Acta Scientific Microbiology (ISSN: 2581-3226)

Volume 8 Issue 1 January 2025

Review Article

The MYBL2 Mechanism as an Oncogene in Cancers-Current Perspective

Binta Sarr[1], Serge Yannick Ouedraogo[2] and Ousman Bajinka[3]*

[1]*Exact Science Corporation, 650 Forward Drive, Madison, Wi 53711, Madison, Wisconsin, United States*

[2]*Shandong Provincial Key Laboratory of Precision Oncology, Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences, 440 Jiyan Road, Jinan, Shandong 250117, P. R. China*

[3]*School of Medicine and Allied Health Sciences, University of The Gambia, The Gambia*

***Corresponding Author:** Ousman Bajinka, School of Medicine and Allied Health Sciences, University of The Gambia, The Gambia.

Received: October 08, 2024

Published: December 10, 2024

Abstract

Background: The abnormal cell division and replication leads to cancerous cells that eventually cause tumors in humans. This is typically due to the metabolic stress as the ultimatal causal factor cancer. Among the therapeutically approaches to cancer, targeted therapy is gaining much grounds on energy reprogramming. One such is to modulate the tumor cell division in order to stop the proliferation, inhibit angiogenesis and cell cycle arrest. Among the recent transcription factors, MYB Proto-Oncogene Like 2 (MYBL2) from Myb-related protein B protein is a very promising target. MYBL2 is studied to modulate cell cycle progression and physiological processes such as cell survival and differentiation.

Objective: Despite the number of recent studies with cutting edge evidence based roles played by this oncogene, the exact mechanism induced by this gene is not established. Since modulating cell cycle progression in oncology is imperative for both combined therapies and monotherapies such as immunotherapies, there is a need to harness the mechanisms associated with gene entities. This review summarized the updated MYBL2 studies as an oncogene based on its biological functions and mechanisms on various cancers. Furthermore, the review discussed the known mechanistic characteristics and associated genes known with MYBL2.

Conclusion: In sum, with this systematic screening on papers based on MYBL2 oncogene, no two studies are absolutely uniform with regards to the molecular reactions and biological mechanism. Although, majority of the studies could establish delay cell cycle proliferation as anti-tumorigenesis, the biological pathways are not even cancer specific and thus, the need for comprehensive studies to harness the biological mechanisms.

Keywords: MYBL2; Cell Cycle; Energy Metabolism; Cancers; Disease Mechanisms

Abbreviation

ABRACL: Actin-binding Rho Activating C-Terminal Like; ADT: Androgen-Deprivation Therapy; ACTN4: Alpha-Actinin-4; Akt: Activates Phosphorylated-Protein Kinase B; ALL: Acute Lymphoblastic Leukemia; AML: Acute Myeloid Leukemia; CAF: Cancer Associated Fibroblasts; CDCA3: Cell Division Cycle-Associated Protein 3; ccRRC: Cell Renal Cell Carcinoma; circular RNA: cirRNA; CRC: Colorectal Cancer; DATS: Diallyl TrisulfideDREAM: GMB: Glioblastoma Multiforme; EC: Endometrial Cancer; ERK: Extracellular Signal-Regulated Kinases; EwS: Ewing sarcoma; FLT3-ITD: FMS-like Tyrosine Kinase-3 Internal Tandem Duplication; FOXMI: Forkhead Box M1; HCC: Hepatocellular Carcinoma; LncRNA: Long Noncoding RNA; MDS: Myelodysplastic Syndromes; MM: Multiple Myeloma; PA: Pancreatic Adenocarcinoma; PDAC: Pancreatic Ductal Adenocarcinoma; PDT: Photodynamic Therapy; PITPNA-AS1: PITPNA

Antisense RNA 1; PTBP1: Polypyrimidine Tract-Binding Protein 1; NCAPH: Non-SMC Condensin I Complex Subunit H; NES: Natural Evolution Signature; PNI: Peri-Neural Invasion; RB-like: E2F and Multi-Vulval Class B; SKCM: Skin Cutaneous Melanoma; TNBC: Triple-Negative Breast Cancer; YAP: Yes-Associated Protein: SS: Synovial Sarcoma; TSCCs: Tongue Squamous Cell Carcinomas; TSS: Transcription Start Site

