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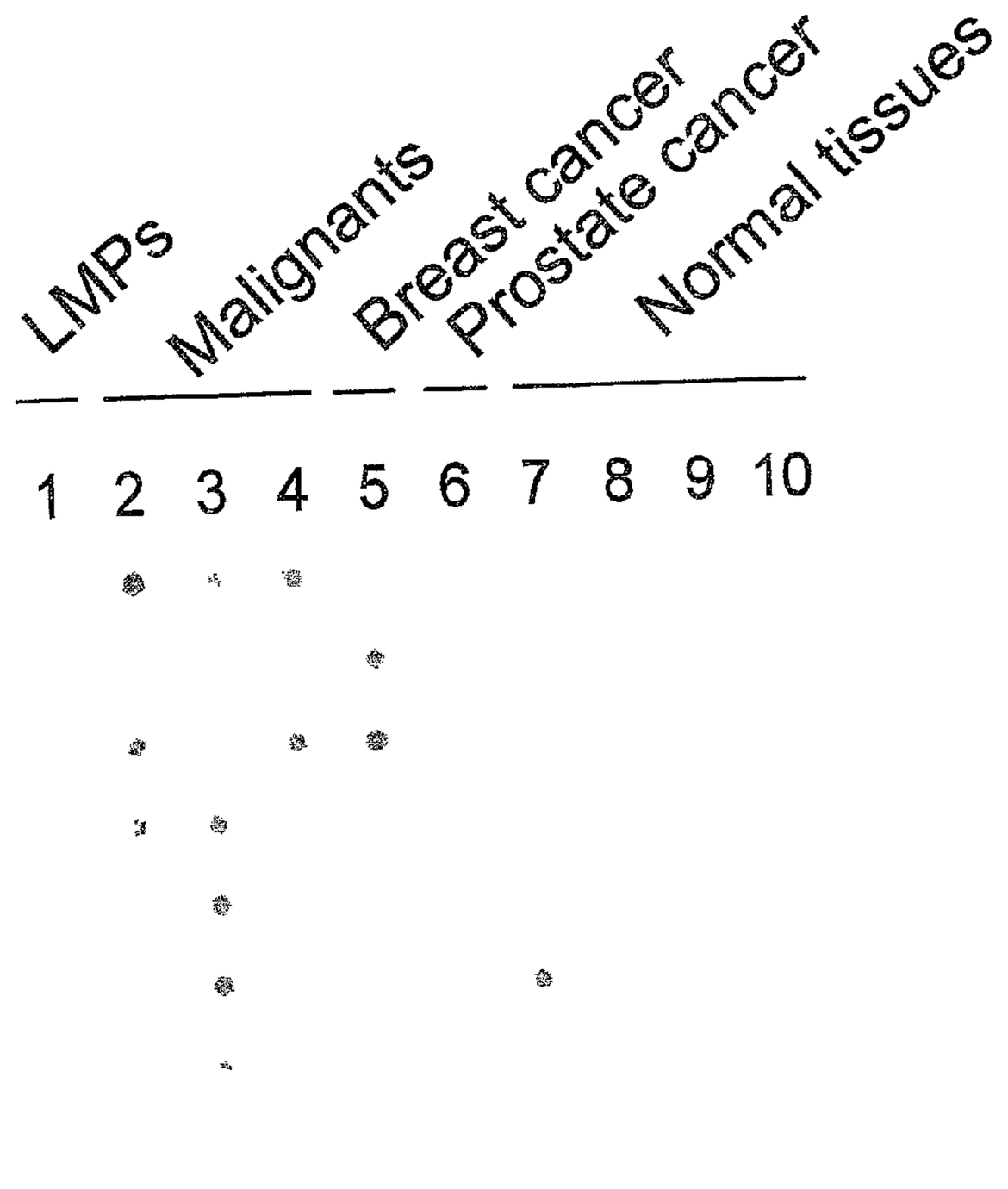
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(54) Title: POLYNUCLEOTIDES AND POLYPEPTIDE SEQUENCES INVOLVED IN CANCER



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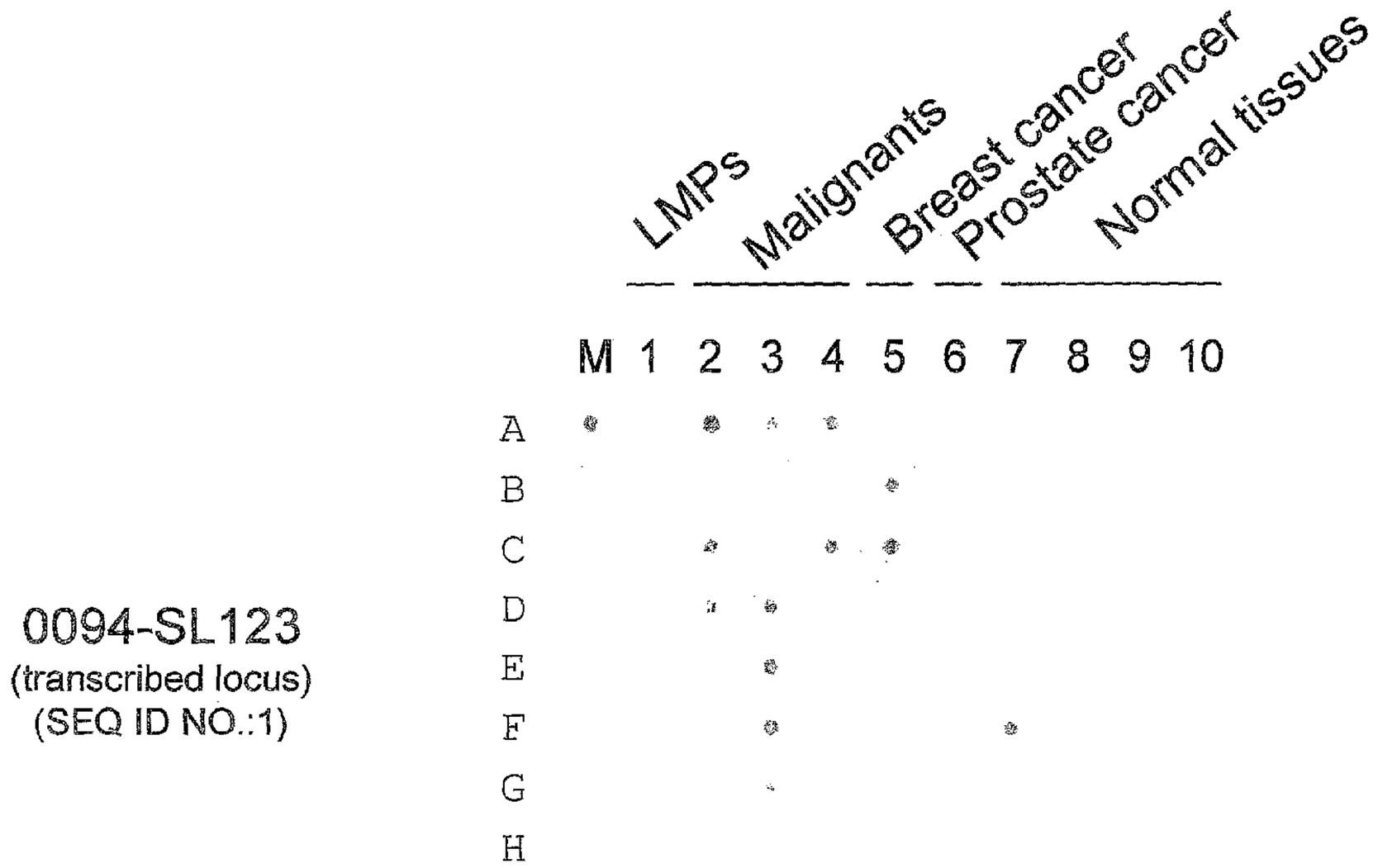
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(54) Title: POLYNUCLEOTIDES AND POLYPEPTIDE SEQUENCES INVOLVED IN CANCER



