Numbering according to the article reference numbering

Table 1. Selected articles in the integrative review.

Authors	Title	Journal of publication	Type of Cancer	Database	Year
Shi et al.[14]	Tumor-associated macrophages in direct contact with prostate cancer cells promote malignant proliferation and metastasis through NOTCH1 pathway.	International Journal Of Biological Sciences	Prostate carcinoma	PubMed	2022
Grilli et al.[18]	Impact of notch signaling on the prognosis of patients with head and neck squamous cell carcinoma.	Oral Oncology	Head and neck carcinoma	PubMed	2020
Nyman, Patrick E. et al.[19]	Loss of Function of Canonical Notch Signaling Drives Head and Neck Carcinogenesis.	Clinical Cancer Research	Head and neck carcinoma	PubMed	2018
Mao, Liang et al. [20]	γ-Secretase inhibitor reduces immunosuppressive cells and enhances tumour immunity in head and neck squamous cell carcinoma.	International Journal Of Cancer	Head and neck carcinoma	PubMed	2017
Fukusumi e Califano[21]	The NOTCH Pathway in Head and Neck Squamous Cell Carcinoma.	Journal Of Dental Research	Head and neck carcinoma	PubMed	2018
RICE, Meghan A. et al.[22]	Loss of Notch1 Activity Inhibits Prostate Cancer Growth and Metastasis and Sensitizes Prostate Cancer Cells to Antiandrogen Therapies.	Molecular Cancer Therapeutics	Prostate carcinoma	SciElo	2019
Cheng Ji-wen et al.[23]	Bone marrow mesenchymal stem cells promote prostate cancer cell stemness via cell–cell contact to activate the Jagged1/Notch1 pathway.	Cell & Bioscience	Prostate carcinoma	Google acadêmico	2021
Bayramoğlu et al.[24]	Evaluation of Notch1 gene expression in prostate carcinoma.	Journal Of Surgery And Medicine	Prostate carcinoma	PubMed	2020
Signoretti e Aster, [25]	penile carcinoma associated with convergent gain-of-function mutations in NOTCH1.	Human Pathology: Case Reports	Penile carcinoma	PubMed	2018
Wang, Yonghua et al.[26]	Mutational landscape of penile squamous cell carcinoma in a Chinese population.	International Journal Of Cancer	Penile carcinoma	PubMed	2019
Canto, Luisa Matos et al.[27]	Mutational Signature and Integrative Genomic Analysis of Human Papillomavirus-Associated Penile Squamous Cell Carcinomas from Latin American Patients.	Cancers	Penile carcinoma	Google acadêmico	2022

Chahoud, Jad et al.[28]	Whole-exome Sequencing in Penile Squamous Cell Carcinoma Uncovers Novel Prognostic Categorization and Drug Targets Similar to Head and Neck Squamous Cell Carcinoma.	Clinical Cancer Research	Penile carcinoma	PubMed	2021
Cao, Jian et al.[29]	Correlation Between the Evolution of Somatic Alterations During Lymphatic Metastasis and Clinical Outcome in Penile Squamous Cell Carcinoma.	Frontiers In Oncology	Penile carcinoma	SciElo	2021
Koury, Jeffrey, et al. [30]	Targeting Signaling Pathways in Cancer Stem Cells for Cancer Treatment.	Stem Cells International	Carcinoma of the breast	PubMed	2017
Jiang, Huimin et al.[31]	Jagged1-Notch1-deployed tumor perivascular niche promotes breast cancer stem cell phenotype through Zeb1.	Nature Communications	Carcinoma of the breast	PubMed	2020
Kałafut, Joanna et al.[32]	Optogenetic control of NOTCH1 signaling.	Cell Communication And Signaling	Carcinoma of the breast	PubMed	2022
MIAO, Kai et al. [33]	NOTCH1 activation compensates BRCA1 deficiency and promotes triple-negative breast cancer formation.	Nature Communications	Carcinoma of the breast	PubMed	2020
Zhang et al.[34]	An essential role of RNF187 in Notch1 mediated metastasis of hepatocellular carcinoma	J Exp Clin Câncer Res	Hepatocellular carcinoma	PubMed	2019
WANG, Fang et al. [35]	ABL1, Overexpressed in Hepatocellular Carcinomas, Regulates Expression of NOTCH1 and Promotes Development of Liver Tumors in Mice.	Gastroenterology	Hepatocellular carcinoma	PubMed	2020
HANY, Heba et al.[36]	Evaluation of the role of Notch1 expression in hepatic carcinogenesis with clinico-pathological correlation.	Pathology	Hepatocellular carcinoma	PubMed	2018
LI, Hui et al.[37]	Correction: ncstn promotes hepatocellular carcinoma cell growth and metastasis via β-catenin activation in a notch1/akt dependent manner.	Journal Of Experimental & Clinical Cancer Research	Hepatocellular carcinoma	PubMed	2023