Introduction

Among the MYB family of transcription factors, MYBL2 is a highly conserved that plays a key role in physiological regulator during the cell cycle progression, survival and differentiation (Martin CM., *et al*. 2015) [1], making diagnostic and prognostic values (Qian X., *et al*. 2023) [2]. The deregulation of MYBL2 biological expression is key for the initiation and the progression in number of cancers tumor microenvironment (TME) (Musa J., *et al*. 2017) [3]. The phosphorylated MYBL2 during late G1 and S phase is facilitated by Cyclin CDK2 and this enhances its transactivation activity (Gautschi O., *et al*. 2018) [4]. This makes it a putative biomarker for anti-CDK2-therapy and the mechanism underpinning is predicted to come from releasing of the nuclear receptor co-repressors N-CoR and SMRT (Musa J., *et al*. 2019) [5]. This maintain MYBL2 in an inhibited state especially when non-phosphorylated. Since MYBL2 overexpression is linked to enhanced transactivation of anti-apoptotic cell, it can diminish cytokine dependence thereby enhancing resistance to apoptosis (Rosa-Ribeiro R., *et al*. 2014) [6]. MYBL2 affects the TME by influencing the cancer associated fibroblasts (CAF), immune infiltration level and expression level of $CD4^+$ T cells, $CD8^+$ T cells, and immune checkpoint-associated cells (Chen X., *et al*. 2021) [7]. The overexpression of MYBL2 in the tumor tissues was significantly correlated with a higher T classification, peri-neural invasion (PNI) and vital status in pancreatic ductal adenocarcinoma (PDAC) (Liu B., *et al*. 2021) [8].

During cell proliferation, *E2F1* and its target gene *MYBL2* contributes to the repression of Arachidonate 5-lipoxygenase, which is also known as 5-LO, ALOX5, 5-LOX or 5-lipoxygenase. This is an enzyme of non-heme iron coded by human gene ALOX5 gene from a family lipoxygenase. The ezymes is able to transform essential fatty acids substrates to leukotrienes in addition to other biologically active products thus, making it a target for pharmaceutical intervention (Rosa-Ribeiro R., *et al*. 2014) [9]. B-MYB promotes the chemoresistance to OXA via regulating the CCAT1/DNMT1/SOCS3 axis and oxaliplatin-resistant (Liu F., *et al*. 2023) [10] in CRC (Chen G, *et al* 2022) [11] and contributes to tamoxifen resistance in breast cancer (Li X., *et al*. 2020) [12]. MYBL2 overexpression with poor patient outcome are significantly correlated in numerous cancer entities (Mullen DJ., *et al*. 2020) [13]. In addition, it contributes to lagging anaphase chromosomes that can initiate aneuploidy in tumors (Pfister K., *et al*. 2018) [14]. MYBL2 is associated with natural evolution signature (NES) in regulating brain development (Wu L., *et al*. 2022) [15] and contribute to the evolution of glioblastoma multiform (GBM) (Jiang L., *et al*. 2020, Liu Y., *et al*. 2020) [16,17]. Among the studied types of cancer associated with MYBL2 oncogene are; Ewing sarcoma (EwS) (Prexler C., *et al*. 2022) [18], hepatocellular carcinoma prognostic (Wang Y., *et al*. 2023) [19], skin cutaneous melanoma (SKCM) (Huang CH., *et al*. 2022) [20], lung adenocarcinoma (Liu C., *et al*. 2017) [21], cell renal cell carcinoma (ccRCC), childhood acute lymphoblastic leukemia (ALL) (de Smith AJ., *et al*. 2018) [22], colorectal cancer (CRC) (Hao S., *et al*. 2019) [23], triple-negative breast cancer (TNBC) (Fiscon G., *et al*. 2021) [24] and TNBC-specific CRC transcription factors (Shi W., *et al*. 2023) [25], gall bladder cancer (Liang HB., *et al*. 2017) [26], basal cell carcinoma (Chae YK., *et al*. 2016) [27] and endometrial cancer (EC) (Le L., *et al*. 2021) [28]. From previous studies, MYBL2 knockdown slows cell proliferation in addition to the expression of G2/M genes with reduced amount of cells in the G2/M phase thus, serving as anti-tumor (Rosa-Ribeiro R., *et al*. 2014) [29]. MYBL2 is an oncogene that participates in carcinogenesis through its role in cell proliferation through cycle regulation, apoptosis, and cell differentiation. To this day, MYBL2's exact function is not known, and conflicting mechanisms of action have been published. Moreover, there is no review with an updated biological functions and mechanisms on MYBL2 on various cancers. To this end, this review gives a summary of the known mechanistic characteristics and associated genes known with MYBL2.

MYBL2 mechanisms in tumor proliferation

MYBL2 is studied for deregulation of the dimerization partner in a number of cancers. This RB-like, E2F and multi-vulval class B (DREAM) complex assembly is a protein complex that regulates the expression of cell cycle-dependent gene. For instace, through Wnt/β-catenin signaling pathway, cell division cycle 20 (CDC20) and MYBL2 inhibit apoptosis (Vera O., *et al*. 2021) [30]. Among the mechanism studied with MYBL2 includes, single nucleotide polymorphisms 20q13 gene coding region amplification and micro