(57) Abstract: The present invention relates to polynucleotide and polypeptide sequences which are differentially expressed in cancer cells compared to normal cells. The present invention more particularly relates to the use of these sequences in the diagnosis, prognosis or treatment of cancer and in the detection of cancer cells.

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POLYNUCLEOTIDES AND POLYPEPTIDE SEQUENCES INVOLVED IN CANCER

FIELD OF THE INVENTION

The present invention relates to polynucleotide and polypeptide sequences which are differentially expressed in cancer compared to normal cells. The present invention more particularly relates to the use of these sequences in the diagnosis, prognosis or treatment of cancer and in the detection of cancer cells.

BACKGROUND OF THE INVENTION

Among gynecologic malignancies, ovarian cancer accounts for the highest tumor-related mortality in women in the United States (Jemal et al., 2005). It is the fourth leading cause of cancer-related death in women in the U.S (Menon et al., 2005). The American Cancer Society estimated a total of 22,220 new cases in 2005 and attributed 16,210 deaths to the disease (Bonome et al., 2005). For the past 30 years, the statistics have remained largely the same - the majority of women who develop ovarian cancer will die of this disease (Chambers and Vanderhyden, 2006). The disease carries a 1:70 lifetime risk and a mortality rate of >60% (Chambers and Vanderhyden, 2006). The high mortality rate is due to the difficulties with the early detection of ovarian cancer when the malignancy has already spread beyond the ovary. Indeed, >80% of patients are diagnosed with advanced staged disease (stage III or IV) (Bonome et al., 2005). These patients have a poor prognosis that is reflected in <45% 5-year survival rate, although 80% to 90% will initially respond to chemotherapy (Berek et al., 2000). This increased success compared to 20% 5-year survival rate years earlier is, at least in part, due to the ability to optimally debulk tumor tissue when it is confined to the ovaries, which is a significant prognostic factor for ovarian cancer (Bristow R. E., 2000 and Brown et al., 2004). In patients who are diagnosed with early disease (stage I), the 5-yr survival ranges from >90 (Chambers and Vanderhyden, 2006).

Ovarian cancer comprises a heterogeneous group of tumors that are derived from the surface epithelium of the ovary or from surface inclusions. They are classified into serous, mucinous, endometrioid, clear cell, and Brenner (transitional) types corresponding to the different types of epithelia in the organs of the female reproductive tract (Shih and Kurman, 2005). Of these, serous tumors account for ~60% of the ovarian cancer cases diagnosed. Each histologic subcategory is further

divided into three groups: benign, intermediate (borderline tumor or low malignancy potential (LMP)), and malignant, reflecting their clinical behavior (Seidman et al., 2002). LMP represents 10% to 15% of tumors diagnosed as serous and is a conundrum as they display atypical nuclear structure and metastatic behavior, yet they are considerably less aggressive than high-grade serous tumors. The 5-year survival for patients with LMP tumors is 95% in contrast to a <45% survival for advanced high-grade disease over the same period (Berek et al., 2000).

Despite improved knowledge of the etiology of the disease, aggressive cytoreductive surgery, and modern combination chemotherapy, there has been only little change in mortality. Poor outcomes have been attributed to (1) lack of adequate screening tests for early disease detection, in combination with only subtle presentation of symptoms at this stage - diagnosis is frequently being made only after progression to later stages, at which point the peritoneal dissemination of the cancer limits effective treatment and (2) the frequent development of resistance to standard chemotherapeutic strategies limiting improvement in the 5-year survival rate of patients. The initial chemotherapy regimen for ovarian cancer includes the combination of carboplatin (Paraplatin™) and paclitaxel (taxol™). Years of clinical trials have proved this combination to be most effective after effective surgery - reduces tumor volume in about 80% of the women with newly diagnosed ovarian cancer and 40% to 50% will have complete regression - but studies continue to look for ways to improve it. Recent abdominal infusion of chemotherapeutics to target hard-to-reach cells in combination with intravenous delivery has increased the effectiveness. However, severe side effects often lead to an incomplete course of treatment. Some other chemotherapeutic agents include doxorubicin, cisplatin, cyclophosphamide, bleomycin, etoposide, vinblastine, topotecan hydrochloride, ifosfamide, 5-fluorouracil and melphalan. The excellent survival rates for women with early stage disease receiving chemotherapy provide a strong rationale for research efforts to develop strategies to improve the detection of ovarian cancer. Furthermore, the discovery of new ovarian cancer-related biomarkers will lead to the development of more effective therapeutic strategies with minimal side effects for the future treatment of ovarian cancer.