Table 2 shows the objective, type of study and results, referring to the topic, found in the studies selected for the integrative review.

Table 2. Description of the articles regarding their objective, type of study, and expected results.

N.º	Objective	Type of study	Results obtained
[14]	To present a new model to demonstrate these cellular communications.	Experimental study	Elevated γ-secretase activity and increased expression of MAML2 induced greater NOTCH1 signaling in prostate cancer cells, which enhanced tumor cell proliferation and invasion. This potentially provided a therapeutic target for prostate cancer.
[18]	To investigate the role of the NOTCH pathway in the prognosis of HNSCC	Cohort study	NOTCH1 expression was significantly associated with early stages (I–II), non-recurrent disease, and higher overall survival (OS) and disease-specific survival (DSS) rates ($p < 0.001$).
[19]	To identify the underlying factors involved in the development of HNSCC, as well as to further distinguish between HPV-positive and HPV-negative HNSCC.	Experimental study	Loss of canonical Notch signaling enhanced tumorigenesis in both contexts and also led to an increase in nuclear β-catenin, a marker of elevated tumorigenic potential.
[20]	To investigate the role of the Notch pathway in immune evasion within the tumor microenvironment of head and neck squamous cell carcinoma (HNSCC).	Experimental study	Notch1 inhibition reduces the number of immunosuppressive cells in Tgfbr1/Pten 2cKO mice.
[21]	To describe recent insights into NOTCH pathway genes, including NOTCH genes, in HNSCC.	Descriptive study	A significant rate of NOTCH1 mutations was revealed, identifying NOTCH1 as the second most frequently mutated gene after TP53. NOTCH activity in HNSCC is therefore context-dependent, and NOTCH in HNSCC is considered to play a bimodal role as both a tumor suppressor and an oncogene.
[22]	To determine the potential of NOTCH1 loss as a strategy to inhibit aggressive prostate cancer growth and metastasis, as well as the synergy of Notch1 inhibition with antiandrogen therapies.	Experimental study	Loss of NOTCH1 in aggressive prostate cancer cells decreases proliferation, invasion, and tumorsphere formation.
[23]	To investigate the effect of direct contact between PCa cells and MSCs on prostate cancer stemness and its underlying mechanisms.	Experimental study	Inhibition of the Notch1 pathway associated with the Jagged1 ligand significantly reduced tumor growth.
[24]]	To investigate the frequency and clinicopathological characteristics associated with Notch1 gene expression using immunohistochemistry and real-time polymerase chain reaction in patients with prostate cancer.	Cohort study	We found significant expression of the Notch1 gene in 17 (28.3%) out of 60 patients with prostate carcinoma, demonstrating an association of this gene with poor prognosis.
[25]	To report a unique case of metastatic penile squamous cell carcinoma associated with high levels of activated NOTCH1 and two different gain-of-function NOTCH1 mutations.	Case report	Here, we report a case of metastatic squamous cell carcinoma, presumably originating from the penis, that harbors two distinct and strong gain-of-function NOTCH1 mutations, resulting in high levels of activated NOTCH1 within the tumor cell population.
[26]	To characterize the genomic landscape of PSCC using whole-exome sequencing.	Experimental study	We observed frequently altered pathways with potential therapeutic implications: alterations in the Notch pathways (30% of the samples showed alterations).
[27]	To characterize the mutational signature of 30 cases of HPV-associated PSCC in Latin American individuals using whole-exome sequencing.	Experimental study	For the most frequently altered genes, variants occur in a single tumor, such as NOTCH1 and TP53.