RNAs regulations changes (Deng Q., *et al*. 2021) [31]. For instance, the uncoupling MYBL2 expression observed with negative transcriptional regulation, due to p53 mutation or the transformation by HPV16 E7 oncogene will enable MYBL2 to progressively bind to MuvB and forkhead box M1 (FOXM1) OV oncogenes. Specifically, FOXM1 plays a role in the control of cell proliferation and DNA break repairs as part of DNA damage checkpoint response (Qin WS *et al*, 2017) [32]. MYBL2-FOXM1 complex knockdown reduces the CHK1i-induced DNA replication stress. This prevention of premature mitosis during late S phase is positively correlated with resistance to CHK1 (Branigan TB., *et al*. 2021) [33]. In addition, MYBL2 interacts with FOXM1 to co-regulate the transcription of cell division cycle-associated protein 3 (CDCA3). Furthermore, MYBL2/FOXM1 and CDCA3 activates Wnt/β-catenin signaling in bladder cancer (Liu W., *et al*. 2022) [34]. FoxM1 expression can be reduced with MTDH knockdown to inhibit the expression of MYBL2 and further reduce tumor proliferation, the cell migration and invasion as seen in glioma cells (Fu J., *et al*. 2022) [35]. B-Myb overexpression activates phosphorylated-protein kinase B (Akt) and extracellular signal-regulated kinases (ERK) signaling pathways in NSCLC (Jin Y., *et al*. 2017) [36].

In MYBL2-dependent manner, oncogene yes-associated protein (YAP) can support cell proliferation (Wei T., *et al*. 2019) [37]. For instance, the YAP -dependent MYB family is studied with postnatal cardiomyocytes (Wang J., *et al*. 2019) [38]. YAP-mediated entry into mitosis is facilitated by MMB subunit B-MYB (Nientiedt M., *et al*. 2021) [39]. Overexpression of MYBL2 facilitates castration-resistant growth and metastatic capacity in androgen-dependent cells by promoting YAP1 transcriptional activity. It facilitates this via modulating the activity of the Rho GTPases RhoA and LATS1 kinase (Li Q., *et al*. 2021) [40]. Another MYBL2 adaptation to androgen deprivation is seen with prostate gland (Li ZB., *et al*. 2020) [41]. Lower MYBL2 levels enhance LNCaP and LAPC4 sensitivity to androgen deprivation and taxanes in prostate cancer (Yoshikawa Y., *et al*. 2022) [42]. B-MYB family is a tumor-promoting gene via suppressing IGFBP3 (Prexler C., *et al*. 2022) [43]. The DNA repair genes to some extent rely on the MYBL2 axis for regulation as in Wnt/β-catenin/MYBL2 axis (Huang CH., *et al*. 2022) [44]. Moreover, MYBL2 and A3B in B-Myb-A3B signaling contributes to cytosine-to-thymine (C-to-T) DNA mutation. Since this signaling can be attenuated with EGF receptor with afatinib, inhibiting EGF receptor seems a targeted therapy (Chou WC., *et al*. 2017) [45]. In synovial sarcoma (SS), MYBL2 contributes to diallyl trisulfide (DATS)-induced increased intracellular reactive oxygen spieces (ROS) and G2/M cell cycle arrest (Xia SL., *et al*. 2021) [46] (Figure 1).

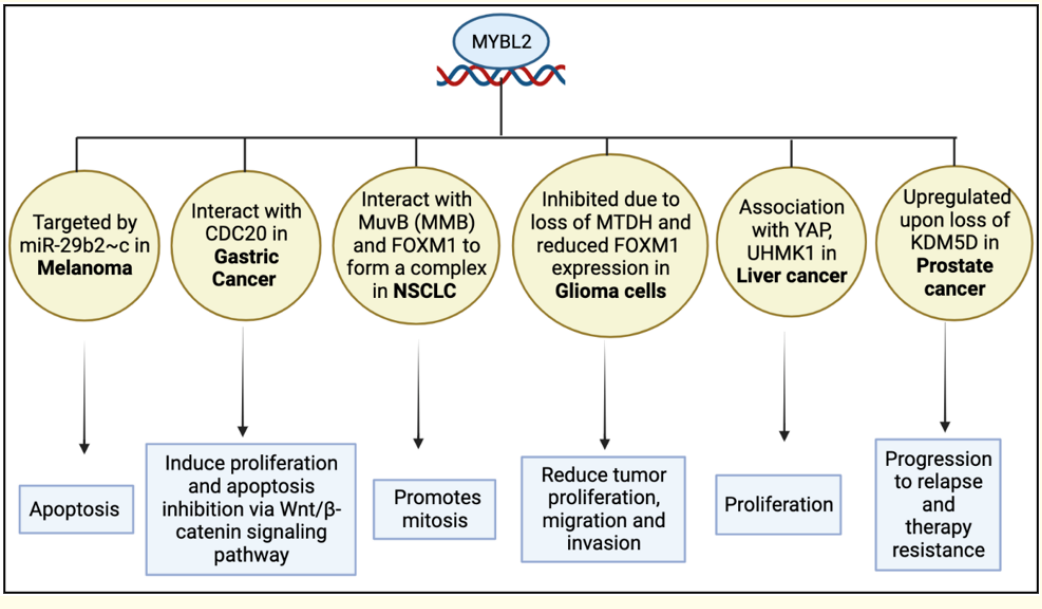

Figure 1: The mecahanisms of transcription factor MYBL2 implication in tumor proliferation across various cancer.

