Enhanced Expression of the N-myc Gene in Wilms’ Tumors

Perry D. Nisen, Kathryn A. Zimmerman, Sean V. Cotter, Fred Gilbert, and Frederick W. Alt

Department of Pediatrics, Division of Hematology-Oncology, Schneider Children's Hospital of Long Island-Jewish Medical Center, New Hyde Park, New York 11042, and School of Medicine, State University of New York at Stony Brook, Stony Brook, New York 11794 [F. D. N.; S. V. C.]; Department of Biochemistry and Molecular Biophysics, and Institute for Cancer Research, Columbia University College of Physicians and Surgeons, New York, New York 10032 [K. A. Z., F. W. A.]; and Department of Pediatrics, Division of Genetics, Mt. Sinai School of Medicine, New York, New York 10029 [F. G.]

ABSTRACT

Activation of myc-family oncogenes has been implicated in the genesis of a variety of neoplasms. In addition, these genes exhibit specific patterns of expression during murine development. We now report that N- and c-myc are differentially expressed in normal developing human renal tissues and in Wilms’ tumor, a neoplasm which derives from primitive kidney cells. Twelve of 13 Wilms’ tumors tested exhibited greatly enhanced levels of expression which occurred in the absence of gene amplification. We also detected N-myc expression in other primitive neoplasms including medulloblastoma and hepatoblastoma. Our observations suggest that N-myc expression is not limited to neuroectodermal tumors as was previously thought, but is a marker for several neoplasms that derive from primitive cell precursors. Finally, high level expression of N-myc was associated with markedly diminished levels of c-myc, suggesting that enhanced expression of N-myc gene might lead to down-regulation of c-myc.

INTRODUCTION

The myc family of cellular oncogenes has three well-characterized members (c-myc, N-myc, and L-myc) as well as several additional members (1). The human and murine N- and c-myc genes have similar 5' noncoding exons and extensive homology in the coding regions (2, 3), and they exhibit similar oncogenic potential in an in vitro transformation assay (4, 5). The L-myc gene has similar structural features to N- and c-myc (1, 6).

Studies of myc gene expression during murine development revealed that high level expression of N- and L-myc is restricted to particular tissues and stages of development and is likely involved in the early stages of multiple differentiation pathways. This is in contrast to the more generalized expression of c-myc in developing tissues (7). Furthermore, myc genes are differentially expressed during the progression of single cell lineages. For example, N- and c-myc are both expressed in pre-B-lymphocytes, but only c-myc is expressed in later stages of B-cell development. Such findings suggested that differential or combinatorial expression of myc genes is associated with mammalian development (1). The distinct expression patterns of myc family genes during development may indicate tumors in which these genes are expressed or activated. For example, high level N-myc expression in developing brain (7) correlates with expression and frequent activation of N-myc in certain human tumors which derive from primitive cells with “neural” characteristics; this set of tumors includes neuroblastoma (8–10), retinoblastoma (8, 11, 12), and small cell lung carcinoma (13). The c-myc gene, on the other hand, is expressed at similar levels in most fetal and neonatal tissues (7), and it is correspondingly activated in a variety of different neoplasms (14).

Received 5/27/86; revised 8/14/86; accepted 8/15/86.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked advertisement in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

1 This work was supported by the Rosalind and Sol Chaikin Institute for Childhood Cancer Research of the Schneider Children's Hospital and by NIH grants 2-PO1 CA23767-06 and CA 42335, American Cancer Society Grant CD-269, and a Searle Scholars Award to F. A. F. A. is an Irma T. Hirschl Career Scientist and Malinckrodt Scholar.

2 To whom requests for reprints should be addressed.

In addition to the brain, N-myc was noted to be expressed at particularly high levels in murine fetal kidney (7). To assess the potential significance of this finding, we have assayed for myc gene expression in developing human kidneys and in Wilms’ tumor, a common renal neoplasm of children that arises from embryonal cells. We have also assayed for N-myc expression in various other human tumors, including a set of neoplasms which also arise from primitive or undifferentiated cells. The results of these studies suggest that enhanced N-myc expression is characteristic of tumors which derive from certain primitive cell lineages and are consistent with the possibility that enhanced N-myc expression could be involved in the development of at least some of these tumors. We also present evidence that high level expression of N-myc is associated with markedly diminished c-myc expression.