Presently, the diagnosis of ovarian cancer is accomplished, in part, through routine analysis of the medical history of patients and by performing physical, ultrasound and x-ray examinations, and hematological screening. Two alternative strategies have been reported for early hematological detection of serum biomarkers. One approach is the analysis of serum samples by mass spectrometry to find proteins or protein fragments of unknown identity that detect the presence or absence of cancer

(Mor et al., 2005 and Kozak et al., 2003). However, this strategy is expensive and not broadly available. Alternatively, the presence or absence of known proteins/peptides in the serum is being detected using antibody microarrays, ELISA, or other similar approaches. Serum testing for a protein biomarker called CA-125 (cancer antigen-125) has long been widely performed as a marker for ovarian cancer. However, although ovarian cancer cells may produce an excess of these protein molecules, there are some other cancers, including cancer of the fallopian tube or endometrial cancer (cancer of the lining of the uterus), 60% of people with pancreatic cancer, and 20%-25% of people with other malignancies with elevated levels of CA-125. The CA-125 test only returns a true positive result for about 50% of Stage I ovarian cancer patients and has a80% chance of returning true positive results from stage II, III, and IV ovarian cancer patients. The other 20% of ovarian cancer patients do not show any increase in CA-125 concentrations. In addition, an elevated CA-125 test may indicate other benign activity not associated with cancer, such as menstruation, pregnancy, or endometriosis. Consequently, this test has very limited clinical application for the detection of early stage disease when it is still treatable, exhibiting a positive predictive value (PPV) of <10%. And, even with the addition of ultrasound screening to CA-125, the PPV only improves to around 20% (Kozak et al., 2003). Thus, this test is not an effective screening test.

Other studies have yielded a number of biomarker combinations with increased specificity and sensitivity for ovarian cancer relative to CA-125 alone (McIntosh et al., 2004, Woolas et al., 1993, Schorge et., 2004). Serum biomarkers that are often elevated in women with epithelial ovarian cancer, but not exclusively, include carcinoembryonic antigen, ovarian cystadenocarcinoma antigen, lipidassociated sialic acid, NB/70,TAG72.3, CA-15.3, and CA-125. Unfortunately, although this approach has increased the sensitivity and specificity of early detection, published biomarker combinations still fail to detect a significant percentage of stage I/II epithelial ovarian cancer. Another study (Elieser et al., 2005) measured serum concentrations of 46 biomarkers including CA-125 and amongst these, 20 proteins in combination correctly recognized more than 98% of serum samples of women with ovarian cancer compared to other benign pelvic disease. Although other malignancies were not included in this study, this multimarker panel assay provided the highest diagnostic power for early detection of ovarian cancer thus far.

Additionally, with the advent of differential gene expression analysis technologies, for example DNA microarrays and subtraction methods, many groups have now reported large collections of genes that are upregulated in epithelial ovarian

cancer (United States Patent Application published under numbers; 20030124579, 20030087250, 20060014686, 20060078941, 20050095592, 20050214831, 20030219760, 20060078941, 20050214826). However, the clinical utilities with respect to ovarian cancer of one or combinations of these genes are not as yet fully determined.

There is a need for new tumor biomarkers for improving diagnosis and/or prognosis of cancer. In addition, due to the genetic diversity of tumors, and the development of chemoresistance by many patients, there exists further need for better and more universal therapeutic approaches for the treatment of cancer. Molecular targets for the development of such therapeutics may preferably show a high degree of specificity for the tumor tissues compared to other somatic tissues, which will serve to minimize or eliminate undesired side effects, and increase the efficacy of the therapeutic candidates.

This present invention tries to address these needs and other needs.

SUMMARY OF THE INVENTION

In accordance with the present invention, there is provided new polynucleotide sequences and new polypeptide sequences as well as compositions, antibodies specific for these sequences, vectors and cells comprising a recombinant form of these new sequences.

The present invention also provides methods of detecting cancer cells using single or multiple polynucleotides and/or polypeptide sequences which are specific to these tumor cells. Some of the polynucleotides and/or polypeptides sequences provided herein are differentially expressed in ovarian cancer compared to normal cells and may also be used to distinguish between malignant ovarian cancer and an ovarian cancer of a low malignancy potential and/or a normal state (individual free of ovarian cancer).

Also encompassed by the present invention are diagnostic methods, prognostic methods, methods of detection, kits, arrays, librairies and assays which comprises one or more polypeptide and/or polynucleotide sequences or antibodies described herein as well as new therapeutic avenues for cancer treatment.

The Applicant has come to the surprising discovery that polynucleotide and/or polypeptide sequences described herein are preferentially upregulated in malignant ovarian cancer compared to low malignancy potential ovarian cancer and/or compared to normal cells. More interestingly, some of these sequences appear to be overexpressed in late stage ovarian cancer.

The Applicant has also come to the surprising discovery that some of the sequences described herein are not only expressed in ovarian cancer cells but in other cancer cells such as cells from breast cancer, prostate cancer, renal cancer, colon cancer, lung cancer, melanoma, leukemia and from cancer of the central nervous system. As such, several of these sequences, either alone or in combination may represent universal tumor markers. Therefore, some NSEQs and PSEQs described herein not only find utility in the field of ovarian cancer detection and treatment but also in the detection and treatment of other types of tumors

Therefore, using NSEQs or PSEQs of the present invention, one may readily identify a cell as being cancerous. As such NSEQs or PSEQs may be used to identify a cell as being a ovarian cancer cell, a prostate cancer cell, a breast cancer cell, a lung cancer cell, a colon cancer cell, a renal cancer cell, a cell from a melanoma, a leukemia cell or a cell from a cancer of the central nervous system.

Even more particularly, NSEQs or PSEQs described herein may be used to identify a cell as being a malignant ovarian cancer or a low malignant potential ovarian cancer.

The presence of some NSEQs or PSEQs in ovarian cancer cell may preferentially be indicative that the ovarian cancer is of the malignant type. Some NSEQs or PSEQs of the present invention may also more particularly indicate that the cancer is a late-stage malignant ovarian cancer.

The NSEQs or PSEQs may further be used to treat cancer or to identify compounds useful in the treatment of cancer including, ovarian cancer (i.e, LMP and/or malignant ovarian cancer), prostate cancer, breast cancer, lung cancer, colon cancer, renal cancer, melanoma, leukemia or cancer of the central nervous system.

