Table 2 Class IV semaphorins implicated in the pathogenesis of cancer

Semaphorins	Types	Promotive function	Inhibitory function	Tumor microenvironment	Clinical significance
Sema4A	Colorectal cancer	[40]	–		p.Val78Met germline mutation [40]
	Myeloma	[41]	–		Targeting for an antibody-drug [41]
	Liver cancer	[42]	–		
	Breast cancer	–	[43]		
	Oral cancer		[44]	Effect for angiogenesis [44]	
Sema4B	Lung cancer	–	[46, 47, 48, 49]		
Sema4C	Breast cancer	[51,52]	–		
Sema4D	Breast cancer	[90, 91, 94, 96]	[99]	Effect for angiogenesis [97]	Expression in *ex vivo*-cultured CTCs [91] Combination therapy with immunomodulatory therapies [94]
	Colorectal carcer	[102, 103, 104, 105, 106, 107, 108]	–		Biomarker for antiangiogenic therapy [103]
	Gastric cancer	[109]	–	Expression in TAMs [109]	
	Esophageal cancer	[110, 111]	–		
	Lung cancer	[112, 113]	[114]	Effect for angiogenesis [112] Effect for osteoblasts [113] Effect for TILs [114]	
	Pancreatic cancer	[107, 115,117]	–	Expression in TILs [115]	Application for an vascular-targeting drug [117]

	Cholangiocarcinoma	[118]	–		
	Prostate cancer	[120, 122]	[119]		Identified through a whole-blood RNA transcriptional profiling [119] Effect for AR expression [121]
	Bladder cancer	[124]	[125]		
	Kidney cancer	–	[125]		
	Cervical cancer	[126]	–		
	Ovarian cancer	[127, 129]	–	Effect for TAMs [129]	
	Osteosarcoma	[132]	–		
	Head and neck cancer	[133, 134, 135, 136]	–	Effect for myeloid cell differentiation [133]	
	Medulloblastoma	–	[138]		
	Leukemia	[139, 142, 143]	[140]		
	Myeloma	[145]	–		
Sema4F	Breast cancer	[99]	–		
	Prostate cancer	[154]	–	Effect for neurogenesis [154]	
	Neurofibromatosis type 1	–	[155]		

Annotated numbers correspond to reference numbers in the main text. Abbreviation: CTCs, circulating tumor cells; TAMs, tumor-associated macrophages; TILs, tumor infiltrating lymphocytes; AR, androgen receptor.