SnapShot: Axon Guidance II

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Axon guidance protein		Chemotrophic effect	Ligand-binding receptor	Receptor processing	Coreceptor	Receptor signaling
BMP	SE	Repulsion	BMP-RIB, BMP-RII	-	-	COFILIN, LIMK1, PI3K, SMAD1, SMAD6
DRAXIN	SE	Repulsion	DCC	-	-	-
EPHRINA	GPI	Repulsion	EPHA	ADAM10	-	α2-CHIMAERIN, EPHEXIN-1, NCK1/2, RAC1, RHOA, SPAR, VAV2/3
EPHRINB	TM	Repulsion	EPHB	MMP2/9	-	NCK1, PAK, p120GAP, RHOA, ROCK, VAV2/3
EPHA	TM	Repulsion	EPHRINA	ADAM10	P75	FYN
		Attraction	EPHRINA	-	RET	-
EPHB	TM	Repulsion	EPHRINB	ADAM10, PS1	-	CDC42, DOCK180, GRB4, NCK2, PAK, RAC1
FGF	SE	Attraction	FGFR1	-	-	-
NETRIN	SE	Attraction	DCC	ADAM10, PS1	APP, HSPG, ROBO1	CDC42, DOCK180, ENA/VASP, ERK1/2, FAK, FYN, NCK1, N-WASP, PAK, PI3K, PIP2, PKC, RAC1, RHOA, TRIO, TRP
		Attraction	NEOGENIN	-	-	-
		Repulsion	UNC5	-	(DCC)	FAK, SHP2, SRC
RGM	GPI	Repulsion	NEOGENIN	TACE, PS1	UNC5	FAK, LARG, LMO4, MYOIIA, p120GAP, PKC, RAS, RHOA
PLEXINA	TM	Repulsion	SEMA1a	-	-	PEBBLE, RHO, p190RHOGAP
SEMA1	TM	Repulsion	PLEXINA	-	OTK	14-3-3ε, GYC76C, MICAL, NERVY, PKA
SEMA2	SE	Repulsion	PLEXINB	-	-	RAC, RHO
		Attraction	PLEXINB	-	-	-
SEMA3	SE	Repulsion	PLEXINA1-4	CALPAIN1	NRP1/2, CAMs, RTKs, ROBO	AKT, COFILIN, CDK5, CRMP, FARP, FYN, GSK3β, LIMK1, PI3K, RAC1, RAP1, RAS, RND
		Attraction	-	-	NRP1/2, CAMs	FAK, SRC
SEMA3E	SE	Repulsion	PLEXIND1	-	-	AKT, GSK3β, PI3K, RAS, RND2
		Attraction	PLEXIND1	-	VEGFR2, NRP1	AKT, GSK3β, PI3K
SEMA4	TM	Repulsion	PLEXINB1-2	PC	ERBB2	AKT, CRMP, GSK3β, LARG, PAK, PI3K, PLCγ, PDZ-RHOGEF, PTEN, RAC1, RAS, RHOA, RND, ROCK, SHP2
SEMA5	TM	Repulsion	PLEXINA1, A3	-	CSPG	-
		Attraction	-	-	HSPG	-
SEMA6	TM	Repulsion	PLEXINA1, A2, A4	-	NrCAM	-
		Attraction	PLEXINA1, NrCAM	-	-	-
SLIT	SE	Repulsion	ROBO	ADAM10	HSPG	CDC42, CROSSGAP, DOCK, RAC1, RHOA, SOS, SRGAP
SHH	SE	Repulsion	BOC	-	-	ILK, PKC, SMOOTHENED
		Repulsion	-	-	-	14-3-3, PKA
		Attraction	BOC	-	-	FYN, SRC, SMOOTHENED
SFRP	SE	Attraction	Frizzled	-	-	Gα
WNT	SE	Attraction	Frizzled	-	CELSR3, VANGL2, ROR	aPKC, PAR3, PAR6
		Repulsion	Frizzled	-	CELSR3, VANGL2	-
		Repulsion	RYK	PS1	-	SRC, TRP

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Axon guidance proteins were originally identified owing to their ability to guide axons in the central and peripheral nervous system. These guidance cues can repel or attract growing axons, and many can serve both functions. They guide axons through interactions with specialized receptor complexes on the neuronal growth cone, and they include both secreted and membrane-associated proteins. Guidance cue-receptor interactions trigger intracellular signal transduction pathways that ultimately impinge upon the growth cone cytoskeleton. In addition to axon guidance, these cues also function to mediate intermediate target navigation, axon sorting within nerves, topographic mapping, target recognition, and circuit organization.

Listed in this table are proteins that function in neurons to mediate long- and short-range axon guidance, along with their (co-)receptors and downstream signaling molecules. Receptors and signaling proteins listed here have been studied at the functional level in neurons, many in vivo. In addition to posttranslational proteolytic processing indicated here, other processes, including regulated receptor endocytosis, clustering, and localized receptor distribution along axons, play critical roles in axon guidance. Owing to space limitations, the effects of axon guidance proteins on neurite growth, branching, and pruning are not included here. We have also limited this table to consideration of "classical" axon guidance proteins; however, neurotrophins essential for neuronal survival and differentiation have also been implicated in regulating neuronal process morphology and guidance. Finally, we have left for future consideration the critical and complex roles played by cell adhesion molecules and extracellular matrix components in selective neuronal process bundling (fasciculation), permissive and nonpermissive growth, and neuronal process self-avoidance.

Abbreviations

CAM, cell adhesion molecule; GPI, glycophosphatidylinositol; PC, proprotein convertase; RTK, receptor tyrosine kinase; SE, secreted; TM, transmembrane.

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