MYBL2 associated genes in cancer

With ChIP-seq data, ASCL1 colocalized on Ras/ErbB signaling gene locus, ZEB1 and HEB are key genes to regulate MYBL2 tumorigenesis mechanisms (Zhong F., *et al*. 2022) [47]. The role of MYBL2 in tumorigenesis are seen with inferior DFS in basal breast cancer (Johnson RH., *et al*. 2015) [48], regulating purine synthesis via regulating IMPDH1 (Zhao JZ., *et al*. 2022) [49] and binding to the protective variant, A allele of rs1024176 in breast cancer (Chou WC., *et al*. 2020) [50]. Induction of proinflammatory cytokines such as IFN-γ, IL-1β and IL-6, IL-8, IL-10 and TGF-β of RPSAP52 overexpression is modulated by MYBL2 in TSSCs proliferation (Wu X., *et al*. 2021) [51]. MYBL2 can be directly bound to the promoter of RRM2 gene and promote its transcription during S-phase together with TAF15 and MuvB components in CRC (Liu Q., *et al*. 2021) [52]. MYBL2 is a crucial regulator of DSB repair and i*MYBL2* expression levels predict cellular response to identify patients with defects in DNA repair. It can transcriptionally activate Actin-binding Rho activating C-terminal like (ABRACL) and can reverse the effects of ABRACL knockdown on cell malignant biological functions (Li J and Chen H., *et al*. 2022) [53]. Upregulating the MYBL2-mTOR axis enables MALAT1 to initiate tumorigenesis (Mu X., *et al.* 2022) [54]. Moreover, MYBL2 directly binds to the transcription start site (TSS) of Non-SMC Condensin I Complex Subunit H (NCAPH) gene in lung adenocarcinoma (LUAD) (Xiong YC., *et al*. 2020) [55]. MYBL2 transcriptional factor is promoted by nuclear translocation of hnRNPD, which is facilitated by PFDN2 in gastric cancer (Fan X., *et al*. 2021) [56]. The directly transactivating of B-Myb and E2F2 to induce malignant phenotypes in CC reveal the molecular mutual collaboration (Geng GJ., *et al*. 2018) [57].

Micro RNA as MYBL2 inhibitor

In apoptosis based therapies, the role of miRNAs as tumor inhibitor is crucial (Lee YJ., *et al*. 2017) [58]. miR-361-3p targets circ-MYBL2 directly and reverse the effects of si-circ-MYBL2 of tumor progression (Mao Y and Wang C., *et al*. 2021) [59]. For instance, with G2 arrest, ginkgetin is studied to regulate bMyb via modulating miR-34a (Bayley R., *et al*. 2020) [60]. Moreover, miR-30b-5p inhibits the progression of tumor via targeting MYBL2 expression in medulloblastoma (MB) (Xu C., *et al*. 2020) [61]. MYBL2 is targeted by miR-143-3p and regulates breast cancer cell proliferation and apoptosis (Chen J and Chen X 2018) [62]. miR-221/222- MYB family-TIMP2 axis regulatory role for breast cancer metastatic is established (Gorbatenko A., *et al*. 2019) [63]. One specific miRNA common with MYBL2 is miR-18a (Luengo-Gil G., *et al*. 2019) [64]. miR-30a inhibits androgen-independent prostate cancer by targeting MYBL2 (Li X., *et al*. 2020) [65]. Moreover, with upregulating MYBL2, long noncoding RNA (LncRNA) LINC01139 can promote tumor progression through competitively binding to miR-30 family (Pattschull G., *et al*. 2019) [66]. In addition, miR-30a overexpression increases cell apoptosis, induce cell cycle arrest and attenuate expression levels of MYBL2 (Druz A., *et al*. 2013) [67].

In regulating cell cycle signaling via miR-30c-2-3p/MYBL2 axis, a tumorigenesis role in LUAD is studied with LINC00346 (He Q., *et al*. 2023) [68]. MYBL2 interacts with a loop of LncRNA LOXL1 antisense RNA 1 (LOXL1-AS1) promoter to give LOXL1-AS1/miR-423-5p/MYBL2, indicating a positive feedback. MYBL2 knockdown could counteract miR-423-5p repression-mediated enhancement on the progression of LOXL1-AS1 downregulated cells in LUAD (Li W., *et al*. 2019) [69]. MYBL2 activated LncRNA PITPNA antisense RNA 1 (PITPNA-AS1) plays an oncogenic role in triple-negative breast cancer (TNBC) via upregulating SIK2 in breast cancer (Liu B., *et al*. 2021) [70]. Another miR-29 target transcription factor is MAFG. This and MYBL2 are partially associated with miR-29b2∼c expression attenuation thereby leading to melanoma (Xu Q., *et al*. 2021) [71].

