

MNT

Subjects: Oncology

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MNT (MAX's Next Tango) is a crucial modulator of MYC, controls several cellular functions, and is activated in most human cancers. It is the largest, most divergent, and most ubiquitously expressed protein of the MXD family. MNT was first described as a MYC antagonist and tumor suppressor. Indeed, 10% of human tumors present deletions of one MNT allele. However, some reports show that MNT functions in cooperation with MYC by maintaining cell proliferation, promoting tumor cell survival, and supporting MYC-driven tumorigenesis in cellular and animal models. Although MAX was originally considered MNT's obligate partner, it is also known that heterodimerize with MLX. Recent findings demonstrate that MNT can also work independently, as MNT forms homodimers and interacts with proteins both outside and inside of the proximal MYC network, as REL. These complexes are involved in a wide array of cellular processes, from transcriptional repression via SIN3 to the modulation of metabolism through MLX as well as immunity and apoptosis via REL.

Keywords: MNT ; MYC ; MAX ; REL ; transcriptional regulation ; proliferation ; cancer

1. MNT discovery and structure

The discovery of MNT (MAX's Next Tango) was reported by two independent laboratories in 1997. One group found MNT through a two-hybrid screening in yeasts using a murine cDNA library with MAX as the bait ^[1], while the other group isolated *MNT* (originally called *ROX*) in a search for transcribed sequences of the human chromosome 17p13.3 ^[2].

The MNT transcription factor belongs to the MXD family (originally called MAD), which shares a basic helix–loop–helix–leucine zipper (bHLHLZ) domain as well as a SIN3 interaction domain (SID) (Figure 1).

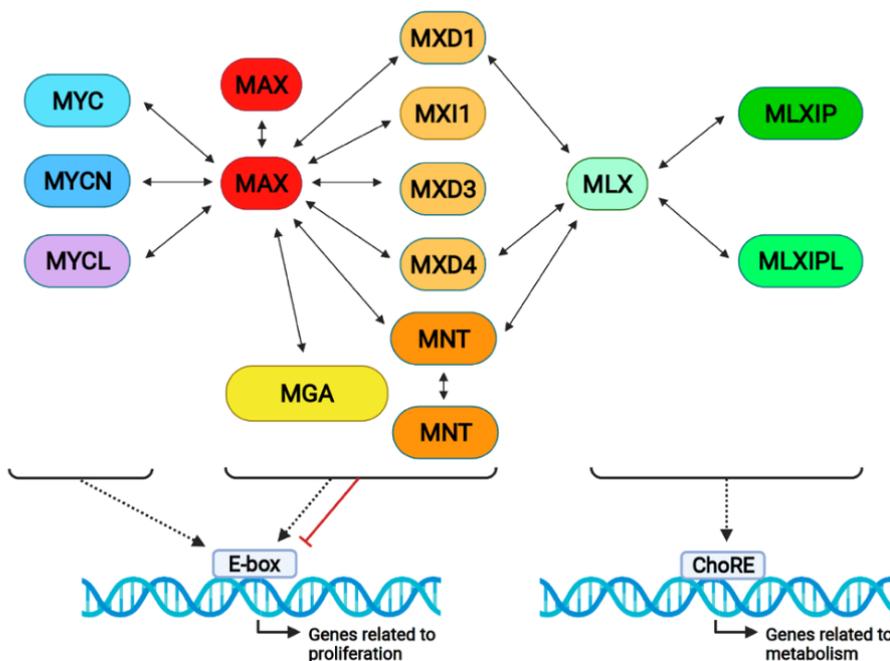


Figure 1. The proximal MYC

network and its interactions. MYC proteins form dimers with MAX and bind DNA on E-boxes, generally activating transcription. All MXD proteins bind to MAX and MXD1, and MXD4 and MNT also bind to MLX, activating or repressing gene transcription. MLX forms complexes with MLXIP (MONDOA) and MLXIPL (MONDOB), binding on ChoRE (carbohydrate response elements) and regulating metabolic genes. Notably, MAX and MNT form homodimers, as represented in the Figure.

