to the Fc portion of human IgG.

FGF-23 (human), mAb (FG322-3)

ALX-804-757-C050 50 µg
ALX-804-757-C100 100 µg

CLONE: FG322-3. **ISOTYPE:** Mouse IgG1. **IMMUNOGEN:** Recombinant human FGF-23. **SPECIFICITY:** Recognizes human FGF-23. Does not cross-react with mouse FGF-23. **APPLICATION:** ELISA, IHC, WB.

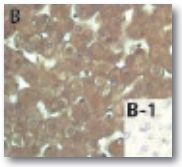


FIGURE: Immunohistochemical staining of FGF-23 with FGF-23 (human), mAb (FG322-3) (Prod. No. ALX-804-757) in human tissue (dilution 1:200).

1. Immunoperoxidase staining of formalin-fixed, paraffin-embedded human liver showing cytoplasmic staining (brown color, 200x).

Klotho – Beyond Spanning the Thread of Life

The klotho gene was identified as a gene mutated in the klotho mouse [1]. The klotho gene encodes a single transmembrane protein and is highest expressed in distal convoluted tubules in the kidney and choroid plexus in the brain. Klotho plays a pivotal role in regulating aging and the development of age-related diseases. First, a loss of klotho results in multiple aging-like phenotypes [1]. Second, overexpression of the klotho gene extends lifespan [2]. Binding of the extracellular domain of Klotho directly to fibroblast growth factor receptors (FGFRs) increases their affinity for FGF-23. Therefore, Klotho functions as a co-factor/co-receptor of FGFRs and is essential for FGF-23 to activate FGF signaling [3].

It was demonstrated that the signal transduction pathways initiated by FGF-23-Klotho signaling prevents tissue atrophy by stimulation proliferation and preventing apoptosis caused by excessive systemic vitamin D [4]. Although Klotho-mediated FGF-23 signaling is well documented, it is not yet clear whether FGF-23 may also have Klotho-independent effects.

In addition the extracellular domain of Klotho can be shed and secreted and may act as a circulating hormone, regulate insulin/insulin-like growth factor 1 (IGF1) signaling, suppress oxidative stress, act as a beta-glucoronidase and activate ion channels (such as TRPV5), protect against endothelial dysfunction, and regulate the production of nitric oxide (NO).

Furthermore, Klotho suppresses the insulin/IGF-1 signal pathway and influences p53/p21, cAMP, PKC and Wnt signaling pathways. Thus Klotho seems to be a multi-functional protein that regulates the phosphate/vitamin D metabolism through the bone derived hormone FGF-23 and plays a role in aging, cancer and stem cell biology. For a recent review see Y. Wang & Z. Sun: Ageing Res. Rev. 8, 43 (2009).

LIT: [1] Mutation of the mouse klotho gene leads to a syndrome resembling ageing: M. Kuro-o, et al.; Nature **6,** 45 (1997) ▪ **[2]** Suppression of aging in mice by the hormone Klotho: H. Kurosu, et al.; Science **309,** 1829 (2005) ▪ **[3]** Klotho converts canonical FGF receptor into a specific receptor for FGF23: I. Urakawa, et al.; Nature **444,** 770 (2006) ▪ **[4]** FGF-23-Klotho signaling stimulates proliferation and prevents vitamin D-induced apoptosis: D. Medici, et al.; J. Cell Biol. **182,** 459 (2008)

Klotho (Extracellular Domain) (human):Fc (human), (rec.)