MM-associated circular RNA (Circ-MYBL2)

circ-MYBL2 can suppress the effects of miR-28 on tumor proliferation and induce apoptosis (Druz A., *et al*. 2013) [72]. In addition, circ-MYBL2 affects the phosphorylation level of its linear isoform, in which it facilitates the binding of Cyclin F to MYBL2, dampening MYBL2 phosphorylation and activation in multiple myeloma (MM) (Yu S., *et al*. 2020) [73]. Moreover, circMYBL2 activates FMS-like tyrosine kinase-3 Internal tandem duplication (FLT3-ITD)-dependent signaling pathways. It enhances the translational efficiency of FLT3 kinase via increasing the binding of polypyrimidine tract-binding protein 1 (PTBP1) to FLT3 messenger RNA (Sun YM., *et al*. 2019) [74]. circ-MYBL2 overexpression increases miR-92b expression while reducing mature miR-92b level. Therefore, circ-MYBL2 inhibits cell proliferation and suppresses the effect of miR-92b in gastric cancer (Luo R. 2022) [75]. MYBL2 is among the frequent miR-29a-downregulated target genes (Dey S., *et al*. 2020) [76]. An instance is the synergistically downregulation of miR-19a via methylation to suppress tumor proliferation in pancreatic adenocarcinoma (PA) (Qian X., *et al*. 2023) [77]. In addition, MYBL2/Ser241 can arrest leukemia at prometaphase (Morita K., *et al*. 2020) [78]. Since MYBL2 binds to OPA3, a promoter region,

and catalyze transcription, *MYBL2* knockdown will seize aerobic glycolysis in hepatocellular carcinoma (HCC) (Liu M., *et al*. 2019) [79]. Alpha-actinin-4 (ACTN4) and MYBL2 association in tumor progression requires further studies (Gründl M., *et al*. 2020) [80].

Conclusion

In a more specific approach to cancer research, in addition to immunotherapy, radiotherapy and chemotherapy, energy metabolism is fundamental. Among the genes and protiens that influence the energy metabolism of tumor mechanism is MYBL2. This gene enhcances cell cycle progression for tumor evasion and dorminanating the immune cells via TME. This review could establish MYBL2 as cell cycle modulator, survival and the differentiation. Based on its biological functions and mechanisms, no two study are seen with a uniform pathway. Although, majority of the studies could establish delay cell cycle proliferation as anti-tumorigenesis, the biological pathways are not even cancer specific and thus, the need for comprehensive studies to harness the biological mechanisms. Moreover, tobacco (Nicotine), liquour, carcinogens as in the packed food additives etc. needs can hold key to the cellular mechanism.

Acknowledgements

Not applicable.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Material

Not applicable.

Competing Interests

The authors declare no competing interest.

Funding

Not applicable.

Authors' Contributions

All authors contributed equally to this manuscript.

Bibliography

1. Bayley R., *et al*. "MYBL2 Supports DNA Double Strand Break Repair in Hematopoietic Stem Cells". *Cancer Research* 78.20 (2018): 5767-5779.

2. Bayley R., *et al*. "MYBL2 amplification in breast cancer: Molecular mechanisms and therapeutic potential". *Biochimica et Biophysica Acta (BBA) - Reviews on Cancer* 1874.2 (2020): 188407.

3. Branigan TB., *et al*. "MMB-FOXM1-driven premature mitosis is required for CHK1 inhibitor sensitivity". *Cell Report* 34.9 (2021): 108808.

4. Chae YK., *et al*. "Inhibition of the fibroblast growth factor receptor (FGFR) pathway: the current landscape and barriers to clinical application". *Oncotarget* 8 (2016): 16052-16074.

5. Chen G., *et al*. "Colorectal cancer organoid models uncover oxaliplatin-resistant mechanisms at single cell resolution". *Cell Oncology (Dordr)* 45.6 (2022): 1155-1167.

6. Chen J and Chen X. "MYBL2 Is Targeted by miR-143-3p and Regulates Breast Cancer Cell Proliferation and Apoptosis". *Oncology Research* 26.6 (2018): 913-922.

7. Chen X., *et al*. "Pan-cancer analysis indicates that MYBL2 is associated with the prognosis and immunotherapy of multiple cancers as an oncogene". *Cell Cycle* 20.21 (2021): 2291-2308.

8. Chou WC., *et al*. "A functional variant near XCL1 gene improves breast cancer survival via promoting cancer immunity". *International Journal of Cancer* 146.8 (2020): 2182-2193.

9. Chou WC., *et al*. "B-Myb Induces APOBEC3B Expression Leading to Somatic Mutation in Multiple Cancers". *Scientific Report* 7 (2017): 44089.

10. de Smith AJ., *et al*. "BMI1 enhancer polymorphism underlies chromosome 10p12.31 association with childhood acute lymphoblastic leukemia". *International Journal of Cancer* 143.11 (2011): 2647-2658.

11. Deng Q., *et al*. "MYBL2 in synergy with CDC20 promotes the proliferation and inhibits apoptosis of gastric cancer cells". *Advances in Clinical and Experimental Medicine* 30.9 (2021): 957-966.