As used herein and in some embodiments of the invention, the term "NSEQ" refers generally to polynucleotides sequences comprising or consisting of any one of SEQ. ID. NOs:1 to 49, and 169 (e.g., an isolated form) or comprising or consisting of a fragment of any one of SEQ. ID. NOs: 1 to 49 and 169. The term "NSEQ" more particularly refers to a polynucleotide sequence comprising or consisting of a transcribed portion of any one of SEQ. ID. NOs:1 to 49 and 169, which may be, for example, free of untranslated or untranslatable portion(s) (i.e., a coding portion of any one of SEQ ID Nos.: 1-49 and 169). The term "NSEQ" additionally refers to a sequence substantially identical to any one of the above and more particularly substantially identical to polynucleotide sequence comprising or consisting of a transcribed portion of any one of SEQ. ID. NOs:1 to 49 and 169, which may be, for example, free of untranslated or untranslatable portion(s). The term "NSEQ"

additionally refers to a nucleic acid sequence region of any one of SEQ. ID. NOs:1 to 49 and 169 which encodes or is able to encode a polypeptide. The term "NSEQ" also refers to a polynucleotide sequence able to encode any one of the polypeptides described herein or a polypeptide fragment of any one of the above. Finally, the term "NSEQ" refers to a sequence substantially complementary to any one of the above.

In other embodiments of the invention such as those which relate to detection and/or treatment of cancers other than ovarian cancer, NSEQ may also relates to SEQ ID NO.:50 including any polynucleotide comprising or consisting of SEQ. ID. NO:50 (e.g., an isolated form) or comprising or consisting of a fragment of any one of SEQ. ID. NO:50, such as a polynucleotide sequence comprising or consisting of a transcribed portion of any one of SEQ. ID. NO:50, which may be, for example, free of untranslated or untranslatable portion(s) (i.e., a coding portion of SEQ. ID. NO:50). The term "NSEQ" additionally refers to a sequence substantially identical to any one of the above and more particularly substantially identical to polynucleotide sequence comprising or consisting of a transcribed portion of SEQ. ID. NO:50, which may be, for example, free of untranslated or untranslatable portion(s). The term "NSEQ" additionally refers to a nucleic acid sequence region of SEQ. ID. NO:50 which encodes or is able to encode a polypeptide. Finally, the term "NSEQ" refers to a sequence substantially complementary to any one of the above.

As such, in embodiments of the invention NSEQ encompasses, for example, SEQ. ID. NOs:1 to 49, 50 and 169 and also encompasses polynucleotide sequences which comprises, are designed or derived from SEQ. ID. NOs:1 to 49, 50 or 169. Non-limiting examples of such sequences includes, for example, SEQ ID NOs.: 103-150 or 151-152.

The term "inhibitory NSEQ" generally refers to a sequence substantially complementary to any one of SEQ. ID. NOs:1 to 49, 50 or 169, substantially complementary to a fragment of any one of SEQ. ID. Nos: 1 to 49, 50 or 169, substantially complementary to a sequence substantially identical to SEQ. ID. NOs:1 to 49, 50 or 169 and more particularly, substantially complementary to a transcribed portion of any one of SEQ. ID. NOs:1 to 49, 50 or 169 (e.g., which may be free of unstranslated or untranslatable portion) and which may have attenuating or even inhibitory action againts the transcription of a mRNA or against expression of a polypeptide encoded by a corresponding SEQ ID NOs.:1 to 49, 50 or 169. Suitable "inhibitory NSEQ" may have for example and without limitation from about 10 to about 30 nucleotides, from about 10 to about 25 nucleotides or from about 15 to about 20 nucleotides.

As used herein the term "PSEQ" refers generally to each and every polypeptide sequences mentioned herein such as, for example, any polypeptide sequences encoded (putatively encoded) by any one of NSEQ described herein (e.g., any one of SEQ. ID. NOs:1 to 49 or 169) including their isolated or substantially purified form. Therefore, in embodiments of the invention, a polypeptide comprising or consisting of any one of SEQ. ID. NOs:51 to 88 or 170 including variants (e.g., an isolated natural protein variant), analogs, derivatives and fragments thereof are collectively referred to herein as "PSEQ". In other embodiments of the invention, such as those related to detection and/or treatment of cancers other than ovarian cancer, PSEQ also refers to polypeptide comprising or consisting of SEQ ID NO.:89 including variants (e.g., an isolated natural protein variant), analogs, derivatives and fragments.

Some of the NSEQs or PSEQs described herein have been previously characterized for purposes other than those described herein. As such dignostics and therapeutics which are known to target those NSEQs or PSEQs (e.g., antibodies and/or inhibitors) may thus now be applied for inhibition of these NSEQ or PSEQ in the context of treatment of ovarian cancer, prostate cancer, renal cancer, colon cancer, lung cancer, melanoma, leukemia or cancer of the central nervous system. The use of these known therapeutics and diagnostics for previously undisclosed utility such as those described herein is encompassed by the present invention.

For example, antibodies capable of binding to folate receptor-1 may thus be used for specific binding of tumor cells other than ovarian cancer cells, such as breast cancer, prostate cancer, renal cancer, colon cancer, lung cancer, melanoma, leukemia and from cancer of the central nervous system. As such the use of antibodies and/or inhibitors of folate receptor-1 (e.g., CB300638, CB300945 which are Cyclopenta[g]quinazoline-based Thymidylate Synthase Inhibitor, those described in US20040242606, US20050009851, etc.) in the use of treatment of prostate cancer, renal cancer, colon cancer, lung cancer, melanoma, leukemia and cancer of the central nervous system is encompassed by the present invention.

NON-LIMITATIVE EXEMPLARY EMBODIMENTS OF THE INVENTION

Use of NSEQ as a Screening Tool

The NSEQ described herein may be used either directly or in the development of tools for the detection and isolation of expression products (mRNA, mRNA precursor, hnRNA, etc.), of genomic DNA or of synthetic products (cDNA, PCR fragments, vectors comprising NSEQ etc.). NSEQs may also be used to prepare suitable tools for detecting an encoded polypeptide or protein. NSEQ may thus be

used to provide an encoded polypeptide and to generate an antibody specific for the polypeptide.