The bHLHLZ is necessary for forming dimers with MAX and for binding to DNA on E-boxes (Enhancer-boxes). The SID establishes the interaction with SIN3 proteins, facilitating transcriptional repression (see below) ^{[3][4]}. Notably, the SID

repressor domain linked to Cas9 has been described as an efficient tool in CRISPR-mediated repression of targeted genes [5]. The canonical MXD proteins are MXD1, MXI1, MXD3, and MXD4. There is yet another member, MGA [6], that shows little similarity with the other MXDs, as it lacks the SID but binds to MAX through its bHLHLZ domain. MGA is a very large protein (3065 amino acids) and besides the bHLHLZ, it contains a T-box domain, which is described in Brachyury proteins and is a characteristic of the TBX (T-Box) transcription factor family. Its structure allows the regulation of both MAX-network and T-domain target genes, either as an activator or repressor [6][7][8]. Inactivation of *MGA* is frequent in human cancer, and a recent study has demonstrated that *MGA* functions as a tumor suppressor in murine models of lung carcinoma and in colorectal cancer organoids, partly due to the de-repression of *MYC* target genes [9].

MNT is a unique member of the MXD family due to several features; it is (i) the largest protein of the family; (ii) the most divergent gene in its sequences; (iii) ubiquitously expressed in human tissues; (iv) essential for mouse development; (v) expressed in both quiescent and proliferating cells; (vi) altered in human cancer; and (vii) is frequently involved in tumorigenesis (**Table 1**). It also plays an important role in modeling the oncogenic activities of *MYC*, as an antagonist in some models or as a cooperator in others (reviewed in [10]).

Table 1. Main differences between the human *MNT*, other human MXD proteins, and *MYC*. The sizes of the proteins are the largest canonical forms, according to the UniProt database. Aa, amino acids; ND, not done; DEL, deletions; AMP, amplifications; MUT, mutations; CTCL, Cutaneous T-cell lymphoma; MB, medulloblastoma; SS, Sezary Syndrome; ALL, acute lymphoblastic leukemia.

| | MNT | MXD1 | MXI1 (MXD2) | MXD3 | MXD4 | MYC | References |
|--|---|---|-------------------------------|--|-----------------------------|-----------------------------|------------------|
| Protein size | 582 aa | 221 aa | 228 aa | 206 aa | 209 aa | 439 aa | UniProt database |
| P-rich sequences | Yes | No | No | No | No | Yes | [2] |
| Phenotype of KO mice | Perinatally lethal/Craniofacial abnormalities | Viable/Increased immature granulocyte progenitors | Viable/Hyperplasia | Viable/Enhanced sensitivity to apoptotic stimuli | ND | Embryonic lethal E9.5–E10.5 | [11][12][13][14] |
| Proximal MYC Network interactors | MNT, MAX, MLX | MAX, MLX | MAX | MAX | MAX, MLX | MAX | Reviewed in [15] |
| Expression in cells | Quiescent and proliferating | Quiescent | Quiescent and proliferating * | Proliferating (S-phase) | Quiescent | Proliferating | Reviewed in [15] |
| Pan-cancer copy number alterations (%) | DEL 10 AMP 3 MUT 1 | DEL 2 AMP 6 MUT < 0.5 | DEL 8 AMP 4 MUT < 0.5 | DEL 7 AMP 8 MUT < 0.5 | DEL 6 AMP 5 MUT < 0.5 | DEL 2 AMP 21 MUT 1 | [16] |

MNT is evolutionarily conserved, an argument for its relevant role in cell biology. It is the sole MXD protein identified in the fly *Drosophila melanogaster* [23]. Flies express a “minimal” network composed of dMax, a single MYC protein (dMyc), and a sole MXD protein (dMnt). In general, *MNT* and *MXD1* are present along the phylogenetic tree, whereas the other MXD are only present in vertebrates (reviewed in [15]). Interestingly, dMnt is recruited to a higher number of *Drosophila* genes than dMyc is [24]. *MNT* orthologues are found in primitive pluricellular organisms from the Cnidaria (*Hydra* spp., *Nematostella* spp.) and Placozoa (*Trichoplax* spp.) phylum [25]. In contrast, the nematodes *C. elegans*, *C. briggsae*, and *Brugia malayi* lack *MNT* or *MYC* orthologs. However, these species, together with the trematode *Schistosoma mansoni*, present orthologs for MAX, MLX, MXD, and MLXIP [15][25][26].

In contrast to the other members of the MXD family, *MNT* is an essential protein during development, as *Mnt* knockout mice die soon after birth [11][27]. Mice with null homozygous deletions for *Mxd1*, *Mxd2*, or *Mxd3* show different defects [12][13][28] but survive to adult ages. *Mnt*-deficient embryos exhibit small size throughout development and, interestingly, show reduced levels of c-Myc and N-Myc [11]. *Mnt*-overexpressing embryos also have developmental defects, are of a smaller size, and have decreased cellularity [1]. These data suggest that a tight control of *MNT* levels is necessary for the correct development.