MATERIALS AND METHODS

DNA and RNA Preparation. Human tumor and normal tissue specimens were obtained as part of an approved Long Island Jewish Medical Center Investigational Review Board protocol. Two hundred to 500 mg of fresh tumor specimens, fetal kidneys, adult kidney, and pellets of cell lines grown in tissue culture were immediately frozen in liquid nitrogen and stored at –70°C. Total cellular and polyadenylate-containing RNA and chromosomal DNA were prepared as described previously (8, 11).

Northern and Southern Blotting Procedure. All RNA and DNA blotting and hybridization procedures were performed as described previously (8, 11).

Densitometry. The level of N-myc and c-myc RNA in the tumors and cell lines was quantitated by densitometric tracing of duplicate autoradiograms as described previously (7) using a Cambridge Instruments Quantimet 920 densitometer. The same instrument was used to determine the extent of N-myc gene amplification on the southern blots as described in the legend to Table 1.

DNA Probes. The N-myc probe is a 1.8-kilobase human complementary DNA clone that contains a part of the second and all of the third exons of the gene (2). The c-myc probe is a 1.4-kilobase human complementary DNA clone that contains the third exon of the gene (15). The human immunoglobulin joining region probe is described by Ravetch ef al. (16).

Tissue Culture. TE671 is a medulloblastoma-derived cell line that was grown as described by McAllister ef al. (17). The growth and characteristics of all other lines have been described previously (8, 11).

RESULTS

N-myc and c-myc Expression in Human Fetal Kidneys and in Wilms’ Tumors. Previous studies of N-myc during murine development revealed that this gene was expressed at particularly high levels in fetal kidneys compared to most other tissues; N-myc expression fell dramatically in adult kidney. In contrast, c-myc expression occurred in the fetal kidney, but the levels did not decrease dramatically in the adult organ (7). To further elucidate this phenomenon, we assayed human fetal and adult kidney specimens for expression of N- and c-myc RNA. As a control for levels of N-myc expression we included RNA from cells that do not express N-myc (HeLa), from a neuroblastoma
cell line (NB69) that expresses detectable \emph{N-myc} levels in the absence of \emph{N-myc} gene amplification, and from a neuroblastoma cell line which, relative to NB69, expresses approximately 100-fold elevated levels of \emph{N-myc} as a result of gene amplification (LAN1) (11) (Fig. 1A). As a control for \emph{c-myc} expression, we included RNA from neuroblastoma cell lines that have either no detectable levels of \emph{c-myc} expression (LAN1; see below) or readily detectable levels of expression (NB69). Because the \emph{N-myc} gene is not expressed in most tumors and cell lines analyzed, expression levels of \emph{N-myc} in the unamplified neuroblastoma cell line NB69 will be referred to arbitrarily as base-line levels (similar levels occur in most unamplified neuroblastomas tested to date), and levels which are more than 10-fold higher, such as those observed in amplified neuroblastoma cell lines, will be referred to as enhanced \emph{N-myc} expression.

Total cellular RNA was isolated from six different freshly obtained human fetal kidney specimens, that were from 17 to 23 wk of gestation, and from an adult kidney. The RNA was screened by northern blot procedures for hybridization to $^{32}$P-labeled human \emph{N-} and \emph{c-myc} DNA probes (Fig. 1B). Base-line levels of \emph{N-myc} expression were detected in fetal kidneys; expression diminished to virtually undetectable levels in adult kidney (Fig. 1B). As in the mouse, \emph{c-myc} expression persisted at somewhat reduced, but significant, levels in the adult kidney (Fig. 1B). The \emph{N-} and \emph{c-myc} genes, therefore, also appear to be differentially expressed during human renal development.

It has been suggested that the unique expression patterns of \emph{myc} genes in normal cells can help to predict the types of tumors in which these genes are expressed (7). Wilms' tumor (nephroblastoma) is a neoplasm that arises from embryonic renal cells. We assayed total cellular RNA preparations from 13 independent fresh Wilms' tumor specimens (W1 to W13) for \emph{N-} and \emph{c-myc} expression (Fig. 1A). Strikingly, 12 of the 13 Wilms' tumor specimens (W1, W3 to W13) exhibited greatly enhanced levels of \emph{N-myc} RNA. The levels in these tumors were elevated from 15- to 40-fold relative to base-line levels and approached those observed in some neuroblastoma lines which had amplified the \emph{N-myc} gene (Table 1).