Those skilled in the art will also recognize that short oligonucleotides sequences may be prepared based on the polynucleotide sequences described herein. For example, oligonucleotides having 10 to 20 nucleotides or more may be prepared for specifically hybridizing to a NSEQ having a substantially complementary sequence and to allow detection, identification and isolation of nucleic sequences by hybridization. Probe sequences of for example, at least 10-20 nucleotides may be prepared based on a sequence found in any one of SEQ ID NO.:1 to 49, 50 or 169 and more particularly selected from regions that lack homology to undesirable sequences. Probe sequences of 20 or more nucleotides that lack such homology may show an increased specificity toward the target sequence. Useful hybridization conditions for probes and primers are readily determinable by those of skill in the art. Stringent hybridization conditions encompassed herewith are those that may allow hybridization of nucleic acids that are greater than 90% homologous but which may prevent hybridization of nucleic acids that are less than 70% homologous. The specificity of a probe may be determined by whether it is made from a unique region, a regulatory region, or from a conserved motif. Both probe specificity and the stringency of diagnostic hybridization or amplification (maximal, high, intermediate, or low) reactions depend on whether or not the probe identifies exactly complementary sequences, allelic variants, or related sequences. Probes designed to detect related sequences may have, for example, at least 50% sequence identity to any of the selected polynucleotides.

Furthermore, a probe may be labelled by any procedure known in the art, for example by incorporation of nucleotides linked to a "reporter molecule". A "reporter molecule", as used herein, may be a molecule that provides an analytically identifiable signal allowing detection of a hybridized probe. Detection may be either qualitative or quantitative. Commonly used reporter molecules include fluorophores, enzymes, biotin, chemiluminescent molecules, bioluminescent molecules, digoxigenin, avidin, streptavidin or radioisotopes. Commonly used enzymes include horseradish peroxidase, alkaline phosphatase, glucose oxidase and β-galactosidase, among others. Enzymes may be conjugated to avidin or streptavidin for use with a biotinylated probe. Similarly, probes may be conjugated to avidin or streptavidin for use with a biotinylated enzyme. Incorporation of a reporter molecule into a DNA probe may be effected by any method known to the skilled artisan, for example by nick translation, primer extension, random oligo priming, by 3' or 5' end labeling or by other

means. In addition, hybridization probes include the cloning of nucleic acid sequences into vectors for the production of mRNA probes. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro. The labelled polynucleotide sequences may be used in Southern or northern analysis, dot blot, or other membrane-based technologies; in PCR technologies; and in micro arrays utilizing samples from subjects to detect altered expression. Oligonucleotides useful as probes for screening of samples by hybridization assays or as primers for amplification may be packaged into kits. Such kits may contain the probes or primers in a pre-measured or predetermined amount, as well as other suitably packaged reagents and materials needed for the particular hybridization or amplification protocol.

The expression of mRNAs identical or substantially identical to the NSEQs of the present invention may thus be detected and/or isolated using methods which are known in the art. Exemplary embodiment of such methods includes, for example and without limitation, hybridization analysis using oligonucleotide probes, reverse transcription and *in vitro* nucleic acid amplification methods.

Such procedures may therefore, permit detection of mRNAs in ovarian cells (e.g., ovarian cancer cells) or in any other cells expressing such mRNAs. Expression of mRNA in a tissue-specific or a disease-specific manner may be useful for defining the tissues and/or particular disease state. One of skill in the art may readily adapt the NSEQs for these purposes.

It is to be understood herein that the NSEQs may hybridize to a substantially complementary sequence found in a test sample (e.g., cell, tissue, etc.). Additionally, a sequence substantially complementary to NSEQ (including fragments) may bind a NSEQ and substantially identical sequences found in a test sample (e.g., cell, tissue, etc.).

Polypeptide encoded by an isolated NSEQ, polypeptide variants, polypeptide analogs or polypeptide fragments thereof are also encompassed herewith. The polypeptides whether in a premature, mature or fused form, may be isolated from lysed cells, or from the culture medium, and purified to the extent needed for the intended use. One of skill in the art may readily purify these proteins, polypeptides and peptides by any available procedure. For example, purification may be accomplished by salt fractionation, size exclusion chromatography, ion exchange chromatography, reverse phase chromatography, affinity chromatography and the like. Alternatively, PSEQ may be made by chemical synthesis.

Natural variants may be identified through hybridization screening of a nucleic acid library or polypeptide library from different tissue, cell type, population, species,

etc using the NSEQ and derived tools.

Use of NSEQ for Development of an Expression System

In order to express a polypeptide, a NSEQ able to encode any one of a PSEQ described herein may be inserted into an expression vector, i.e., a vector that contains the elements for transcriptional and translational control of the inserted coding sequence in a particular host. These elements may include regulatory sequences, such as enhancers, constitutive and inducible promoters, and 5′ and 3′ un-translated regions. Methods that are well known to those skilled in the art may be used to construct such expression vectors. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination.

A variety of expression vector/host cell systems known to those of skill in the art may be utilized to express a polypeptide or RNA from NSEQ. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with baculovirus vectors; plant cell systems transformed with viral or bacterial expression vectors; or animal cell systems. For long-term production of recombinant proteins in mammalian systems, stable expression in cell lines may be effected. For example, NSEQ may be transformed into cell lines using expression vectors that may contain viral origins of replication and/or endogenous expression elements and a selectable or visible marker gene on the same or on a separate vector. The invention is not to be limited by the vector or host cell employed.

Alternatively, RNA and/or polypeptide may be expressed from a vector comprising NSEQ using an *in vitro* transcription system or a coupled *in vitro* transcription/translation system respectively.

In general, host cells that contain NSEQ and/or that express a polypeptide encoded by the NSEQ, or a portion thereof, may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA/DNA or DNA/RNA hybridizations, PCR amplification, and protein bioassay or immunoassay techniques that include membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or amino acid sequences. Immunological methods for detecting and measuring the expression of polypeptides using either specific polyclonal or monoclonal antibodies are known in the art. Examples of such techniques include enzyme-linked immunosorbent assays

(ELISAs), radioimmunoassays (RIAs), and fluorescence activated cell sorting (FACS). Those of skill in the art may readily adapt these methodologies to the present invention.

