High-Level Expression of the Ribosomal Protein L19 in Human Breast Tumors That Overexpress erbB-2

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ABSTRACT

The erbB-2 (or HER-2 or neu) gene is amplified and overexpressed in approximately one-third of cancers of the breast, stomach, and ovary. Evidence is accumulating that erbB-2 overexpression is associated with decreased survival of breast cancer patients. In an effort to understand how erbB-2 overexpression might impart a more malignant potential to breast cancer cells, we have searched for evidence of changes in gene expression associated with erbB-2 overexpression. Using differential screening of a complementary DNA library we identified several complementary DNAs that represent mRNAs the expression of which may vary according to erbB-2 level. One complementary DNA was studied in detail. The mRNA encoding the ribosomal protein L19 (1.9 kilobases) was more abundant in breast cancer samples that express high levels of erbB-2 ($P < 6 \times 10^{-7}$). The level of L19 mRNA expression varied over a 1- to 64-fold range among the tumor samples. No evidence of gene amplification (P < 6 X 10^{-7}). The level of IA9 mRNA expression varied over a 1- to 64-fold range among the tumor samples. No evidence of gene amplification (P < 6 X 10^{-7}).

INTRODUCTION

Three lines of evidence suggest that overexpression of the erbB-2 gene contributes to the malignancy of breast cancer cells. First, the close similarity of the protein structure to the EGFR receptor indicates a function in control of growth or differentiation (1–3). Second, artificially induced erbB-2 overexpression can transform fibroblasts (NIH/3T3) (4, 5). Third, and most important, many studies have linked erbB-2 gene amplification or overexpression with poor patient prognosis (6–10; reviewed in Refs. 11 and 12). Estimations for the magnitude of this effect have been as high as a 5-fold increase in risk of death in some patient groups (9). There is not yet a mechanistic understanding of the increased malignancy of breast cancers that overexpress erbB-2. Clinical evidence has been reported that erbB-2 overexpression may effect either the response of cells to chemotherapy or the division rate (12).

In this study we attempted to determine if erbB-2 overexpression alters cells qualitatively as evidenced by measurable changes in gene expression. We used techniques designed to identify mRNAs the level of which is consistently altered in association with erbB-2 overexpression. Candidate cDNA clones were identified by differential plaque hybridization. Differential expression of mRNA was then confirmed by analysis of breast cell lines and primary tumors. One cDNA clone identified in this way indicates that the mRNA for ribosomal protein L19 has dramatically different expression in tumors that overexpress erbB-2. This expression pattern is not associated with a general increase in expression of mRNAs for other ribosomal proteins.

MATERIALS AND METHODS

Screening of a Human Breast Cancer Cell Line cDNA Library by Plus/Minus Hybridization. A MCF-7 Agt10 cDNA library (a gift of Dr. Fran Kern, Georgetown University) was screened by plating approximately 8000 plaque/plate with competent C600 cells. Triplicate plaque lifts onto nitrocellulose were made and denatured by successive rewettings in 0.5 M NaOH, 0.5 M NaOH, 0.5 M Tris-Cl (pH 7.5), 0.5 M Tris-Cl (pH 7.5), and 1.5 M NaCl. Each of the plaque lifts were hybridized with a $^3$P-labeled total cDNA probe from either the SK-BR-3, MDA-MB-468, or MCF-7 cells.

Cell Lines and Tissue Culture. Human breast cancer cell lines SK-BR-3, T47D, MCF-7, BT474, BT20, MDA-MB-468, MDA-MB-231, and HBL-100 were obtained from the American Type Culture Collection. Cells were grown in Dulbecco's modified Eagle's medium with 5% fetal bovine serum (Gibco). Cells were grown in Dulbecco’s modified Eagle’s medium with 5% fetal bovine serum (Gibco), and the medium was changed every 2 days.

Tissue Specimens. Archived frozen breast cancer tissue samples with previously determined diagnostic and prognostic parameters were obtained from the Molecular Oncology, Inc., Tumor Repository.