12. Dey S., *et al*. "miR-29a Is Repressed by MYC in Pancreatic Cancer and Its Restoration Drives Tumor-Suppressive Effects via Downregulation of LOXL2". *Molecular Cancer Research* 18.2 (2020): 311-323.

13. Druz A., *et al*. "Large-scale screening identifies a novel microRNA, miR-15a-3p, which induces apoptosis in human cancer cell lines". *RNA Biology* 10.2 (2013): 287-300.

14. Gautschi O., *et al*. "Aurora kinases as anticancer drug targets". *Clinical Cancer Research* 14 (2008): 1639–1648.

15. Geng GJ., *et al*. "MicroRNA-30a suppresses non-small-cell lung cancer by targeting Myb-related protein B". *Experimental and Therapeutic Medicine* 15.2 (2018): 1633-1639.

16. Gorbatenko A., *et al*. "HER2 and p95HER2 differentially regulate miRNA expression in MCF-7 breast cancer cells and downregulate MYB proteins through miR-221/222 and miR-503". *Scientific Report* 9.1 (2019): 3352.

17. Göbel T., *et al*. "Three-dimensional growth reveals fine-tuning of 5-lipoxygenase by proliferative pathways in cancer". *Life Science Alliance* 6.5 (2023): e202201804.

18. Gründl M., *et al*. "Interaction of YAP with the Myb-MuvB (MMB) complex defines a transcriptional program to promote the proliferation of cardiomyocytes". *PLoS Genetics* 16.5 (2020): e1008818.

19. Fan X., *et al*. "B-Myb Mediates Proliferation and Migration of Non-Small-Cell Lung Cancer via Suppressing IGFBP3". *International Journal of Molecular Sciences* 19.5 (2018): 1479.

20. Fan X., *et al*. "B-Myb accelerates colorectal cancer progression through reciprocal feed-forward transactivation of E2F2". *Oncogene* 40.37 (2021): 5613-5625.

21. Fiscon G., *et al*. "Gene network analysis using SWIM reveals interplay between the transcription factor-encoding genes HMGA1, FOXM1, and MYBL2 in triple-negative breast cancer". *FEBS Letter* 595.11 (2021): 1569-1586.

22. Fu J., *et al*. "Knockdown MTDH Inhibits Glioma Proliferation and Migration and Promotes Apoptosis by Downregulating MYBL2". *Mediators of Inflammation* 2022 (2022): 1706787.

23. Hao S., *et al*. "MicroRNA-related transcription factor regulatory networks in human colorectal cancer. *Medicine (Baltimore)* 98.15 (2019): e15158.

24. He Q., *et al*. "PFDN2 promotes cell cycle progression via the hnRNPD-MYBL2 axis in gastric cancer". *Frontiers in Oncology* 13 (2023): 1164070.

25. Huang CH., *et al*. "Identification of aberrantly methylated differentially expressed genes and pro-tumorigenic role of KIF2C in melanoma". *Frontiers in Genetics* 13 (2022): 817656.

26. Hui YJ., *et al*. "Up-regulation of ABCG2 by MYBL2 deletion drives Chlorin e6-mediated photodynamic therapy resistance in colorectal cancer". *Photodiagnosis and Photodynamic Therapy* 42 (2023): 103558.

27. Jiang L., *et al*. "Gene regulation network analysis reveals core genes associated with survival in glioblastoma multiforme". *Journal of Cellular and Molecular Medicine* 24.17 (2020): 10075-10087.

28. Jin Y., *et al*. "B-Myb Is Up-Regulated and Promotes Cell Growth and Motility in Non-Small Cell Lung Cancer". *International Journal of Molecular Sciences* 18.6 (2017): 860.

29. Johnson RH., *et al*. "Gene expression in "young adult type" breast cancer: a retrospective analysis". *Oncotarget* 6.15 (2015): 13688-13702.

30. Lee YJ., *et al*. "Ginkgetin induces G2-phase arrest in HCT116 colon cancer cells through the modulation of b Myb and miRNA34a expression". *International Journal of Oncology* 51.4 (2017): 1331-1342.

31. Le L., *et al*. "Overexpression of MYBL2 predicts poor prognosis and promotes oncogenesis in endometrial carcinoma". *European Journal of Histochemistry* 65.2 (2021): 3226.

32. Li J and Chen H. "Actin-binding Rho activating C-terminal like (ABRACL) transcriptionally regulated by MYB proto-oncogene like 2 (MYBL2) promotes the proliferation, invasion, migration and epithelial-mesenchymal transition of breast cancer cells". *Bioengineered* 13.4 (2022): 9019-9031.

33. Li M., *et al*. "Circ_0006332 promotes growth and progression of bladder cancer by modulating MYBL2 expression via miR-143". *Aging (Albany NY)* 11.22 (2019): 10626-10643.

34. Li Q., *et al*. "MYBL2 disrupts the Hippo-YAP pathway and confers castration resistance and metastatic potential in prostate cancer". *Theranostics* 11.12 (2021): 5794-5812.