ALX-201-433-C010 10 µg

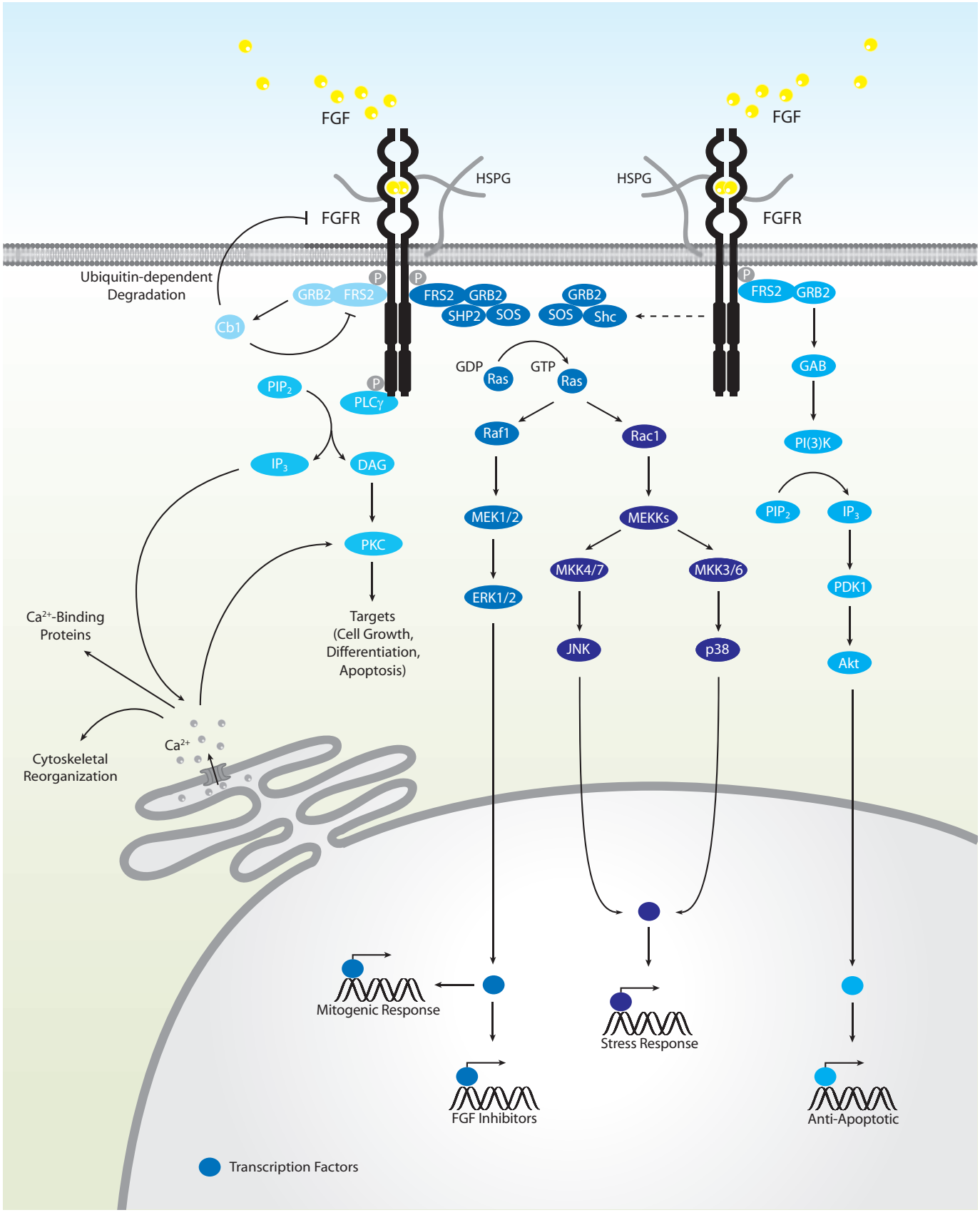
Produced in HEK 293 cells. The signal peptide and the extracellular domain of human klotho (aa 1-981) are fused at the C-terminus to the Fc portion of human IgG.

βKlotho (Extracellular Domain) (human):Fc (human), (rec.)

ALX-201-434-C010 10 µg

Produced in HEK 293 cells. The extracellular domain of human βklotho (aa 1-996) is fused at the C-terminus to the Fc portion of human IgG.

FGF Signaling Pathway



Purified (PF) = Purified (Preservative free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide

Fibroblast Growth Factor Receptors (FGFRs)

FGFR1 (human), (rec.)

BML-SE480-0005 5 µg

BML-SE480-0020 20 µg

Produced in *E. coli*. Active FGFR1 (aa 399-822) is fused a the N-terminus to a GST-tag. **APPLICATION:** Kinetic and functional studies, phosphorylation of target substrates, drug screening.