RNA Isolation from Tissue Samples and Cultured Cells. Total RNA was isolated from tissue samples and cultured cells by a modified Chigwin method (13). Frozen tumor samples were lyopholized for 12 h and then ground to a fine powder with a mortar and pestle. The ground tumor powders or culture cell pellets were solubilized in 4 M guanidine isothiocyanate, 0.5% sodium Sarkosyl, 5 mm sodium citrate (pH 7.0), and 0.1 M β-mercaptoethanol by homogenization in a Polytron. CsCl was added to 0.25% (w/v), mixed, and layered on a 5.7 M CsCl cushion containing 5 mM EDTA and 1% sodium Sarkosyl and centrifuged at 100,000 g for >16 h. The RNA band was recovered by ethanol precipitation. The RNA pellet was resuspended in 10 mM Tris-Cl (pH 7.5), 5 mM EDTA, and 1% sodium Sarkosyl, extracted with CHCl$_3$/isobutyl alcohol (4:1), and then precipitated with ethanol. Polyadenylated RNA was isolated by incubation with oligo(dT)$_24$-cellulose.

Northern Blot Analysis. Total RNA (5 μg) isolated from tumor samples or cultured cells was denatured in 2.2 M formaldehyde at 65°C for 5 min and electrophoresed in a 1% agarose gel containing 0.66 M formaldehyde. Comparison of the total RNA loaded per well and the integrity of the RNA were visualized by ethidium bromide staining of the 28S and 18S rRNA in the gel. The gel was soaked in 50 mM NaOH, 10 mM NaCl followed by 1 M ammonium acetate and then transferred to a ZetaProbe nylon filter (Bio-Rad) in 1 M ammonium acetate and cross-linked to the filter by exposure to 0.3 J/cm$^2$ of 312-nm UV radiation in a BiosLink (Bios Corp.).

Dot-Blot Analysis. The total RNA samples were denatured in 50 mM NaOH, 1.5 mM NaCl and then neutralized with 1 M ammonium acetate. Approximately 2 μg of each sample were serially diluted 2-fold in 1 M ammonium acetate with transfer RNA added to maintain constant total RNA concentration and then vacuum filtered onto ZetaProbe nylon filters in a dot-blot manifold. The RNA was cross-linked to the filter as described above. The dot-blot quantitation of the various experimental mRNA levels was normalized by hybridizing the same blots with a β-actin cDNA probe. The hybridization intensities of the various experimental probes were then compared to that of the β-actin probe at their different dilution levels, and their expression ratios were determined (14).

Polymerase Chain Reaction and Cloning of the Isolated Library Sequences. The cDNA portions of recombinant phage were isolated by polymerase chain reaction (15) using primers adjacent to the 3' and 5' cloning sites. The insert (~690 base pairs) was then used as a hybridization probe for the initial screening of breast cell lines by Northern blot analysis. The L19 cDNA insert was isolated by EcoRI digestion of a Agt10 phage DNA preparation, band purified, and then cloned into pUC18 or M13 RF at the EcoRI cloning site for sequencing.

Probes and Hybridizations. cDNA probes used to screen the cDNA library plagues were made by reverse transcription of polyadenylated RNA isolated from the SK-BR-3, MDA-MB-468, or MCF-7 cell lines in the pres-
ence of $^{[32P]}$dCTP (Amersham). The S16 and L26 probes (a gift of Dr. Ira Wool, University of Chicago) as well as the erbB-2 and β-actin probes were labeled by random prime polymerization (Pharmacia) of their complete cDNA sequence in the presence of $^{[32P]}$dCTP. The isolated library cDNA inserts were labeled by random priming with $^{[32P]}$dCTP as probes for the cell line Northern blot and tumor sample dot blots.

Probe hybridization was conducted at 42°C in 50% formamide, 5 × SSC, 5 × Denhardt’s solution, 10% dextran sulfate, and 0.5% sodium dodecyl sulfate with 250 μg/ml salmon sperm DNA. Blots were washed at 54°C with two 15-min washes of 2 × SSC, then 0.2 × SSC 0.1% sodium dodecyl sulfate, and finally 0.2 × SSC. Successive probe hybridizations were accomplished by stripping the blot at 65°C in 50% formamide, 10 × SSC, and 10 mM sodium pyrophosphate (pH 7.2), verified by 24-h autoradiographic exposure.

DNA Sequencing and Analysis. The isolated cDNA inserts subcloned into pUC18 and M13 vectors (BRL-Gibco) were sequenced in the 5' and 3' directions by the dideoxynucleotide chain termination method (16) using Sequenase 2.0 (U.S. Biochemicals).

Statistical Analysis. Correlations between the L19 relative expression levels and various prognostic factors were evaluated by performing the $\chi^2$ contingency table analysis where appropriate. Fisher’s exact test was performed when the assumptions of the $\chi^2$ analysis were violated.