2. MNT Alterations in Cancer

MNT has been classified both as an oncogene or as a tumor suppressor gene based on its diverse activities in the cells. The data arguing that it behaves as tumor suppressor gene can be summarized as follows: (a) the tissue-specific loss of

Mnt in mouse models results in thymic lymphoma [29] or mammary tumors [27][30] (discussed below in point 7.1); (b) MEFs deficient in *Mnt* proliferate faster than wild-type cells and prematurely enter into the S phase [27] (discussed below in point 7.1); (c) in a pan-cancer study of The Cancer Genome Atlas (TCGA) data, heterozygous *MNT* deletion was found in 10% of the tumors (overall frequency) and in more than 20% of liver hepatocellular carcinomas, lung adenocarcinomas, sarcomas, and uterine carcinosarcomas [16].

The *MNT* locus at chromosome 17p13.3 is a hot spot for the loss of heterozygosity (LOH) in tumors such as sporadic breast cancer, medulloblastomas, or chronic lymphocytic leukemia (CLL) [21][31][32][33] as well as in ovarian cancer [34], astrocytomas [35], bladder cancer [36], or osteosarcoma [37]. However, no inactivating mutations in *MNT* have been found in these tumors. *MNT* deletions were also found in acute lymphoblastic leukemia [20], and a decrease in its levels in medulloblastomas, which was caused by the haploinsufficiency of chromosome 17p13.3 [21]. In the Sézary Syndrome, a malignant variant of cutaneous T-cell lymphoma, more than 60% of the patients show a loss of one or both *MNT* alleles [17][18], thus being the tumor with the highest frequency of *MNT* deletions. In agreement, the down-regulation of *MNT* expression has also been reported in Sézary Syndrome [19].

The analysis of the genomic data available in TCGA shows that 0.6% of tumors carry *MNT* mutations, with missense mutations being the most common. Most of these missense mutations are observed in colorectal, endometrial, melanoma, esophageic, and head and neck cancer. The majority of mutations map in the C-terminal half of the protein, i.e., downstream of the bHLHLZ domain.

Analysis of *MNT* mRNA expression in tumors shows that it is down-regulated in tumor samples compared to their normal tissue counterparts, including testicular germ cell tumors, uterine corpus endometrial carcinoma, and uterine carcinosarcoma. However, the opposite occurs in other tumor types, including cervical carcinoma, cholangiocarcinoma, acute myeloid leukemia, and pancreatic adenocarcinoma (Figure 2). These differences likely reflect the complex biological activities of *MNT*, which depend on the cellular context and the repertoire of proteins to interact with.