Host cells comprising NSEQ may thus be cultured under conditions for the transcription of the corresponding RNA (mRNA, siRNA, shRNA etc.) and/or the expression of the polypeptide from cell culture. The polypeptide produced by a cell may be secreted or may be retained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing NSEQ may be designed to contain signal sequences that direct secretion of the polypeptide through a prokaryotic or eukaryotic cell membrane. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode the same, substantially the same or a functionally equivalent amino acid sequence may be produced and used, for example, to express a polypeptide encoded by NSEQ. The nucleotide sequences of the present invention may be engineered using methods generally known in the art in order to alter the nucleotide sequences for a variety of purposes including, but not limited to, modification of the cloning, processing, and/or expression of the gene product. DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. For example, oligonucleotide-mediated site-directed mutagenesis may be used to introduce mutations that create new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, and so forth. In addition, a host cell strain may be chosen for its ability to modulate expression of the inserted sequences or to process the expressed polypeptide in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing, which cleaves a "prepro" form of the polypeptide, may also be used to specify protein targeting, folding, and/or activity. Different host cells that have specific cellular machinery and characteristic mechanisms for post-translational activities (e.g., CHO, HeLa, MDCK, HEK293, and W138) are available commercially and from the American Type Culture Collection (ATCC) and may be chosen to ensure the correct modification and processing of the expressed polypeptide.

Those of skill in the art will readily appreciate that natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence resulting in translation of a fusion polypeptide containing heterologous polypeptide moieties in any of the aforementioned host systems. Such heterologous polypeptide moieties may facilitate purification of fusion polypeptides using commercially available

affinity matrices. Such moieties include, but are not limited to, glutathione S-transferase (GST), maltose binding protein, thioredoxin, calmodulin binding peptide, 6-His (His), FLAG, c-myc, hemaglutinin (HA), and antibody epitopes such as monoclonal antibody epitopes.

In yet a further aspect, the present invention relates to a polynucleotide which may comprise a nucleotide sequence encoding a fusion protein, the fusion protein may comprise a fusion partner fused to a peptide fragment of a protein encoded by, or a naturally occurring allelic variant polypeptide encoded by, the polynucleotide sequence described herein.

Those of skill in the art will also readily recognize that the nucleic acid and polypeptide sequences may be synthesized, in whole or in part, using chemical or enzymatic methods well known in the art. For example, peptide synthesis may be performed using various solid-phase techniques and machines such as the ABI 431A Peptide synthesizer (PE Biosystems) may be used to automate synthesis. If desired, the amino acid sequence may be altered during synthesis and/or combined with sequences from other proteins to produce a variant protein.

The present invention additionally relates to a bioassay for evaluating compounds as potential antagonists of the polypeptide described herein, the bioassay may comprise:

a) culturing test cells in culture medium containing increasing concentrations of at least one compound whose ability to inhibit the action of a polypeptide described herein is sought to be determined, wherein the test cells may contain a polynucleotide sequence described herein (for example, in a form having improved trans-activation transcription activity, relative to wild-type polynucleotide, and comprising a response element operatively linked to a reporter gene); and thereafter

b) monitoring in the cells the level of expression of the product of the reporter gene (encoding a reporter molecule) as a function of the concentration of the potential antagonist compound in the culture medium, thereby indicating the ability of the potential antagonist compound to inhibit activation of the polypeptide encoded by, the polynucleotide sequence described herein.

The present invention further relates to a bioassay for evaluating compounds as potential agonists for a polypeptide encoded by the polynucleotide sequence described herein, the bioassay may comprise:

a) culturing test cells in culture medium containing increasing

concentrations of at least one compound whose ability to promote the action of the polypeptide encoded by the polynucleotide sequence described herein is sought to be determined, wherein the test cells may contain a polynucleotide sequence described herein (for example, in a form having improved trans-activation transcription activity, relative to wild-type polynucleotide, and comprising a response element operatively linked to a reporter gene); and thereafter

b) monitoring in the cells the level of expression of the product of the reporter gene as a function of the concentration of the potential agonist compound in the culture medium, thereby indicating the ability of the potential agonist compound to promote activation of a polypeptide encoded by the polynucleotide sequence described herein.

Use of NSEQ as a Identification Tool or as a Diagnostic Screening Tool

The skilled artisan will readily recognize that NSEQ may be used to identify a particular cell, cell type, tissue, disease and thus may be used for diagnostic purposes to determine the absence, presence, or altered expression (i.e. increased or decreased compared to normal) of the expression product of a gene. Suitable NSEQ may be for example, between 10 and 20 or longer, i.e., at least 10 nucleotides long or at least 12 nucleotides long, or at least 15 nucleotides long up to any desired length and may comprise, for example, RNA, DNA, branched nucleic acids, and/or peptide nucleic acids (PNAs). In one alternative, the polynucleotides may be used to detect and quantify gene expression in samples in which expression of NSEQ is correlated with disease. In another alternative, NSEQ may be used to detect genetic polymorphisms associated with a disease. These polymorphisms may be detected, for example, in the transcript, cDNA or genomic DNA.

The invention provides for the use of at least one of the NSEQ described herein on an array and for the use of that array in a method of detection of a particular cell, cell type, tissue, disease for the prognosis or diagnosis of cancer. The method may comprise hybridizing the array with a patient sample (putatively comprising or comprising a target polynucleotide sequence substantially complementary to a NSEQ) under conditions to allow complex formation (between NSEQ and target polynucleotide), detecting complex formation, wherein the complex formation is indicative of the presence of the polynucleotide and wherein the absence of complex formation is indicative of the absence of the polynucleotide in the patient sample. The presence or absence of the polynucleotide may be indicative of cancer such as, for

example, ovarian cancer or other cancer as indicated herein.

The method may also comprise the step of quantitatively or qualitatively comparing (e.g., with a computer system, apparatus) the level of complex formation in the patient sample to that of standards for normal cells or individual or other type, origin or grade of cancer.

The present invention provides one or more compartmentalized kits for detection of a polynucleotide and/or polypeptide for the diagnosis or prognosis of ovarian cancer. A first kit may have a receptacle containing at least one isolated NSEQ or probe comprising NSEQ. Such a probe may bind to a nucleic acid fragment which is present/absent in normal cells but which is absent/present in affected or diseased cells. Such a probe may be specific for a nucleic acid site that is normally active/inactive but which may be inactive/active in certain cell types. Similarly, such a probe may be specific for a nucleic acid site that may be abnormally expressed in certain cell types. Finally, such a probe may identify a specific mutation. The probe may be capable of hybridizing to the nucleic acid sequence which is mutated (not identical to the normal nucleic acid sequence), or may be capable of hybridizing to nucleic acid sequences adjacent to the mutated nucleic acid sequences. The probes provided in the present kits may have a covalently attached reporter molecule. Probes and reporter molecules may be readily prepared as described above by those of skill in the art.