The relative level of \emph{c-myc} expression in Wilms' tumors appeared to be, approximately, inversely correlated with relative \emph{N-myc} expression levels. Thus, the tumors with greatly enhanced \emph{N-myc} expression exhibited lower relative levels of \emph{c-myc} expression, whereas the tumor that had undetectable levels of \emph{N-myc} (W2) expressed higher levels of \emph{c-myc} relative to that of the other Wilms' tumors (see below) (Fig. 1A; Table 1).

\begin{figure}
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{Expression of \emph{N-myc} and \emph{c-myc} in tumors and normal tissues. Approximately 10 \(\mu\)g of total cellular RNA were fractionated by gel electrophoresis, transferred to nitrocellulose filters, and assayed for hybridization to $^{32}$P-labeled \emph{N-myc} (top) and \emph{c-myc} (bottom) probes as described previously (7). The filters were sequentially hybridized to the two different probes; the signal from the \emph{N-myc} probe was removed before the \emph{c-myc} probe was applied. \(A\), Wilms' tumors and tumor cell lines. Sources of RNA are indicated on the figure and described in more detail in the text. The \emph{N-} and \emph{c-myc} mRNA species of approximately 2.9 kilobases (2) and 2.3 kilobases (38), respectively, are indicated. \(B\), normal kidney samples and hepatoblastoma. Sources of RNA are indicated on the figure. A Wilms' tumor sample (W5) is included from \(A\) to facilitate comparative analyses of samples in \(A\) and \(B\). The numbers corresponding to the different fetal kidney specimens (17, 18, 19.5, 20+, 21, 21+) refer to the approximate gestational age of the fetuses.}
\end{figure}

\begin{table}
\centering
\caption{Expression of \emph{N-myc} and \emph{c-myc} in tumors and normal tissues. (Fig. 1A; Table 1).}
\begin{tabular}{|c|c|c|}
\hline
Specimen & RNA Source & RNA Level \\
\hline
W1 & Wilms' Tumor & Enhanced \\
W2 & Wilms' Tumor & Base-line \\
W3 to W13 & Wilms' Tumor & Enhanced \\
W14 & Normal Kidney & Base-line \\
\hline
\end{tabular}
\end{table}

\section*{Diminished \emph{c-myc} Expression in Cells with Enhanced \emph{N-myc} Expression}

The Wilms' tumors were primary surgical specimens that likely contained several different normal cell types which could have contributed to the overall levels of \emph{N-} and \emph{c-myc} expression in the tumor RNA. Therefore, lymphocytes or normal adult kidney cells (which continue to express the \emph{c-myc} gene), as opposed to neoplastic cells, could have been the source of the detected levels of \emph{c-myc} gene expression in the tumor specimens. To further study the potential relationship between enhanced \emph{N-myc} expression and \emph{c-myc} expression, we examined the relative levels of \emph{N-} and \emph{c-myc} RNA in clonal cell lines which expressed the \emph{N-myc} gene at varying levels (Fig. 2). With few exceptions, nonneuroblastoma lines that do not express detectable \emph{N-myc} RNA, such as HeLa cells, all express readily detectable levels of \emph{c-myc} (e.g., Fig. 2, Lanes 1 to 3); to facilitate comparisons, these levels, which vary somewhat, will be arbitrarily referred to as base-line levels. Several human neuroblastoma cell lines assayed that have not amplified the \emph{N-myc} gene express base-line levels of both \emph{N-} and \emph{c-myc} (Fig. 2, Lanes 4 to 6). Similar findings were previously reported for murine pre-B-lymphocytes and a murine neuroblastoma (7). However, eight independent neuroblastoma lines in which \emph{N-myc} is amplified and consequently overexpressed by 50-fold or more over base-line levels have little or no detectable levels of \emph{c-myc} expression (Fig. 2, Lanes 7 to 13; Table 1). Thus, the relative expression levels of \emph{N-} and \emph{c-myc} genes in neuroblastoma lines and Wilms' tumors are consistent with the possibility that enhanced expression of the \emph{N-myc} gene can in some way lead to down-regulation of the \emph{c-myc} gene. Similar findings have also been
reported with respect to the expression of myc-family genes in small cell lung carcinomas; tumors that have amplified and expressed enhanced levels of one myc-family member (e.g., N-myc) do not express other family members (e.g., c- and L-myc) (13).