RESULTS

Identification of cDNAs Cooverexpressed with erbB-2. A two-step approach was devised to identify cDNA clones corresponding to mRNAs the expression levels of which vary significantly in breast cancers with erbB-2 overexpression. First, a MCF-7 Agt10 cDNA library was screened by comparing the hybridization intensity for each candidate cDNA insert against their corresponding cDNA alone. In the initial screening of 80,000 phage plaques, 388 discrete plaques exhibited distinct hybridization intensity differences when the SK-BR-3 and the MCF-7 probes were compared. A second screening of these 388 candidates was conducted by picked each into an array. This allowed for a more quantitative comparison of the hybridization signal intensity differences when the SK-BR-3 and the MCF-7 probes were compared. The cDNA inserts from these recombinant phage were isolated by polymerase chain reaction.

In the second step of our isolation approach, these cDNAs were used to confirm the erbB-2 expression status of each cell line (Fig. 1). One candidate cDNA clone (later identified as ribosomal protein L19 mRNA) was used in Northern blot hybridization experiments using each candidate cDNA insert. Control blots of the same RNA samples were hybridized with a β-actin or erbB-2 probe to allow comparison of the amount of each RNA sample on the blot and to confirm the erbB-2 expression status of each cell line (Fig. 1). One candidate cDNA clone (later identified as ribosomal protein L19 DNA; see below) detected a strong RNA band at 1.9 kilobases in all three cell lines (SK-BR-3, BT474, T47D) that overexpress erbB-2 (5 kilobases), as well as one (MDA-MB-231) of the two cell lines that overexpress EGF receptor. Much lower hybridization signals were detected in the control cell lines (MCF-7, HBL-100) that have low erbB-2 levels. These results suggested to us a relationship between the L19 mRNA level and erbB-2 overexpression.

To determine the expression level of L19 with respect to erbB-2 levels, dot-blot analysis was carried out on these same samples, and the amount of loaded mRNA was normalized by a comparative hybridization with a β-actin probe. As shown in Table 1, the breast cancer cell lines that express the highest levels of erbB-2 (~128) also express the highest L19 mRNA levels (~64). Cell lines

<table>
<thead>
<tr>
<th>Cell line (reference)</th>
<th>L19 mRNA expression level</th>
<th>erbB-2 mRNA expression level</th>
<th>erbB-2 gene amplification</th>
<th>EGF receptor mRNA expression level</th>
<th>EGFR gene amplification</th>
</tr>
</thead>
<tbody>
<tr>
<td>SK-BR-3 (14)</td>
<td>64</td>
<td>128</td>
<td>4–8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>BT474 (14)</td>
<td>64</td>
<td>128</td>
<td>4–8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>MDA-MB-453 (14)</td>
<td>64</td>
<td>64</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>T47D (current study)</td>
<td>8</td>
<td>16</td>
<td>1</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>MDA-MB-468 (14)</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>MDA-MB-231 (Ref. 17 and current study)</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>BT20 (14)</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>16</td>
<td>4–8</td>
</tr>
<tr>
<td>HBL-100 (14)</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>MCF-7 (14)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

The erbB-2 and epidermal growth factor receptor mRNA and gene amplification levels where determined by Kraus et al. (14), Hynes et al. (17), or the current study.

* ND. Not determined.

Fig. 1. Northern blot of human breast cancer cell lines. Northern blot analysis using 5 μg total RNA from human breast cancer cell lines. Top, blot hybridized with the isolated L19 cDNA (1.9-kilobase) probe. Middle, blot hybridized with the erbB-2 cDNA (5.0-kilobase) probe. Bottom, blot hybridized with the β-actin cDNA (2.0-kilobase) probe. The same blot filter was used for each hybridization. The figure is a composite generated from a single autoradiographic exposure for each probe.

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that express an intermediate level of erbB-2 (>8) also express elevated L19 levels (>4). The cell lines that do not overexpress erbB-2 express low levels of L19. Through the two-tier screening procedure L19 displayed the most dramatic differences in expression of the candidate cDNA clones. For this reason, L19 is the focus of this study. Other candidate cDNAs were isolated. These may represent mRNAs of which also varies according to erbB-2 levels, suggesting that gene expression alterations associated with erbB-2 overexpression may be complex. Somewhat surprisingly, none of the final four clones examined represented the erbB-2 mRNA. It is therefore likely that additional sequences exist that have very different expression levels between the MCF-7 cell line and the SK-BR-3 cell line.

DNA Sequence Determination of Human L19 Clone. The cDNA insert of the clone was subcloned into the pUC18 and M13 vectors and found to be 690 base pairs long (including the polyadenylated tail), by dideoxy nucleotide sequencing. A computer search of the Genebank DNA database found 87% and 84% homology with the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and human ribosomal protein L19 sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively. The computer program generated protein translation of the L19 sequence gave a protein sequence of 196 amino acids that had 100% identity to the rat and mouse ribosomal protein L19 cDNA sequences, respectively.