FGFR1 (human), (rec.)

BML-SE291-0010 10 µg

Produced in insect cells. Cytoplasmic domain of human FGFR1 (aa 308-731). **APPLICATION:** Kinetic and functional studies, phosphorylation of target substrates, drug screening.

FGFR3 (human), (rec.)

BML-SE292-0010 10 µg

Produced in insect cells. Cytoplasmic domain of human FGFR3 (aa 399-806). **APPLICATION:** Kinetic and functional studies, phosphorylation of target substrates, drug screening.

FGFR Peptide Substrate

[Lys-Glu-Ala-Pro-Glu-Asp-Leu-Tyr-Lys-Asp-Phe-Leu-Thr-Leu]

BML-P244-0001 1 mg

This peptide is derived from the KDR sequence and is a substrate for FGFR.

FGFR Peptide Substrate (Biotinylated)

[Biotin-Ahx-Lys-Glu-Ala-Pro-Glu-Asp-Leu-Tyr-Lys-Asp-Phe-Leu-Thr-Leu]

BML-P245-0001 1 mg

This peptide is derived from the KDR sequence and is a substrate for FGFR. The biotin allows peptide to be used in kinase assays with streptavidin-bound membranes.

FGF Ligands & their Receptors

Subfamily	Ligand	FGFR-1b	FGFR-1c	FGFR-2b	FGFR-2c	FGFR-3b	FGFR-3c	FGFR-4
FGF-1 Subfamily	FGF-1	x	x	x	x	x	x	x
	FGF-2	x	x		x		x	x
FGF-4 Subfamily	FGF-4		x		x		x	x
	FGF-5		x		x			
	FGF-6		x		x			x
FGF-7 Subfamily	FGF-3	x		x				
	FGF-7			x				
	FGF-10	x		x				
	FGF-22	x		x				
FGF-8 Subfamily	FGF-8		x		x		x	x
	FGF-17		x		x		x	x
	FGF-18				x		x	x
FGF-9 Subfamily	FGF-9				x	x	x	x
	FGF-16				x	x	x	x
	FGF-20		x	x	x	x	x	x
FGF-11 Subfamily	FGF-11							
	FGF-12							
	FGF-13							
	FGF-14							
FGF-19 Subfamily	FGF-19*		x		x		x	x
	FGF-21*		x		x		x	x
	FGF-23*		x		x		x	x

* Requires a klotho factor for signaling.

LIT: Receptor specificity of the fibroblast growth factor family: D. M. Ornitz, et al.; J. Biol. Chem. **271,** 15292 (1996) ▪ Receptor specificity of the fibroblast growth factor family. The complete mammalian FGF family: X. Zhang, et al.; J. Biol. Chem. **281,** 15694 (2006)

FGFs & Stem Cells

Fibroblast growth factors (FGFs) play an important role in the regulation of proliferation and differentiation in stem cells. For research in stem cells and clinical application of these cells, it is important to establish *in vitro* culture conditions that maintain the self-renewal ability of stem cells along with their fully pluripotent or multipotent differentiation capacity as well as efficient proliferative ability. FGFs are amongst the most common growth factors used to expand stem cells, including human embryonic stem (hES) cells, trophoblast stem (TS) cells and neural stem (NS) cells. Moreover, it has been recently recognized that FGFs are useful for culturing cancer stem cells.

FGFs & Embryonic Stem Cells

Emerging evidence indicates that there are many differences between mouse embryonic stem (mES) cells and human embryonic stem (hES) cells. In particular, the required growth factors for maintaining self-renewal ability in culture are clearly different. Leukemia inhibitory factor (LIF) is essential for mES cells. In mES cells, FGF-4 acts as an autoinductive stimulus that propels mES cells toward lineage specification. The main role of LIF is to block the FGF-4 signaling to keep pluripotency of mES cells. However, LIF signaling does not support self-renewal ability of hES cells. In hES cells, under serum-free conditions, FGF-2 and activin/nodal factors maintain self-renewal ability. It was shown that FGF-4 perpetuates the pluripotency of hES cells as well. Interestingly, FGF-4 is secreted with a novel FGF-4 splice isoform (FGF-4si). FGF-4si is an antagonist of FGF-4, shutting down FGF-4 induced undifferentiated growth of hES cells.