35. Li X., *et al*. "miR-30a inhibits androgen-independent growth of prostate cancer via targeting MYBL2, FOXD1, and SOX4". *Prostate* 80.9 (2020): 674-686.

36. Li X., *et al*. "The role of MYB proto-oncogene like 2 in tamoxifen resistance in breast cancer". 52.1 (2021): 21-30.

37. Li W., *et al*. "LncRNA LOXL1-AS1 regulates the tumorigenesis and development of lung adenocarcinoma through sponging miR-423-5p and targeting MYBL2". *Cancer Medicine* 9.2 (2020): 689-699.

38. Li ZB., *et al*. "Long noncoding RNA LINC01139 promotes the progression of hepatocellular carcinoma by upregulating MYBL2 via competitively binding to miR-30 family". *Biochemical and Biophysical Research Communications* 525.3 (2020): 581-588.

39. Liang HB., *et al*. "MYBL2 is a Potential Prognostic Marker that Promotes Cell Proliferation in Gallbladder Cancer". *Cellular Physiology and Biochemistry* 41.5 (2017): 2117-2131.

40. Liu Z., *et al*. "Circular RNA circFAT1 (e2) Facilitates Cell Progression through the miR-30e-5P/MYBL2 Pathway in Glioma". *Dis Markers* 2023 (2023): 7418365.

41. Liu B., *et al*. "MYBL2-induced PITPNA-AS1 upregulates SIK2 to exert oncogenic function in triple-negative breast cancer through miR-520d-5p and DDX54". *Journal of Translational Medicine* 19.1 (2021): 333.

42. Liu C., *et al*. "Identification of transcription factors that may reprogram lung adenocarcinoma". *Artificial Intelligence in Medicine* 83 (2017): 52-57.

43. Liu F., *et al*. "Transcription factor B-MYB activates lncRNA CCAT1 and upregulates SOCS3 to promote chemoresistance in colorectal cancer". *Chemico-Biological Interactions* 374 (2023): 110412.

44. Liu M., *et al*. "MYB proto-oncogene like 2 promotes hepatocellular carcinoma growth and glycolysis via binding to the Optic atrophy 3 promoter and activating its expression". *Bioengineered* 13.3 (2022): 5344-5356.

45. Liu W., *et al*. "MYBL2 promotes proliferation and metastasis of bladder cancer through transactivation of CDCA3". *Oncogene* 41.41 (2022): 4606-4617.

46. Liu Q., *et al*. "A MYBL2 complex for RRM2 transactivation and the synthetic effect of MYBL2 knockdown with WEE1 inhibition against colorectal cancer". *Cell Death Disease* 12.7 (2021): 683.

47. Liu Y., *et al*. "Integrated regulatory models for inference of subtype-specific susceptibilities in glioblastoma". *Molecular Systems Biology* 16.9 (2020): e9506.

48. Luengo-Gil G., *et al*. "Clinical and biological impact of miR-18a expression in breast cancer after neoadjuvant chemotherapy". *Cell Oncology (Dordr)* 42.5 (2019): 627-644.

49. Luo R. "CircRNA circ-MYBL2 absorbs precursor miR-92b in the nucleus to suppress its role in enhancing gastric cancer cell proliferation". *The American Journal of the Medical Sciences* 364.4 (2022): 454-460.

50. Kaur A., *et al*. "WNT inhibition creates a BRCA-like state in Wnt-addicted cancer". *EMBO Molecular Medicine* 13.4 (2021): e13349.

51. Mao Y., *et al*. "A Cytoplasm-Enriched circRNA circ-MYBL2 is Downregulated in Non-Small Cell Lung Cancer and Sponges Oncogenic miR-28 to Regulate Cancer Cell Proliferation and Apoptosis". *Cancer Management Research* 13 (2021): 6499-6506.

52. Martin CM., *et al*. "The use of MYBL2 as a novel candidate biomarker of cervical cancer". *Methods in Molecular Biology* 1249 (2015): 241-251.

53. Morita K., *et al*. "Allosteric Activators of Protein Phosphatase 2A Display Broad Antitumor Activity Mediated by Dephosphorylation of MYBL2". *Cell* 181.3 (2020): 702-715.e20.

54. Mullen DJ., *et al*. "TENET 2.0: Identification of key transcriptional regulators and enhancers in lung adenocarcinoma". *PLoS Genetics* 16.9 (2020): e1009023.

55. Mu X., *et al*. "LncRNA-MALAT1 Regulates Cancer Glucose Metabolism in Prostate Cancer via MYBL2/mTOR Axis". *Oxidative Medicine and Cellular Longevity* 2022 (2022): 8693259.

56. Musa J., *et al*. "MYBL2 (B-Myb): a central regulator of cell proliferation, cell survival and differentiation involved in tumorigenesis". *Cell Death Disease* 8.6 (2017): e2895.

57. Musa J., *et al*. "Cooperation of cancer drivers with regulatory germline variants shapes clinical outcomes". *Nature Communication* 10.1 (2019): 4128.

