Supplementary information S1 | **Role of Notch in solid tumors**

Tumor	Observation	Role of Notch	Refs
Breast Cancer	Increased NOTCH 4 and decreased NOTCH 1 activity in the tumor initiating cell population	Oncogenic and tumor suppressive	1
	Increased expression of NOTCH receptors, ligands and HES-1 and HES-5	Tumor progression	2
	Increased Notch mediated EMT under hypoxic conditions	Tumor maintenance and progression	3
	Increased Notch signaling is associated with increased metastatic potential of breast cancer cells	Tumor progression	4
	Increased NOTCH activation in ER negative breast cancer results in increased cell proliferation	Drug resistance and tumor progression	5
	NOTCH 2 over expression associated with invasive breast cancer	Tumor progression	6
	Increased JAG 1 expression correlated with recurrence in lymph node negative breast cancer	Tumor progression	7
	Notch activation induces Slug, promotes tumor growth and metastases and inhibits anoikis	Tumor progression	8
	Notch 2 signaling inhibits xenograft growth and promotes apoptosis. Notch 4 signaling promotes tumor growth	Isoform specific Oncogenic and tumor suppressive	9
	Increased JAG1 indicates poor prognosis	Tumor progression	10
	Increased nuclear accumulation of NICD and increased signaling	Tumor progression	11
	Increased NOTCH 1 and decreased NOTCH 2 in poorly differentiated tumors	Isoform specific Oncogenic and tumor suppressive	12
	Loss of NUMB activity resulting in	Tumor progression	13

	increased Notch signaling		
Colorectal cancer	Somatic mutations of FBXW7 which can result in increased NOTCH activity	Oncogenic	14
	Increased Jagged (Notch Signaling) due to active Wnt	Oncogenic	15,16
	Increased NOTCH 1 activation confers chemoresistance	Drug resistance	17
	Notch inhibits the expression of the tumor suppressor KLF4	Oncogenic	18
	Increased expression of JAGGED1, NOTCH 1 and HES-1	Tumor progression	19
	Notch signaling can overcome taxane induced mitotic arrest and apoptosis	Drug Resistance	20
	Increased JAGGED 1 results in loss of contact inhibition and goblet cell differentiation	Oncogenic	21
Prostate cancer	Activation of Notch signaling results in inhibition of growth	Tumor suppressor	22
	Loss of Notch 1 resulting in loss of PTEN expression	Tumor suppressor	23
	Loss of Notch 1 results in reduced MMP-9 and uPA and decreased invasion	Tumor progression	24
	Increased Jagged 1	Tumor progression	25
	Increased Jagged 1 associated with metastases and recurrence	Tumor progression	26
	Notch signaling important for bone metastasis	Tumor progression	27
Liver cancer	Lower expression of NOTCH and JAGGED correlates with increased nuclear b CATENIN and tumor progression	Tumor Suppressor	28
	Notch signaling induces p53 by inhibiting the AKT/HDM2 mediated degradation	Drug Resistance	29

	and sensitize the cells to TRAIL mediated apoptosis		
	Loss of NOTCH 3 increases p53 and cell death by doxirubicin	Drug Resistance	[30]
	Inhibition of Notch signaling by GSI results in reduced proliferation in HepG2 cells	Tumor progression	[31]
	Notch expression deregulated	Tumor progression	[32]
	NOTCH3, JAGGED 1, DELTA like 1 and HES-1 overexpressed in HepG2	Tumor progression	[33]
	Notch 1 overexpressed in cholangicarcinoma	Tumor progression	[34]
	NOTCH 1 overexpression results in cell cycle arrest and increased p53 levels	Tumor Suppressor	[35]
Pancreatic cancer	Inhibition of NOTCH 3 inactivates PI3K/AKT and sensitizes the cells to gemcitabine	Drug Resistance	[36]
	Active NOTCH signaling synergizes with KRAS in acinar cells for initiation and progression of PanINs	Tumor Progression	[37]
	Inhibition of cell proliferation by exosomal nano particles requires downregulation of Notch	Drug Resistance	[38]
	Anti-tumor activity of TW-37 (small molecule inhibitor of Bcl-2) acts by attenuating Notch signaling	Drug Resistacne	[39]
	Notch signaling linked to the EMT phenotype (cancer stem cells) and resistance to gemcitabine.	Drug resistance	[40]
	Over-expression of NOTCH1, 2; JAGGED2; DLL3 (amplification) and DLL4 suggesting a role for ligand dependent Notch signaling in tumor	Oncogenic and tumor progression	[41]