FGFs & Trophoblast Stem Cells

Mouse trophoblast stem (mTS) cells are tissue-specific stem cells of the trophoblast lineage, that give rise to embryonic portion of the placenta. FGF-4 in combination with conditioned medium are the key for the self-renewal ability of mTS cells *in vitro*. In the absence of either FGF-4, or conditioned medium, mTS cells lose multipotency and differentiate into giant cells, which resemble trophoblast giant cells. *In vivo*, FGF-4, produced from the inner cell mass (ICM) of the blastocyst and the epiblast of embryos, signals to neighboring mTS cells in a paracrine manner. Therefore, it is proposed that FGF-4 functions as a secretory factor in the mTS cell niche.

FGFs & Neural Stem Cells

Neural stem (NS) cells possess the characteristics of multipotent stem cells: first, the self-renewal ability and second, the ability to differentiate into neurons, astrocytes and oligodendrocytes. FGF-2 and/or epidermal growth factors (EGFs) are required for the *in vitro* culturing of NS cells. By withdrawal of FGF-2 *in vitro*, the differentiation of NS cells can be driven. *In vivo*, FGF-2 also plays an important role. In the event of brain damage, endogenous production of FGF-2 is necessary and sufficient to stimulate proliferation and differentiation of neural progenitor cells to repair brain lesions.

Selected Literature References

LIT: Fibroblast Growth Factor 4 and Its Novel Splice Isoform Have Opposing Effects on the Maintenance of Human Embryonic Stem Cell Self-Renewal: Y. Mayshar, et al.; Stem Cells **26,** 767 (2008) ▪ Stem Cells and Early Lineage Development: J. Rossant; Cell **132,** 527 (2008) (Review) ▪ Control of Stemness by Fibroblast Growth Factor Signaling in Stem Cells and Cancer Stem Cells: N. Gotoh; Curr. Stem Cell Res. Ther. **4,** 9 (2009) (Review)

Purified (PF) = Purified (Preservative free); FC = Flow Cytometry; ICC = Immunocytochemistry; IP = Immunoprecipitation; IHC = Immunohistochemistry (FS = Frozen Sections, PS = Paraffin Sections); WB = Western blot; BP = Blocking Peptide

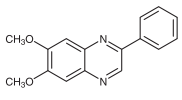
Related Products

AG-1296

BML-EI303-0005 5 mg

BML-EI303-0025 25 mg

A potent inhibitor of PDGF receptor tyrosine kinase (IC_{50}=1μM). Also inhibits FGF receptor tyrosine kinase and c-kit. Induces apoptosis in a small-cell lung cancer cell line (H526).



Fumagillin

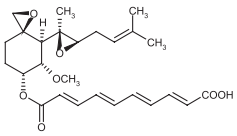
[Fumidil B; Fumadil B; TNP-470]

BML-CT100-0001 1 mg

BML-CT100-0005 5 mg

Isolated from *Aspergillus fumigatus*. Inhibitor of angiogenesis and endothelial cell proliferation. Binds to the cytoplasmic domain of FGFR-1 and inhibits FGF-1 induced angiogenesis. Specific inhibitor of methionine aminopeptidase type II (MetAP-II). Antineoplastic.

LIT: Fumagillin (H-3), a new antibiotic with amebicidal properties: C. M. Mc, et al.; Science **113,** 202 (1951) ▪ Molecular recognition of angiogenesis inhibitors fumagillin and ovalicin by methionine aminopeptidase 2: E. C. Griffith, et al.; PNAS **95,** 15183 (1998) ▪ Fumagillin treatment of hepatocellular carcinoma in rats: an in vivo study of antiangiogenesis: I. S. Sheen, et al.; World J. Gastroenterol. **11,** 771 (2005) ▪ **For a comprehensive bibliography please visit our website.**



SC-236

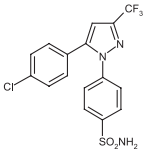
[4-[5-(4-Chlorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide]

ALX-270-377-M005 5 mg

ALX-270-377-M025 25 mg

Highly selective and potent inhibitor of cyclooxygenase-2 (COX-2) (IC_{50}=10nM for COX-2 versus IC_{50}=17.8μM for COX-1) with antitumor properties. Induces apoptosis and bFGF and VEGF-driven angiogenesis.