Antibodies (e.g., isolated antibody) that may specifically bind to a protein or polypeptide described herein (a PSEQ) as well as nucleic acids encoding such antibodies are also encompassed by the present invention.

As used herein the term "antibody" means a monoclonal antibody, a polyclonal antibody, a single chain antibody, a chimeric antibody, a humanized antibody, a deimmunized antibody, an antigen-binding fragment, an Fab fragment; an $F(ab')_2$ fragment, and Fv fragment; CDRs, or a single-chain antibody comprising an antigen-binding fragment (e.g., a single chain Fv).

The antibody may originate for example, from a mouse, rat or any other mammal or from other sources such as through recombinant DNA technologies.

The antibody may also be a human antibody which may be obtained, for example, from a transgenic non-human mammal capable of expressing human Ig genes. The antibody may also be a humanised antibody which may comprise, for example, one or more complementarity determining regions of non-human origin. It may also comprise a surface residue of a human antibody and/or framework regions of a human antibody. The antibody may also be a chimeric antibody which may

comprise, for example, variable domains of a non-human antibody and constant domains of a human antibody.

The antibody of the present invention may be mutated and selected based on an increased affinity, solubility, stability, specificity and/or for one of a polypeptide described herein and/or based on a reduced immunogenicity in a desired host or for other desirable characteristics.

Suitable antibodies may bind to unique antigenic regions or epitopes in the polypeptides, or a portion thereof. Epitopes and antigenic regions useful for generating antibodies may be found within the proteins, polypeptides or peptides by procedures available to one of skill in the art. For example, short, unique peptide sequences may be identified in the proteins and polypeptides that have little or no homology to known amino acid sequences. Preferably the region of a protein selected to act as a peptide epitope or antigen is not entirely hydrophobic; hydrophilic regions are preferred because those regions likely constitute surface epitopes rather than internal regions of the proteins and polypeptides. These surface epitopes are more readily detected in samples tested for the presence of the proteins and polypeptides. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, and single chain antibodies, Fab fragments, and fragments produced by a Fab expression library. The production of antibodies is well known to one of skill in the art and is not intended to be limited herein.

Peptides may be made by any procedure known to one of skill in the art, for example, by using in vitro translation or chemical synthesis procedures or by introducing a suitable expression vector into cells. Short peptides which provide an antigenic epitope but which by themselves are too small to induce an immune response may be conjugated to a suitable carrier. Suitable carriers and methods of linkage are well known in the art. Suitable carriers are typically large macromolecules such as proteins, polysaccharides and polymeric amino acids. Examples include serum albumins, keyhole limpet hemocyanin, ovalbumin, polylysine and the like. One of skill in the art may use available procedures and coupling reagents to link the desired peptide epitope to such a carrier. For example, coupling reagents may be used to form disulfide linkages or thioether linkages from the carrier to the peptide of interest. If the peptide lacks a disulfide group, one may be provided by the addition of a cysteine residue. Alternatively, coupling may be accomplished by activation of carboxyl groups.

The minimum size of peptides useful for obtaining antigen specific antibodies may vary widely. The minimum size must be sufficient to provide an antigenic epitope

that is specific to the protein or polypeptide. The maximum size is not critical unless it is desired to obtain antibodies to one particular epitope. For example, a large polypeptide may comprise multiple epitopes, one epitope being particularly useful and a second epitope being immunodominant, etc. Typically, antigenic peptides selected from the present proteins and polypeptides will range without limitation, from 5 to about 100 amino acids in length. More typically, however, such an antigenic peptide will be a maximum of about 50 amino acids in length, and preferably a maximum of about 30 amino acids. It is usually desirable to select a sequence of about 6, 8, 10, 12 or 15 amino acids, up to about 20 or 25 amino acids (and any number therebetween).

Amino acid sequences comprising useful epitopes may be identified in a number of ways. For example, preparing a series of short peptides that taken together span the entire protein sequence may be used to screen the entire protein sequence. One of skill in the art may routinely test a few large polypeptides for the presence of an epitope showing a desired reactivity and also test progressively smaller and overlapping fragments to identify a preferred epitope with the desired specificity and reactivity.

As mentioned herein, antigenic polypeptides and peptides are useful for the production of monoclonal and polyclonal antibodies. Antibodies to a polypeptide encoded by the polynucleotides of NSEQ, polypeptide analogs or portions thereof, may be generated using methods that are well known in the art. For example, monoclonal antibodies may be prepared using any technique that provides for the production of antibody molecules by continuous cell lines in culture. These include, but are not limited to, the hybridoma, the human B-cell hybridoma, and the EBV-hybridoma techniques. In addition, techniques developed for the production of chimeric antibodies may be used. Alternatively, techniques described for the production of single chain antibodies may be employed. Fabs that may contain specific binding sites for a polypeptide encoded by the polynucleotides of NSEQ, or a portion thereof, may also be generated. Various immunoassays may be used to identify antibodies having the desired specificity. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art.

To obtain polyclonal antibodies, a selected animal may be immunized with a protein or polypeptide. Serum from the animal may be collected and treated according to known procedures. Polyclonal antibodies to the protein or polypeptide of interest may then be purified by affinity chromatography. Techniques for producing polyclonal antisera are well known in the art.

Monoclonal antibodies (MAbs) may be made by one of several procedures available to one of skill in the art, for example, by fusing antibody producing cells with immortalized cells and thereby making a hybridoma. The general methodology for fusion of antibody producing B cells to an immortal cell line is well within the province of one skilled in the art. Another example is the generation of MAbs from mRNA extracted from bone marrow and spleen cells of immunized animals using combinatorial antibody library technology.

One drawback of MAbs derived from animals or from derived cell lines is that although they may be administered to a patient for diagnostic or therapeutic purposes, they are often recognized as foreign antigens by the immune system and are unsuitable for continued use. Antibodies that are not recognized as foreign antigens by the human immune system have greater potential for both diagnosis and treatment. Methods for generating human and humanized antibodies are now well known in the art.