L19 Expression Level in Human Breast Tumor Samples. We next attempted to determine if the coincidence of high-level expression of L19 and erbB-2 also occurs in primary human breast cancers. Quantitative determination of L19 and erbB-2 expression levels was accomplished by dot-blot analysis on total RNA from the tumor samples. The samples were judged by histological evaluation to contain an average of 43% tumor cells (SE = 3.1). Hybridization intensity using probes for L19 or erbB-2 was determined and normalized to β-actin hybridization signal intensity as previously described. Total RNA from the SK-BR-3, T47D, and MCF-7 cell lines were used as high-, medium-, and low-expression level controls on each blot. As shown in Fig. 3, relative expression levels of L19 in the tumor samples varied from 1 to 64, while the SK-BR-3, T47D, and MCF-7 controls gave 128, 16, and 2 values, respectively. For these experiments the lowest hybridization intensity was arbitrarily assigned the value of 1.

Based on these results the tumor samples were divided into two groups according to their L19 expression levels determined by the population distribution of these samples. The low group had L19 relative expression values of ≤8, while the high group had relative expression values of >8 and comprised 18 of 54 of the sample population. These groups were analyzed for the association of high-level L19 expression with available clinical information for each tumor. These included estrogen receptor status, progesterone receptor status, nuclear and histological grading, Ki-67 values, node status, tumor size, and erbB-2 expression levels (Table 2). The expression level for erbB-2 mRNA was measured and varied from 1 to 64, as previously reported (19). High-level L19 mRNA expression was very closely associated with the erbB-2 mRNA levels (P < 6 × 10^-7; Fig. 4). This strong association confirms the predictions of our screening approach and suggests that L19 gene expression may be caused by overexpression of erbB-2. Comparison of L19 expression found a possible association to the excised tumor size (P < 0.03 by χ² analysis). No statistical relationship between L19 expression and either estrogen receptor or progesterone receptor histological or nuclear grade or lymph node status was observed. In the case of lymph node status, the number of samples for which relevant diagnostic information was available makes a conclusion difficult. Unfortunately, no follow-up information was available for these patients.

Since L19 is a ribosomal protein, we reasoned that high-level expression might reflect an increased protein synthesis capability and that this might mirror cellular proliferation. To test the association of
Table 2 Clinical correlations with L19 overexpression in tumor samples

Excised tumor size was measured as the greatest dimension in centimeters. Positive estrogen and progesterone receptors samples had values of >45 fmol/mg. Ki-67-positive samples had values of >15. P values were determined by χ² analysis. The erbB-2-positives (+) had mRNA levels of ≥4, while the L19-positives had mRNA levels of ≥8.

<table>
<thead>
<tr>
<th></th>
<th>High-level L19 mRNA</th>
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<tbody>
<tr>
<td>erbB-2 overexpression</td>
<td>+ 14 5 6E-07</td>
</tr>
<tr>
<td>Tumor size</td>
<td>0-1 1 10</td>
</tr>
<tr>
<td>1-2</td>
<td>2 4 18</td>
</tr>
<tr>
<td>2-3</td>
<td>9 10</td>
</tr>
<tr>
<td>&gt;3</td>
<td>2 0.03</td>
</tr>
<tr>
<td>Estrogen receptor</td>
<td>+ 13 19</td>
</tr>
<tr>
<td>-</td>
<td>5 14</td>
</tr>
<tr>
<td>Progesterone receptor</td>
<td>+ 10 13</td>
</tr>
<tr>
<td>-</td>
<td>6 20</td>
</tr>
<tr>
<td>Histological grade</td>
<td>1 0 0</td>
</tr>
<tr>
<td>2</td>
<td>0 1</td>
</tr>
<tr>
<td>3</td>
<td>4 11</td>
</tr>
</tbody>
</table>
| 4                              | 8 17                 | 0.6
| Nuclear grade                  | 1 0 0                |
| 2                              | 1 11                 |
| 3                              | 3 7                  | 0.4
| 4                              | 0                   |
| Ki-67                          | + 3 5 11             |
| -                              | 11 16                | 0.5
| Lymph nodes                    | + 8 12               |
| -                              | 2 6                  | 0.6

L19 expression with the division rate, we measured the Ki-67 values determined by automated image analysis (20). No statistical correlation was found. These results indicate that high-level L19 expression is most tightly associated with erbB-2 overexpression of the clinical parameters measured for the primary tumor samples.