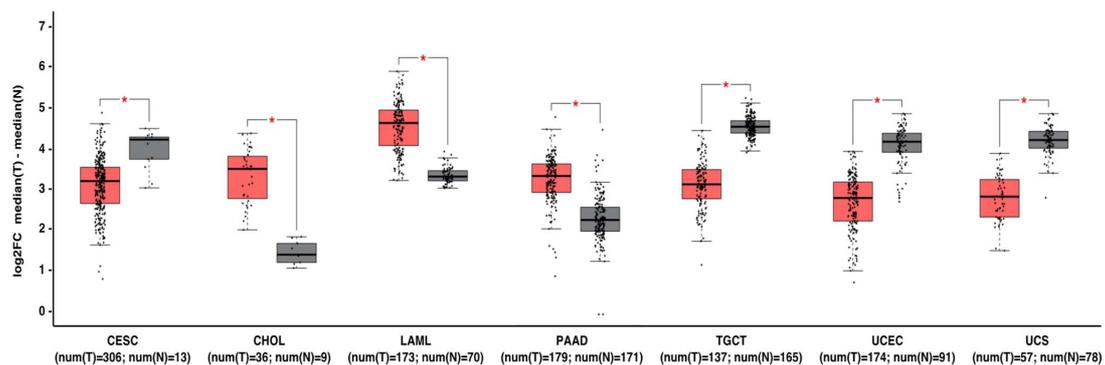


Figure 2. *MNT* can act as a tumor suppressor gene or oncogene depending on the tumor type. Gene expression profiling interactive analysis (GEPIA, <http://gepia.cancer-pku.cn/>) was performed to validate *MNT* mRNA expression in selected cancer type samples (in red) vs. normal samples (in grey). The expression data were first log₂(TPM+1) transformed for differential analysis, and the log₂FC was defined as median (tumor)–median (normal). Data are represented as mean ± SD (* *p* < 0.01). Abbreviations: CESC, cervical squamous cell carcinoma and endocervical adenocarcinoma; CHOL, Cholangiocarcinoma; LAML, acute myeloid leukemia; PAAD, pancreatic adenocarcinoma; TGCT, testicular germ cell tumors; UCEC, uterine corpus endometrial carcinoma; UCS, uterine carcinosarcoma.

3. Concluding Remarks

MYC has been one main focus of cancer research since it was identified in 1977–1979 as the oncogene captured by an avian oncogenic retrovirus [38][39][40] and was later found deregulated in 70% of human tumors [41]. However, in recent years, the interest in understanding the entire proximal MYC network has grown. The studies mentioned herein place *MNT* in a key position as a MYC modulator and demonstrate its diverse and essential roles in cell biology.

The functions of *MNT* are generally connected to MYC. Yet, studies in *MYC* knockout cells raised the question of whether MYC is a *MNT* antagonist rather than *MNT* a MYC antagonist [22]. *Mnt* knockdown in *Myc*-deficient rat fibroblasts showed that *Mnt* also conducts pro-survival functions in the absence of *Myc* [42]. Thus, the most important role of MYC might be to relieve *MNT*-mediated repression rather than activating transcription. In this scenario, *MNT* functions would remain unaffected by the presence or absence of MYC, while excessive MYC levels would impact *MNT* by impairing its transcriptional repressing activity.

The dual role of MNT in cancer, either as a MYC antagonist and or as a MYC cooperators, offers the possibility of using MNT as a therapeutic target. For instance, in MYC-driven lymphomas, tumor cells depend on MNT to survive. Thus, drugs that inhibit MNT activities (e.g., impairing critical interactions) would increase the efficacy of current therapies by enhancing apoptosis [43]. One possibility would be to test the MYC:MAX inhibitors Omomyc, 10058-F4, 10074-G5, Mad, or MYCMI-6, 11, and 14 on MNT. Some of these, such as Omomyc or Mad peptides, preferentially bind to MAX and not to MYC. Hence, they might be used as MNT inhibitors by impairing MNT–MAX interaction. However, this possibility has not been formally addressed yet [41][44][45][46][47]. In addition, as MNT downregulation stimulates NF- κ B signaling through the interaction with REL, NF- κ B inhibitors could be used in tumors with MNT loss, such as in CTCL (**Table 1**). Further research will uncover new roles of MNT in cell biology and will provide strategies for its use as a clinical target.

