# Fibroblast Growth Factor Superfamily

Fibroblast growth factors (FGFs) constitute a large family of proteins involved in many aspects of development including cell proliferation, growth, and differentiation. Determining how common FGF signaling pathways generate specific cellular responses is essential to our understanding of how enhanced expression or disruption of these pathways can lead to developmental defects and cancer.



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# R&D Systems Tools for Cell Biology Research Blobrief TAKE-AWAY REFERENCE TOOL

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## **Fibroblast Growth Factor Superfamily**

FGFs are grouped into seven subfamilies based on sequence similarity and functional characteristics. FGFs bind to heparan sulfate proteoglycans (HSPGs) and FGF receptor tyrosine kinases to activate intracellular signaling pathways initiated by receptor dimerization, autophosphorylation, and the recruitment and docking of SH2 domain-containing proteins. There are four FGF signaling receptors (FGF R1-4) which exhibit alternative splicing in the Ig-like repeat domains and one decoy receptor that binds ligand, but does not propagate a signal (FGF R5). Splice forms of FGF R1-4 that affect the ligand-binding domains are indicated in the table: b and c denote alternate forms of the Ig-like repeat III. Splice forms that indicate the presence (α form) or absence (β form) of Ig-like repeat I, or those representing truncated, non-signaling forms are not shown. Although FGF Receptor binding is necessary, it is not sufficient for activating signaling. Activation depends on the presence of accessory proteins, such as glycosaminoglycans and Klotho. In addition, the degree, pattern, and location of sulfation, acetylation, etc. of these cofactors may impact FGF liqand/receptor binding and subsequent pathway activation.

### **FGF PATHWAYS** Sprouty UBIQUITIN-DEPENDENT DEGRADATION Sprouty TARGET SUBSTRATES Ca<sup>2+</sup>-BINDING PROTEINS p38 MAPK Caspase-9 JNK ERK1/2 GSK-3B Akt/PKB -CYTOSKELETAL REORGANIZATION ERK1/2 ANTI-APOPTOTIC -Transcriptional regulators MKP3 CYTOSKELETAL REORGANIZATION ➤ Stress response genes MKP1 NEGATIVE FEEDBACK ➤ FGF Inhibitors: Sprouty, Sef, MKP1, MKP3 ➤ Mitogenic response genes

#### **FGF LIGANDS**

SUBFAMILY	LIGAND	ALTERNATE NAME	FGF RECEPTORS						
			R1b	R1c	R2b	R2c	R3b	R3c	R4
FGF-1	FGF-1	FGF acidic	•	•	•	•	•	•	•
	FGF-2	FGF basic		•				•	•
FGF-4	FGF-4	K-FGF, hst-1		•		•		•	•
	FGF-5	HBGF-5		1		•			
	FGF-6	HBGF-6		•		•			
FGF-7	FGF-3	int-2	•		•				
	FGF-7	KGF			•				
	FGF-10	KGF-2	•		•				
	FGF-22		•		•				
FGF-8	FGF-8a	AIGF			2 8				
	FGF-8b	AIGF		•				•	•
	FGF-8e	AIGF						•	•
	FGF-8f	AIGF						•	•
	FGF-17			•		•		•	•
	FGF-18							•	•
FGF-9	FGF-9	GAF				•		•	•
	FGF-16								•
	FGF-20					•			
FGF-11	FGF-11	FHF-3							
	FGF-12	FHF-1							
	FGF-13	FHF-2							
	FGF-14	FHF-4							
FGF-19	FGF-19*	FGF-15 (mouse)		•		•		•	•
	FGF-21*		1	•		•		•	•
	FGF-23*					-			•

\*Requires a Klotho cofactor for signaling

#### FGF R DOMAINS