	initiation and maintenance		
	GSI treatment inhibits tumor formation in a mouse model of PDAC	Oncogenic	42
	MMP-7 induced NOTCH activation leads to acinar to ductal transdifferentiation and increases risk of tumorigenesis	Oncogenic	43
	NOTCH 3 expression correlates with poor prognosis	Tumor progression	44
	Notch signaling is essential for DMBA (dimethyl benzathracene) induced pancreatic cancer in mice	Oncogenic	45
	NOTCH is down-regulated by curcumin, genistein treatment leading to growth inhibition and apoptosis	Drug resistance	46-48
	Down-regulation of NOTCH results in inhibition of NF-kB, MMP-9 and VEGF and reduced metastasis	Tumor progression	49
	Notch signaling causes neurovascular progression in pancreatic cancer and causes an invasive phenotype	Tumor progression	50
	Ablation of Notch 2, but not Notch 1 leads to abrogation of PanIN progression and increased survival	Tumor progression	51
Glioblastoma	Notch signaling increases radio resistance of glioma stem cells	Radioresistance	52
	NOTCH1 and NOTCH3 are over-expressed in cell lines and tumors, along with HES-1 and/or HES-2, and HEY-1 expression increases with GBM grade	Tumor progression	53
	Knockdown of *NOTCH1* resulted in growth suppression, increased apoptosis, and morphological changes, indicating Notch has a role in maintaining cells in	Tumor maintenance/progression	54

	an undifferentiated state		
	Knockdown of *DLL1* or *JAG1* resulted in decreased cell growth and/or cell death	Tumor progression	[55]
	Non-canonical Notch signaling through the ligand DNER has a differentiating and tumor suppressive effect in GBM	Tumor Suppressor	[56]
Cervical cancer	NOTCH activation activates the NF-kB via association with IKKalpha and protects CasKi cells against cisplatin induced apoptosis	Drug Resistance	[57]
	Co-activation of Notch and NF-KB pathways	Tumor progression	[58]
	Disruption of *NOTCH* by HPV-16 integration - NOTCH1 activation is seen only in late stages of HPV-positive tumors	Tumor progression	[59,60]
	NOTCH activity is correlated with tumor progression and inhibition of Notch with GSI resulted in decreased cell proliferation and increased apoptosis	Tumor progression	[56]
Squamous cell carcinoma (Oral)	NOTCH 1 levels correlated to LN metastasis and invasion	Tumor progression	[61]
	Overexpression of NOTCH results in cell cycle arrest and apoptosis. There is decrease in b-CATENIN, SKP and BCL-2 and increase in p21 and p53	Tumor Suppressor	[62]
	Amplification and overexpression of *JAG1, RBP/SUH, FJX1, DLL1 and NOTCH 4*	Tumor progression	[63]
Skin	NOTCH 1 is down regulated in UV-induced squamous cell carcinoma	Tumor Suppressor	[64]
	Mice expressing dominant negative MAML in the epidermis develop	Tumor Suppressor	[65]

	spontaneous SCC with increased nuclear b-CATENIN and CYCLIN-D1 which is also observed in human SCC		
Head and neck	High NOTCH1 and STAT3 correlate with cisplatin resistance indicating active survival pathways	Drug Resistance	[66]
Medulloblastoma	High *NOTCH2*, but not *NOTCH1* transcripts	Tumor progression	[67]
	HES-1 expression negatively associated with patient survival	Tumor progression	[67]
	Blocking NOTCH with GSI decreases cell proliferation and increases apoptosis	Tumor Maintenance and progression	[68]
Melanoma	Tumors have increased NOTCH activity compared to non-transformed controls	Tumor progression	[69,70]
	NOTCH1 activation increases metastasis and tumor cell survival *in vivo*	Tumor maintenance and progression	[71,72]
	NOTCH over-expression leads to increased cell proliferation and dysregulated adhesion and migration	Tumor maintenance and progression	[69,70]
	Blocking NOTCH activation suppresses melanoma growth *in vitro* and *in vivo*	Tumor progression	[71,72]
Lung Cancer	NOTCH3 expression seen in 39% of resected human lung tumors	Tumor progression	[73]
	One-third of NSCLC have increased NOTCH activity due to gain-of-function mutations or loss of NUMB	Oncogenic/ Tumor Progression	[74]
	Blocking interaction between NOTCH3 and JAG1 results in increased apoptosis and decreased transcription of *HEY-1*	Tumor Progression	[75,76]
	Over-expression of NOTCH1 or NOTCH2 in SCLC cells results in growth arrest	Tumor Suppressor	[77]

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