References

1. Hurlin, P.J.; Quéva, C.; Eisenman, R.N. Mnt, a novel Max-interacting protein is coexpressed with Myc in proliferating cells and mediates repression at Myc binding sites. *Genes Dev.* 1997, 11, 44–58.
2. Meroni, G.; Reymond, A.; Alcalay, M.; Borsani, G.; Tanigami, A.; Tonlorenzi, R.; Lo Nigro, C.; Messali, S.; Zollo, M.; Ledbetter, D.H.; et al. Rox, a novel bHLHZip protein expressed in quiescent cells that heterodimerizes with Max, binds a non-canonical E box and acts as a transcriptional repressor. *EMBO J.* 1997, 16, 2892–2906.
3. Ayer, D.E.; Lawrence, Q.A.; Eisenman, R.N. Mad-max transcriptional repression is mediated by ternary complex formation with mammalian homologs of yeast repressor Sin3. *Cell* 1995, 80, 767–776.
4. Grzenda, A.; Lomberk, G.; Zhang, J.S.; Urrutia, R. Sin3: Master scaffold and transcriptional corepressor. *Biochim. Biophys. Acta Gene Regul. Mech.* 2009, 1789, 443–450.
5. Raffener, P.; Hart, J.R.; García-Caballero, D.; Bar-Peled, L.; Weinberg, M.S.; Vogt, P.K. An MXD1-derived repressor peptide identifies noncoding mediators of MYC-driven cell proliferation. *Proc. Natl. Acad. Sci. USA* 2020, 117, 6571–6579.
6. Hurlin, P.J.; Steingrimsson, E.; Copeland, N.G.; Jenkins, N.A.; Eisenman, R.N. Mga, a dual-specificity transcription factor that interacts with Max and contains a T-domain DNA-binding motif. *EMBO J.* 1999, 18, 7019–7028.
7. Rikin, A.; Evans, T. The Tbx/bHLH Transcription Factor mga regulates gata4 and Organogenesis. *Dev. Dyn.* 2010, 239, 535–547.
8. Ogawa, H.; Ishiguro, K.; Gaubatz, S.; Livingston, D.M.; Nakatani, Y. A Complex with Chromatin Modifiers That Occupies E2F- and Myc-Responsive Genes in G0 Cells. *Science* 2002, 296, 1132–1136.
9. Mathsyaraja, H.; Catchpole, J.; Eastwood, E.; Babaeva, E.; Geuenich, M.; Cheng, P.F.; Freie, B.; Ayers, J.; Yu, M.; Wu, N.; et al. Loss of MGA mediated Polycomb repression promotes tumor progression and invasiveness. *Elife* 2021, 28, e64212.
10. Yang, G.; Hurlin, P.J. MNT and Emerging Concepts of MNT-MYC Antagonism. *Genes* 2017, 8, 83.
11. Toyo-oka, K.; Hirotsune, S.; Gambello, M.J.; Zhou, Z.; Olson, L.; Rosenfeld, M.G.; Eisenman, R.; Hurlin, P.; Wynshaw-Boris, A. Loss of the Max-interacting protein Mnt in mice results in decreased viability, defective embryonic growth and craniofacial defects: Relevance to Miller-Dieker syndrome. *Hum. Mol. Genet.* 2004, 13, 1057–1067.
12. Foley, K.P.; McArthur, G.A.; Quéva, C.; Hurlin, P.J.; Soriano, P.; Eisenman, R.N. Targeted disruption of the MYC antagonist MAD1 inhibits cell cycle exit during granulocyte differentiation. *EMBO J.* 1998, 17, 774–785.
13. Schreiber-Agus, N.; Meng, Y.; Hoang, T.; Hou, H.; Chen, K.; Greenberg, R.; Cordon-Cardo, C.; Lee, H.-W.; DePinho, R.A. Role of Mxi1 in ageing organ systems and the regulation of normal and neoplastic growth. *Nature* 1998, 393, 483–487.
14. Queva, C.; McArthur, G.A.; Iritani, B.M.; Eisenman, R.N. Targeted Deletion of the S-Phase-Specific Myc Antagonist Mad3 Sensitizes Neuronal and Lymphoid Cells to radiation-induced apoptosis. *Mol. Cell. Biol.* 2001, 21, 703–712.
15. Diolaiti, D.; McFerrin, L.; Carroll, P.A.; Eisenman, R.N. Functional interactions among members of the MAX and MLX transcriptional network during oncogenesis. *Biochim. Biophys. Acta* 2015, 1849, 484–500.
16. Schaub, F.X.; Dhankani, V.; Berger, A.C.; Trivedi, M.; Richardson, A.B.; Shaw, R.; Zhao, W.; Zhang, X.; Ventura, A.; Liu, Y.; et al. Pan-cancer Alterations of the MYC Oncogene and Its Proximal Network across the Cancer Genome Atlas. *Cell Syst.* 2018, 6, 282–300.e2.
17. Boonk, S.E.; Zoutman, W.H.; Marie-Cardine, A.; van der Fits, L.; Out-Luiting, J.J.; Mitchell, T.J.; Tosi, I.; Morris, S.L.; Moriarty, B.; Booken, N.; et al. Evaluation of Immunophenotypic and Molecular Biomarkers for Sézary Syndrome Using Standard Operating Procedures: A Multicenter Study of 59 Patients. *J. Investig. Dermatol.* 2016, 136, 1364–1372.