N-myc Expression in Wilms' Tumors Is Not Due to Gene Amplification. High level expression of N-myc in neuroblastoma tumors is generally associated with amplification of the N-myc gene (8-11). To determine whether enhanced N-myc expression in the Wilms' tumors resulted from gene amplification, we assayed EcoRI-digested chromosomal DNA prepared from the various Wilms' samples for hybridization to an N-myc probe (2) and to a probe specific for a human immunoglobulin joining region (JH) (8, 11) (Fig. 3). The JH probe serves to standardize the amount of DNA in each lane. In all tested Wilms' DNA samples, the JH- and N-myc-hybridizing bands were of similar relative intensity to those observed with normal lymphocyte DNA, in contrast to the tremendous increase in the relative level of hybridization to the N-myc sequence in the amplified neuroblastoma lines LAN5 and CHP134. Thus, greatly enhanced expression of the N-myc gene in many Wilms' tumors occurs in the absence of gene amplification. The level of N-myc expression per gene copy in such tumors is, on the average, 25-fold greater than that of human neuroblastomas (Table 1).

N-myc Expression in Other Primitive Tumors. The murine developmental studies also demonstrated that N-myc was expressed at high levels in tissues of the fetal CNS, but at greatly diminished levels in adult CNS tissues (7). Screening a variety of brain tumors for N-myc expression revealed enhanced expression over base-line levels in a medulloblastoma tumor and base-line levels of expression in a medulloblastoma-derived cell line TE671 (17) (Fig. 1A; Table 1); medulloblastoma arises from primitive neuroectodermal tissue in the brain. Significantly, we did not detect N-myc expression in 15 adult CNS tumors, none of which is of primitive cell origin (see legend to Table 1). These results are consistent with the previous suggestion that N-myc may be a marker of tumors that arise from primitive cell precursors (7). To further test this possibility, we assayed for N-myc expression in hepatoblastoma tumors; these also originate from primitive cell precursors. Total cellular RNA was isolated from two different hepatoblastoma specimens and screened by northern hybridization techniques. Both specimens exhibited base-line levels of N-myc expression (Fig. 1B; Table 1). These findings support the conclusion that N-myc expression can selectively occur in a variety of neoplasms that derive from primitive or undifferentiated precursor cells (7).

DISCUSSION

We have shown that N-myc is expressed at significant levels in human fetal kidneys and that expression levels decline dramatically in adult kidneys. In contrast, c-myc expression levels are similar in human fetal and adult kidneys. These findings extend the previous findings that early stage-specific expression of N-myc and differential expression of N-, L-, and c-myc occur during murine differentiation (7). The results of the murine analyses suggested that N- and L-myc expression patterns during early development might help point to tumors in which these genes are expressed or activated (7). Our current findings support this idea. Thus, N-myc is expressed at particularly high levels in the developing kidney (7, this study); and, correspondingly, expression is greatly enhanced in Wilms' tumor, a neoplasm which arises from embryonal kidney cells. In addition to Wilms' tumor, we have also found N-myc expression in several other tumors derived from primitive cells, including medulloblastoma and hepatoblastoma. Our findings extend the spec-
trum of human neoplasms which express N-myc beyond the limited set of neural tumors in which it was previously detected, and they further suggest that N-myc expression may be a characteristic of a variety of different tumors which arise from primitive cells.