LIT: COX-2 inhibitors. A new class of antiangiogenic agents: J. L. Masferrer, et al.; Ann. NY Acad. Sci. **889,** 84 (1999) ▪ **For a comprehensive bibliography please visit our website.**



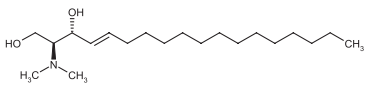
D-*erythro*-Sphingosine, N,N-Dimethyl-

[N,N-Dimethyl-D-*erythro*-sphingosine]

BML-SL105-0005 5 mg

BML-SL105-0025 25 mg

Synthetic. Potent and specific inhibitor of sphingosine kinase (IC_{50}=5μM) which blocks conversion of sphingosine to sphingosine-1-phosphate (Prod. No. BML-SL140). Inhibitor of protein kinase C (PKC) which also stimulates Src-kinase. Inhibits bFGF induced proliferation of human coronary smooth muscle cells.



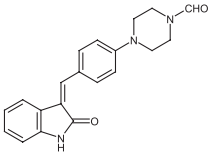
SU 4984

[3[4-(1-Formylpiperazin-4-yl)benzylidenyl]-2-indolinone]

ALX-270-330-M001 1 mg

Inhibitor of tyrosine kinase activity of fibroblast growth factor receptor 1 (FGFR-1). Inhibits αFGF-induced tyrosine phosphorylation of ERK1 and ERK2 (IC_{50}=20-4μM) and the tyrosine phosphorylation of the PDGF receptor and the insulin receptor. Does not inhibit the kinase activity of the EGF receptor.

LIT: Structures of the tyrosine kinase domain of fibroblast growth factor receptor in complex with inhibitors: M. Mohammadi, et al.; Science **276,** 955 (1997)



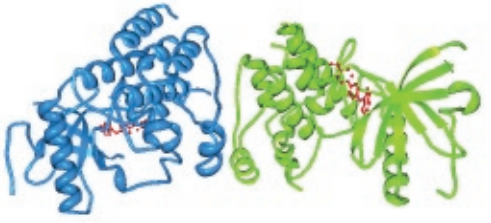


FIGURE: Crystal structure of the tyrosine kinase domain of human FGFR-1 in complex with the inhibitor SU 4984 (ALX-270-330).

Suramin . hexasodium salt

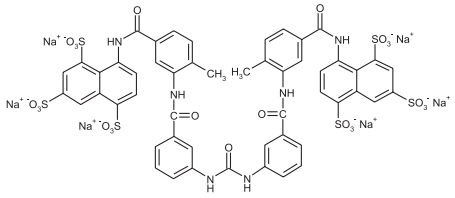
ALX-430-022-M050 50 mg

ALX-430-022-M250 250 mg

ALX-430-022-G001 1 g

Polysulfonated naphthylurea. P_{2x} and P_{2y} purinergic receptor antagonist. Antitumor, antiangiogenic and antiparasitic compound. Inhibits sirtuin 1, sirtuin 5, topoisomerase II and several growth factors, including FGFa, FGFb and PGDF. Blocks association of G protein α and β/γ-subunits.

LIT: Suramin: a potent inhibitor of the reverse transcriptase of RNA tumor viruses: E. De Clerq; Cancer Lett. **8,** 9 (1979) ▪ Suramin disrupts receptor-G protein coupling by blocking association of G protein alpha and betagamma subunits: W. C. Chung & J. C. Kermode; J. Phamacol. Exp. Ther. **313,** 191 (2005) ▪ DBC1 is a negative regulator of SIRT1: J. E. Kim, et al.; Nature **451,** 583 (2008) ▪ The Sirtuin family: therapeutic targets to treat diseases of aging: J. C. Milne & J. M. Denu; Curr. Opin. Chem. Biol. **12,** 11 (2008) ▪ **For a comprehensive bibliography please visit our website.**



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