18. Van Doorn, R.; Dijkman, R.; Vermeer, M.H.; Out-Luiting, J.J.; Van Der Raaij-Helmer, E.M.H.; Willemze, R.; Tensen, C.P. Aberrant expression of the tyrosine kinase receptor EphA4 and the transcription factor twist in Sézary syndrome identified by gene expression analysis. *Cancer Res.* 2004, 64, 5578–5586.
19. Vermeer, M.H.; Van Doorn, R.; Dijkman, R.; Mao, X.; Whittaker, S.; Van Voorst Vader, P.C.; Gerritsen, M.J.P.; Geerts, M.L.; Gellrich, S.; Söderberg, O.; et al. Novel and highly recurrent chromosomal alterations in Sézary Syndrome. *Cancer Res.* 2008, 68, 2689–2698.
20. Guo, X.; Pan, L.; Zhang, X.; Suo, X.; Niu, Z.; Zhang, J.; Wang, F.; Dong, Z.; Da, W.; Ohno, R. Expression and mutation analysis of genes that encode the Myc antagonists Mad1, Mxi1 and Rox in acute leukaemia. *Leuk. Lymphoma* 2007, 48, 1200–1207.
21. Cvekl, A.; Zavadil, J.; Birshtein, B.K.; Grotzer, M.A.; Cvekl, A. Analysis of transcripts from 17p13.3 in medulloblastoma suggests ROX/MNT as a potential tumour suppressor gene. *Eur. J. Cancer* 2004, 40, 2525–2532.
22. Wahlström, T.; Henriksson, M. Mnt Takes Control as Key Regulator of the Myc/Max/Mxd Network. *Adv. Cancer Res.* 2007, 97, 61–80.
23. Loo, L.W.M.; Secombe, J.; Little, J.T.; Leni-Sue Carlos, L.-S.; Yost, C.; Cheng, P.-F.; Flynn, E.M.; Edgar, B.A.; Eisenman, R.N. The Transcriptional Repressor dMnt Is a Regulator of Growth in *Drosophila melanogaster*. *Mol. Cell. Biol.* 2005, 25, 7078–7091.
24. Orian, A.; van Steensel, B.; Delrow, J.; Bussemaker, H.J.; Li, L.; Sawado, T.; Williams, E.; Loo, L.W.M.; Cowley, S.M.; Yost, C.; et al. Genomic binding by the *Drosophila* Myc, Max, Mad/Mnt transcription factor network. *Genes Dev.* 2003, 17, 1101–1114.
25. McFerrin, L.G.; Atchley, W.R. Evolution of the Max and Mix networks in animals. *Genome Biol. Evol.* 2011, 3, 915–937.
26. Johnson, D.W.; Llop, J.R.; Farrell, S.F.; Yuan, J.; Stolzenburg, L.R.; Samuelson, A.V. The *Caenorhabditis elegans* Myc-Mondo/Mad Complexes Integrate Diverse Longevity Signals. *PLoS Genet.* 2014, 10, e1004278.
27. Hurlin, P.J.; Zhou, Z.; Toyo-oka, K.; Ota, S.; Walker, W.L.; Hirotsune, S.; Wynshaw-boris, A. Deletion of Mnt leads to disrupted cell cycle control and tumorigenesis. *EMBO J.* 2003, 22, 4584–4596.
28. Schreiber-Agus, N.; Chin, L.; Chen, K.; Torres, R.; Rao, G.; Guida, P.; Skoutchi, A.; Depinho, R.A. An Amino-Terminal Domain of Mxi1 Mediates Anti-Myc Oncogenic Activity and Interacts with a Homolog of the Yeast Transcriptional Repressor SIN3. *Cell* 1995, 80, 777–786.
29. Dezfouli, S.; Bakke, A.; Huang, J.; Wynshaw-Boris, A.; Hurlin, P.J. Inflammatory Disease and Lymphomagenesis Caused by Deletion of the Myc Antagonist Mnt in T Cells. *Mol. Cell. Biol.* 2006, 26, 2080–2092.
30. Toyo-oka, K.; Bowen, T.J.; Hirotsune, S.; Li, Z.; Jain, S.; Ota, S.; Lozach, L.E.; Bassett, I.G.; Lozach, J.; Rosenfeld, M.G.; et al. Mnt-Deficient Mammary Glands Exhibit Impaired Involution and Tumors with Characteristics of Myc Overexpression. *Cancer Res.* 2006, 66, 5565–6894.
31. Edelmann, J.; Holzmann, K.; Miller, F.; Winkler, D.; Buhler, A.; Zenz, T.; Bullinger, L.; Kuhn, M.W.M.; Gerhardinger, A.; Bloehdorn, J.; et al. High-resolution genomic profiling of chronic lymphocytic leukemia reveals new recurrent genomic alterations. *Blood* 2012, 6, 4783–4794.
32. Lo Nigro, C.; Venesio, T.; Reymond, A.; Meroni, G.; Alberici, P.; Cainarca, S.; Enrico, F.; Stack, M.; Ledbetter, D.H.; Liscia, D.S.; et al. The Human ROX Gene: Genomic Structure and Mutation Analysis in Human Breast Tumors. *Genomics* 1998, 282, 275–282.
33. Sommer, A.; Waha, A.; Tonn, J.; Sörensen, N.; Hurlin, P.J.; Eisenman, R.N.; Lüscher, B.; Pietsch, T. Analysis of the MAX-binding protein MNT in human medulloblastomas. *Int. J. Cancer* 1999, 82, 810–816.
34. Phillips, N.; Ziegler, M.; Saha, B.; Xynos, F. Allelic loss on chromosome 17 in human ovarian cancer. *Int. J. Cancer* 1993, 54, 85–91.
35. Saxena, A.; Clark, W.C.; Robertson, J.T.; Ikejiri, B.; Oldfield, E.H.; Ali, I.U. Erratum: Evidence for the involvement of a potential second tumor suppressor gene on chromosome 17 distinct from p53 in malignant astrocytomas (*Cancer Research* (December 1, 1992) (6716–6721)). *Cancer Res.* 1993, 53, 1472.
36. Williamson, M.P.; Elder, P.A.; Knowles, M.A. The spectrum of TP53 mutations in bladder carcinoma. *Genes Chromosom. Cancer* 1994, 9, 108–118.
37. Andreassen, Å.; Oyjord, T.; Hovig, E.; Holm, R.; Florenes, V.A.; Nesland, J.M.; Myklebost, O.; Hoie, J.; Bruland, S.; Borresen, A.-L.; et al. p53 Abnormalities in Different Subtypes of Human Sarcomas. *Cancer Res.* 1993, 53, 468–471.
38. Sheiness, D.; Fanshier, L.; Bishop, J.M. Identification of nucleotide sequences which may encode the oncogenic capacity of avian retrovirus MC29. *J. Virol.* 1978, 28, 600–610.