Expression of S16 and L26 Ribosomal Proteins Compared to L19. In order to determine if high-level L19 expression is indicative of a general increase in the ribosomal content, we examined the expression levels of two other ribosomal proteins. The identical dot-blot hybridization filters containing mRNA from human breast cancer cell lines and primary human tumor samples were hybridized with specific DNA probes corresponding to mRNA for encoding the S16 and L26 ribosomal proteins (21, 22). Determination of relative hybridization intensity was again normalized to the β-actin hybridization signal.

Neither S16 nor L26 expression was consistently elevated with high-level L19 expression for either cell lines or primary tumor samples. The expression levels for three cell lines are shown in Table 3. The maximum difference in expression for both S16 and L26 among the tested lines and tumors was 4- and 12-fold, respectively. Evidence of coordinated expression for S16 and L26 is shown in Fig. 5. No evidence of coordination of expression was detected with either L19 or erbB-2. These results suggest that the L19 gene is not a member of a tightly coregulated set of genes encoding ribosomal proteins. These results also suggest that erbB-2 overexpression is not a general stimulator of ribosomal proteins.

DISCUSSION

Our results indicate that the human ribosomal protein L19 is expressed at increased levels up to a 64-fold greater level in erbB-2-overexpressing tumors and cell lines. Our analysis of cell lines suggests that high-level expression of L19 is not a consequence of EOF receptor overexpression. The association of high-level expression of L19 with erbB-2 overexpression in the human breast cancers was remarkably consistent among 46 samples (P < 6 x 10⁻⁷). High-level L19 expression was more weakly associated (P = 0.03) with the excised tumor size. This is not unexpected, since previous studies have indicated a link between erbB-2 overexpression and tumor size. In fact, in the present study erbB-2 overexpression was associated with increased tumor size (P < 0.01).

Our results are not consistent with a model in which erbB-2 overexpression causes a coordinated increase in activity of protein synthesis machinery and L19 levels simply reflect an increased synthesis of ribosomes. Among different tumor samples there were limited differences in the expression level of the S16 and L26 ribosomal proteins. Higher levels of S16 mRNA were associated with higher L26 mRNA levels (P < 6 x 10⁻⁴). In contrast, the variation of S16 and L26 mRNA levels was independent of L19 and erbB-2 expression. These results suggest that L19 expression is not tightly linked to the expression of other ribosomal proteins in breast cancers. Variation in the expression of mRNAs of specific ribosomal proteins has been demonstrated in association with other cancers. Studies comparing...
malignant colon carcinomas to normal colon mucosa have reported increases in the mRNA for the acidic ribosomal phosphoprotein p2 (23) and L31 (24). More recently, the ribosomal protein mRNAs S3, S6, S8, S12, PO (25), and S19 (26) have been shown to be expressed at increased levels in both colon carcinomas and polyps. As yet, none of these changes have been implicated in the process of malignant transformation.

As is the case for many ribosomal proteins, it is not known what exact function is contributed by the L19 protein. Changes in L19 expression independent of other ribosomal proteins suggest that L19 is not simply a required structural element. Other ribosomal proteins have been implicated in regulatory processes that may be important in carcinogenesis. The ribosomal protein S6 is a serine kinase and is suggested to be important in cell transformation (28). It is also conceivable that L19 may serve functions other than contributing to the ribosomal structure. Interesting evidence for this comes from a study that artificially induced high-level expression of L19 mRNA can impart to a transfected cell a distinct characteristic that may contribute to the highly malignant behavior of some cancers.

At present, our studies do not indicate the mechanism responsible for high-level L19 expression found in erbB-2-overexpressing tumors. However, one mechanism can be ruled out. Coamplification of the erbB-2 and L19 genes does not occur in any cell lines analyzed as determined by comparative Southern blot analysis (data not shown). Moreover, no apparent structural alterations to the L19 genes were identified, as evidence by identical Southern blot band patterns. Two potential mechanisms that might be responsible for increases in L19 mRNA are transcriptional activation or mRNA stabilization. Our data do not allow us to discriminate between these possibilities. Either mechanism would suggest a role for erbB-2 overexpression in altering cellular gene expression. In this context, our data are consistent with erbB-2 overexpression regulating the "phenotype" of the cancer cell. If high-level L19 expression is characteristic of a phenotype it may be interesting to explore whether L19 protein expression can be used to evaluate the malignant potential of breast or other cancers.

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REFERENCES


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