N-myc clearly appears to be associated with the increased oncogenic potential of tumors in which its expression is enhanced as a result of gene amplification (18). It is not known whether base-line or enhanced levels of N-myc expression in tumors in which the gene is not amplified reflect a role in tumorigenesis or merely the inherent expression properties of the cell from which the tumor derived and is incidental to oncogenesis (7, 19). Although N-myc expression levels in Wilms' tumors are greatly elevated relative to the base-line levels of bulk fetal kidney, it is possible that such enhanced N-myc expression levels occur in a subset of normal kidney cells from which the tumor derives. For example, barely detectable levels of N-myc RNA in the developing liver appear to be contributed, at least in part, by a subpopulation of developing lymphocytes which express the gene at base-line levels (7). Enhanced N-myc expression levels can occur by different mechanisms in different tumors. Thus, N-myc expression, when normalized to gene copy number, occurred at base-line levels in all neuroblastomas tested to date (7, 8, 10); greatly enhanced N-myc expression in neuroblastoma is generally limited to the more progressive forms of the disease and results from gene amplification (18, 20). On the other hand, Wilms' tumors frequently display enhanced levels of N-myc expression, and in these tumors the enhanced expression usually occurs in the absence of gene amplification. Currently, Wilms' tumor is the only known cell which expresses such high levels of N-myc from a single gene copy, although conflicting reports exist about the possibility that some retinoblastomas may express high level N-myc from a single copy gene (12, 21). If high level N-myc expression is linked to oncogenesis in Wilms' tumor, it most likely would occur at an early stage.

Previous models of oncogenesis have focused on the necessity of two steps for malignant transformation in tumors that possess a recessive genetic predisposition (22–25). The first step is the inherited or spontaneously arising recessive cancer allele; the second step could be any of several genetic rearrangements that result in homozygosity or hemizygosity for this recessive allele. It has been suggested that the recessive genes in Wilms' tumor (and retinoblastoma) may encode a function which regulates the expression of a "transforming" gene active only during embryogenesis (26). The products of such putative transforming genes were proposed to be involved in regulating differentiation and/or proliferation of the primitive precursor cells; continual expression of these genes was postulated to occur in cells which had inactivated both regulatory alleles. In the context of such a model, N-myc possesses three necessary features of this putative transforming gene: (a) oncogenic potential in an in vitro transforming assay (4, 5); (b) expression primarily during the early stages of differentiation (7, 19); and (c) expression at greatly enhanced levels in most Wilms' tumors. Thus, an interesting possibility is that N-myc expression levels may be related to the homozygous mutations associated with these tumors. In this regard, it would be interesting to determine the status of the recessive alleles in the few Wilms' tumors which do not show enhanced levels of N-myc expression relative to those of tumors in which expression is enhanced.

The IGF-II gene is another proposed candidate for the embryonic transforming gene of Wilms' tumor; expression of this potential transforming gene in Wilms' tumor has recently been reported (27, 28). IGF-II is a somatomedin that has mitogenic properties and is normally expressed at high levels in embryonic, but not adult tissues (29). IGF-II expression appears to be restricted to a more limited set of embryonic tumors than those in which N-myc is expressed; IGF-II expression was not detected in a limited number of neuroblastoma and retinoblastoma tumors assayed (28).

The c-, N-, and L-myc genes clearly appear to be members of a myc-gene family. Furthermore, because the murine L-myc gene was identified from a large pool of unique murine myc genes originally isolated on the basis of homology to both the second and third exons of the human N-myc gene, it seems likely that the myc gene family contains additional members (7). Although current studies suggest that individual members of this family may have important roles within specific lineages and/or at specific developmental stages, the function of myc-
The level of N-myc and c-myc mRNA in the tumors, cell lines, and fetal tissues was quantitated by densitometric tracing of duplicate autoradiograms similar to those depicted in Figs. 1 to 3 (see “Materials and Methods”). The intensity of the signal was calculated as a percentage of the signal intensity generated with RNA from the most highly expressing source (LAN1 for N-myc and NB69 for c-myc) which was arbitrarily set at 100%; in the table, each value given was rounded off to the nearest multiple of five. A value of <1 indicates that the expression level of the sequence in that tissue was detectable, although clearly below the 1% level, and too low to obtain an accurate reading. A reading of “<0.1” indicates that there was no detectable signal. In addition to the pediatric medulloblastoma tumor, 14 fresh adult brain tumors were similarly examined and were not found to express detectable N-myc. These included: 3 glioblastomas; 3 meningiomas; 1 malignant epidermoidoma; 1 schwannoma; 1 acoustic neuroma; 1 optic glioma; and 4 presumed metastatic tumors to the brain. The N-myc gene copy number for the neuroblastoma lines was taken from Ref. 11. The amount of N-myc RNA per gene copy number of N-myc was determined by dividing the extent of RNA expression by the number of copies of the gene in chromosomal DNA.