[28]	To identify novel common targets.	Experimental study	We observed that multiple genes associated with oncogenic pathways were highly mutated in PSCC samples. The Notch pathway was the most frequently affected in PSCC samples, with 70.6% of the cases (n = 24) showing mutations in at least one of the 17 Notch-related genes, including NOTCH1 (n = 15, 44.1%).
[29]	To characterize the somatic mutation landscape and compare genetic features among PSCC patients with different lymph node statuses using whole-exome sequencing.	Cohort study	These studies revealed that somatic alterations are associated with penile carcinogenesis, including frequent mutations in the TP53, CDKN2A, NOTCH1, and PIK3CA genes.
[30]	To evaluate the roles of the Wnt, Hedgehog, and Notch pathways in the stemness and functions of CSCs, and to summarize therapeutic studies targeting these pathways to eliminate CSCs and improve overall cancer treatment outcomes.	Descriptive study	High Notch1 expression was correlated with a lower degree of cellular differentiation in 80% of usual-type epithelial hyperplasias, 67% of ductal carcinoma in situ cases, 89% of invasive ductal carcinomas, and 57% of invasive lobular carcinomas, in addition to playing a key role in epithelial–mesenchymal transition.
[31]	Elucidating the microenvironmental signals (i.e., the tumor perivascular niche) that influence aggressive breast cancer cells may provide effective treatment strategies.	Experimental study	In this study, we provide evidence that endothelial Jag1, derived from tumor microenvironmental signals, elevates Zeb1 expression in neighboring breast CSCs through a Notch1-mediated juxtacrine mechanism.
[32]	To demonstrate a designed OptoNotch (oN) system capable of regulating NOTCH1 activity with spatiotemporal precision.	Experimental study	They confirmed that Notch1 activity is indeed involved in cell proliferation as well as in resistance to chemotherapeutic agents used in the treatment of breast cancer.
[33]	To identify 169 potential cancer drivers, among which Notch1 is one of the main candidates for accelerating TNBC by promoting epithelial–mesenchymal transition (EMT) and regulating the cell cycle.	Experimental cohort study	It was suggested that NOTCH1 activation abolishes mitotic catastrophe caused by BRCA1 deficiency by reducing DNA damage.
[34]	To explore the regulatory role of Notch1 in HCC metastasis.	Cohort study	They emphasized that patients with hepatic carcinoma showing high hepatic expression levels of Notch1 had lower disease-free survival compared to those with low hepatic expression levels of Notch1.
[35]	We investigated whether ABL proto-oncogene 1, non-receptor tyrosine kinase (ABL1), is involved in the development of hepatocellular carcinoma.	Experimental study	NOTCH1 knockdown in HCC cells significantly reduced cell growth.
[36]	To investigate the exact role of Notch1 in hepatocarcinogenesis and its influence on survival, as well as to determine its potential as a targeted therapy.	Retrospective study	Notch1 expression was higher in low-grade HCC than in high-grade hepatic carcinoma ($p = 0.036$). Notch1 expression showed an inverse correlation with mitotic count ($p = 0.008$) and necrosis ($p = 0.005$). Disease-free survival was lower in patients with low levels of Notch1 expression ($p = 0.045$).
[37]	To elucidate the molecular mechanisms underlying HCC progression, as well as to identify effective therapeutic strategies against HCC progression.	Experimental study	HCC patients with high levels of NOTCH1 expression showed increased life expectancy. On the other hand, NOTCH1 may contribute to tumor formation in HCC by activating the epithelial–mesenchymal transition (EMT) pathway.