58. Nientiedt M., *et al*. "B-MYB-p53-related relevant regulator for the progression of clear cell renal cell carcinoma". *Journal of Cancer Research and Clinical Oncology* 147.1 (2021): 129-138.

59. Pattschull G., *et al*. "The Myb-MuvB Complex Is Required for YAP-Dependent Transcription of Mitotic Genes". *Cell Report* 27.12 (2019): 3533-3546.e7.

60. Pfister K., *et al*. "Identification of Drivers of Aneuploidy in Breast Tumors". *Cell Report* 23.9 (2018): 2758-2769.

61. Prexler C., *et al*. "Correlation of Transcriptomics and FDG-PET SUVmax Indicates Reciprocal Expression of Stemness-Related Transcription Factor and Neuropeptide Signaling Pathways in Glucose Metabolism of Ewing Sarcoma". *Cancers (Basel)* 14.23 (2022): 5999.

62. Qian X., *et al*. "MM-associated circular RNA downregulates microRNA-19a through methylation to suppress proliferation of pancreatic adenocarcinoma cells". *Bioengineered* 13.4 (2022): 9294-9300.

63. Qin WS., *et al*. "The Short Isoform of Nuclear Mitotic Apparatus Protein 1 Functions as a Putative Tumor Suppressor". *Chinese Medical Journal (Engl)* 130.15 (2017): 1824-1830.

64. Rosa-Ribeiro R., *et al*. "Transcription factors involved in prostate gland adaptation to androgen deprivation". *PLoS One* 9.6 (2014): e97080.

65. Shi W., *et al*. "Super enhancer-driven core transcriptional regulatory circuitry crosstalk with cancer plasticity and patient mortality in triple-negative breast cancer". *Frontiers in Genetics* 14 (2023): 1258862.

66. Sun YM., *et al*. "circMYBL2, a circRNA from MYBL2, regulates FLT3 translation by recruiting PTBP1 to promote FLT3-ITD AML progression". *Blood* 134.18 (2019): 1533-1546.

67. Vera O., *et al*. "A MAPK/miR-29 Axis Suppresses Melanoma by Targeting MAFG and MYBL2". *Cancers (Basel)* 13.6 (2021): 1408.

68. Wang J., *et al*. "circ-MYBL2 Serves As A Sponge For miR-361-3p Promoting Cervical Cancer Cells Proliferation And Invasion". *Oncology Targets Therapy* 12 (2019): 9957-9964.

69. Wang Y., *et al*. "Construction and Analysis of Hepatocellular Carcinoma Prognostic Model Based on Random Forest". *Canadian Journal of Gastroenterology and Hepatology* 2023 (2023): 6707698.

70. Wei T., *et al*. "YAP-dependent induction of UHMK1 supports nuclear enrichment of the oncogene MYBL2 and proliferation in liver cancer cells". *Oncogene* 38.27 (2019): 5541-5550.

71. Wu L., *et al*. "Natural Coevolution of Tumor and Immunoenvironment in Glioblastoma". *Cancer Discovery* 12.12 (2022): 2820-2837.

72. Wu X., *et al*. "lncRNA RPSAP52 induced the development of tongue squamous cell carcinomas via miR-423-5p/MYBL2". *Journal of Cellular and Molecular Medicine* 25.10 (2021): 4744-4752.

73. Xia SL., *et al*. "In vitro anti-synovial sarcoma effect of diallyl trisulfide and mRNA profiling". *Gene* 816 (2022): 146172.

74. Xiong YC., *et al*. "Overexpression of MYBL2 promotes proliferation and migration of non-small-cell lung cancer via upregulating NCAPH". *Molecular and Cellular Biochemistry* 468.1-2 (2020): 185-193.

75. Xu C., *et al*. "MiR-30b-5p inhibits proliferation and promotes apoptosis of medulloblastoma cells via targeting MYB proto-oncogene like 2 (MYBL2)". *Journal of Investigative Medicine* 68.6 (2020): 1179-1185.

76. Xu Q., *et al*. "LINC00346 Sponges miR-30c-2-3p to Promote the Development of Lung Adenocarcinoma by Targeting MYBL2 and Regulating CELL CYCLE Signaling Pathway". *Frontiers in Oncology* 11 (2021): 687208.

77. Yoshikawa Y., *et al*. "Increased MYBL2 expression in aggressive hormone-sensitive prostate cancer". *Molecular Oncology* 16.22 (2022): 3994-4010.

78. Yu S., *et al*. "circRNA circ-MYBL2 is a novel tumor suppressor and potential biomarker in multiple myeloma". *Human Cell* 34.1 (2021): 219-228.

79. Zhao JZ., *et al*. "MYBL2 regulates de novo purine synthesis by transcriptionally activating IMPDH1 in hepatocellular carcinoma cells". *BMC Cancer* 22.1 (2022): 1290.

80. Zhong F., *et al*. "Combinatorial transcriptional regulation of HEB/ZEB1/ASCL1 and MYBL2 on Ras/ErbB signaling". *Biochemical and Biophysical Research Communications* 622 (2022): 170-176.