### Acknowledgments

We wish to thank A. Evans, G. D’Angio, J. Garvin, A. Shende, and A. Sherbani for providing tumor specimens. We also wish to thank F. Rauschbaum for providing fetal tissue samples and E. Valderrama for the adult kidney specimen. We thank Dr. Connie Gee for critical reading of the manuscript.

### References


### Table 1 Expression and gene amplification of N-myc and c-myc in Wilms' tumors and fetal kidneys

<table>
<thead>
<tr>
<th>Expression in</th>
<th>N-myc</th>
<th>c-myc</th>
<th>N-myc gene copy no.</th>
<th>N-myc RNA/gene copy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilms' tumors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>W1</td>
<td>15</td>
<td>1</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>W2</td>
<td>25</td>
<td>1</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>W3</td>
<td>35</td>
<td>1</td>
<td>1</td>
<td>35</td>
</tr>
<tr>
<td>W4</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>W5</td>
<td>25</td>
<td>1</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>W6</td>
<td>30</td>
<td>1</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>W7</td>
<td>40</td>
<td>1</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>W8</td>
<td>40</td>
<td>1</td>
<td>1</td>
<td>40</td>
</tr>
<tr>
<td>W9</td>
<td>30</td>
<td>1</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>W10</td>
<td>15</td>
<td>1</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>W11</td>
<td>30</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>W12</td>
<td>30</td>
<td>1</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>W13</td>
<td>40</td>
<td>1</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Fetal kidneys</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17 wk F1</td>
<td>5</td>
<td>5</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>18 wk F2</td>
<td>2.5</td>
<td>5</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>19.5 wk F3</td>
<td>1</td>
<td>5</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>20 wk F4</td>
<td>2.5</td>
<td>5</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>21 wk F5</td>
<td>1</td>
<td>&lt;1</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>21 wk F6</td>
<td>&lt;1</td>
<td>1</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Adult kidney</td>
<td>&lt;0.1</td>
<td>1</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Hepatoblastoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H1</td>
<td>1</td>
<td>5</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>H2</td>
<td>5</td>
<td>20</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Medulloblastoma tumor</td>
<td>10</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Medulloblastoma line TE671</td>
<td>1</td>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Teratoma</td>
<td>1</td>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Neuroblastoma lines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NB69</td>
<td>1</td>
<td>100</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>LAN1</td>
<td>80</td>
<td>100</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>LAN5</td>
<td>100</td>
<td>200</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>SKNSH</td>
<td>1</td>
<td>10</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CHP100</td>
<td>2</td>
<td>90</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>IMR32</td>
<td>100</td>
<td>&lt;25</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>CHP126</td>
<td>50</td>
<td>100</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NB16</td>
<td>400</td>
<td>&lt;300</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NB9</td>
<td>200</td>
<td>&lt;300</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>NB19</td>
<td>ND</td>
<td>&lt;600</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>CHP134</td>
<td>ND</td>
<td>700</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>HeLa</td>
<td>–</td>
<td>90</td>
<td>&lt;0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>AML (promyelocytic) K56</td>
<td>–</td>
<td>70</td>
<td>&lt;0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>CML (HL60)</td>
<td>–</td>
<td>90</td>
<td>&lt;0.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Human lymphocytes</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

*a* No detectable RNA per gene copy.

*b* ND, not determined.

N-myc gene products are nuclear proteins which bind DNA in vitro (30–33), and sequence comparisons have suggested similar properties for the N-myc protein (1–3). Thus, it is possible that the myc-gene products may have a direct role in regulating the expression of other genes (34), as previously suggested by the homology of c-myc to the adenovirus transcriptional regulatory
N-myc EXPRESSION IN WILMS’ TUMORS


Enhanced Expression of the N-myc Gene in Wilms' Tumors

Perry D. Nisen, Kathryn A. Zimmerman, Sean V. Cotter, et al.


Updated version  Access the most recent version of this article at: http://cancerres.aacrjournals.org/content/46/12_Part_1/6217

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, use this link http://cancerres.aacrjournals.org/content/46/12_Part_1/6217. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.