39. Sheiness, D.; Bishop, J.M. DNA and RNA from uninfected vertebrate cells contain nucleotide sequences related to the putative transforming gene of avian myelocytomatosis virus. *J. Virol.* 1979, 31, 514–521.
40. Duesberg, P.H.; Bister, K.; Vogt, P.K. The RNA of avian acute leukemia virus MC29. *Proc. Natl. Acad. Sci. USA* 1977, 74, 4320–4324.
41. Massó-Vallés, D.; Soucek, L. Blocking Myc to Treat Cancer: Reflecting on Two Decades of Omomyc. *Cells* 2020, 9, 883.
42. Nilsson, J.A.; Maclean, K.H.; Keller, U.B.; Pendeville, H.; Baudino, T.A.; Cleveland, J.L. Mnt loss triggers Myc transcription targets, proliferation, apoptosis, and transformation. *Mol. Cell. Biol.* 2004, 24, 1560–1569.
43. Nguyen, H.V.; Vandenberg, C.J.; Ng, A.P.; Robati, M.R.; Anstee, N.S.; Rimes, J.; Hawkins, E.D.; Cory, S. Development and survival of MYC-driven lymphomas require the MYC antagonist MNT to curb MYC-induced apoptosis. *Blood* 2020, 135, 1019–1031.
44. Vita, M.; Henriksson, M. The Myc oncoprotein as a therapeutic target for human cancer. *Semin. Cancer Biol.* 2006, 16, 318–330.
45. Castell, A.; Yan, Q.; Fawkner, K.; Hydbring, P.; Zhang, F.; Verschut, V.; Franco, M.; Zakaria, S.M.; Bazzar, W.; Goodwin, J.; et al. A selective high affinity MYC-binding compound inhibits MYC:MAX interaction and MYC-dependent tumor cell proliferation. *Sci. Rep.* 2018, 8, 10064.
46. Demma, M.J.; Hohn, M.J.; Sun, A.; Mapelli, C.; Hall, B.; Walji, A.; O'Neil, J. Inhibition of Myc transcriptional activity by a mini-protein based upon Mxd1. *FEBS Lett.* 2020, 594, 1467–1476.
47. Demma, M.J.; Mapelli, C.; Sun, A.; Bodea, S.; Ruprecht, B.; Javaid, S.; Wiswell, D.; Muise, E.; Chen, S.; Zelina, J.; et al. Omomyc Reveals New Mechanisms To Inhibit the MYC Oncogene. *Mol. Cell. Biol.* 2019, 39, 1–27.

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