Chimeric antibodies may be constructed in which regions of a non-human MAb are replaced by their human counterparts. A preferred chimeric antibody is one that has amino acid sequences that comprise one or more complementarity determining regions (CDRs) of a non-human Mab that binds to a polypeptide encoded by the polynucleotides of NSEQ, or a portion thereof, grafted to human framework (FW) regions. Methods for producing such antibodies are well known in the art. Amino acid residues corresponding to CDRs and FWs are known to one of average skill in the art.

A variety of methods have been developed to preserve or to enhance affinity for antigen of antibodies comprising grafted CDRs. One way is to include in the chimeric antibody the foreign framework residues that influence the conformation of the CDR regions. A second way is to graft the foreign CDRs onto human variable domains with the closest homology to the foreign variable region. Thus, grafting of one or more non-human CDRs onto a human antibody may also involve the substitution of amino acid residues which are adjacent to a particular CDR sequence or which are not contiguous with the CDR sequence but which are packed against the CDR in the overall antibody variable domain structure and which affect the conformation of the CDR. Humanized antibodies of the invention therefore include human antibodies which comprise one or more non-human CDRs as well as such antibodies in which additional substitutions or replacements have been made to preserve or enhance binding characteristics.

Chimeric antibodies of the invention also include antibodies that have been

humanized by replacing surface-exposed residues to make the MAb appear human. Because the internal packing of amino acid residues in the vicinity of the antigen-binding site remains unchanged, affinity is preserved. Substitution of surface-exposed residues of a polypeptide encoded by the polynucleotides of NSEQ (or a portion thereof)-antibody according to the invention for the purpose of humanization does not mean substitution of CDR residues or adjacent residues that influence affinity for a polypeptide encoded by the polynucleotides of NSEQ, or a portion thereof.

Chimeric antibodies may also include antibodies where some or all non-human constant domains have been replaced with human counterparts. This approach has the advantage that the antigen-binding site remains unaffected. However, significant amounts of non-human sequences may be present where variable domains are derived entirely from non-human antibodies.

Antibodies of the invention include human antibodies that are antibodies consisting essentially of human sequences. Human antibodies may be obtained from phage display libraries wherein combinations of human heavy and light chain variable domains are displayed on the surface of filamentous phage. Combinations of variable domains are typically displayed on filamentous phage in the form of Fab's or scFvs. The library may be screened for phage bearing combinations of variable domains having desired antigen-binding characteristics. Preferred variable domain combinations are characterized by high affinity for a polypeptide encoded by the polynucleotides of NSEQ, or a portion thereof. Preferred variable domain combinations may also be characterized by high specificity for a polypeptide encoded by the polynucleotides of NSEQ, or a portion thereof, and little cross-reactivity to other related antigens. By screening from very large repertoires of antibody fragments, (2-10 x 10^{10}) a good diversity of high affinity Mabs may be isolated, with many expected to have sub-nanomolar affinities for a polypeptide encoded by the polynucleotides of NSEQ, or a portion thereof.

Alternatively, human antibodies may be obtained from transgenic animals into which un-rearranged human Ig gene segments have been introduced and in which the endogenous mouse Ig genes have been inactivated. Preferred transgenic animals contain very large contiguous Ig gene fragments that are over 1 Mb in size but human polypeptide-specific Mabs of moderate affinity may be raised from transgenic animals containing smaller gene loci. Transgenic animals capable of expressing only human Ig genes may also be used to raise polyclonal antiserum comprising antibodies solely of human origin.

Antibodies of the invention may include those for which binding characteristics

have been improved by direct mutation or by methods of affinity maturation. Affinity and specificity may be modified or improved by mutating CDRs and screening for antigen binding sites having the desired characteristics. CDRs may be mutated in a variety of ways. One way is to randomize individual residues or combinations of residues so that in a population of otherwise identical antigen binding sites, all twenty amino acids may be found at particular positions. Alternatively, mutations may be induced over a range of CDR residues by error prone PCR methods. Phage display vectors containing heavy and light chain variable region gene may be propagated in mutator strains of E. coli. These methods of mutagenesis are illustrative of the many methods known to one of skill in the art.

The antibody may further comprise a detectable label (reporter molecule) attached thereto.

There is provided also methods of producing antibodies able to specifically bind to one of a polypeptide, polypeptide fragments, or polypeptide analogs described herein, the method may comprise:

a) immunizing a mammal (e.g., mouse, a transgenic mammal capable of producing human Ig, etc.) with a suitable amount of a PSEQ described herein including, for example, a polypeptide fragment comprising at least 6 (e.g., 8, 10, 12 etc.) consecutive amino acids of a PSEQ;

b) collecting the serum from the mammal; and

c) isolating the polypeptide-specific antibodies from the serum of the mammal.

The method may further comprise the step of administering a second dose to the mammal (e.g., animal).

Methods of producing a hybridoma which secretes an antibody that specifically binds to a polypeptide are also encompassed herewith and are known in the art.

The method may comprise:

a) immunizing a mammal (e.g., mouse, a transgenic mammal capable of producing human Ig, etc.) with a suitable amount of a PSEQ thereof;

b) obtaining lymphoid cells from the immunized animal obtained from (a);

c) fusing the lymphoid cells with an immortalizing cell to produce hybrid cells; and

d) selecting hybrid cells which produce antibody that specifically binds to a PSEQ thereof.

Also encompassed by the present invention is a method of producing an antibody that specifically binds to one of the polypeptide described herein, the method may comprise:

a) synthesizing a library of antibodies (e.g., antigen binding fragment) on phage or ribosomes;

b) panning the library against a sample by bringing the phage or ribosomes into contact with a composition comprising a polypeptide or polypeptide fragment described herein;

c) isolating phage which binds to the polypeptide or polypeptide fragment, and;

d) obtaining an antibody from the phage or ribosomes.

The antibody of the present invention may thus be obtained, for example, from a library (e.g., bacteriophage library) which may be prepared, for example, by

a) extracting cells which are responsible for production of antibodies from a host mammal;

b) isolating RNA from the cells of (a);

c) reverse transcribing mRNA to produce cDNA;

d) amplifying the cDNA using a (antibody-specific) primer; and

e) inserting the cDNA of (d) into a phage display vector or ribosome display cassette such that antibodies are expressed on the phage or ribosomes.

In order to generate antibodies, the host animal may be immunized with polypeptide and/or a polypeptide fragment and/or analog described herein to induce an immune response prior to extracting the cells which are responsible for production of antibodies.

The antibodies obtained by the means described herein may be useful for detecting proteins, variant and derivative polypeptides in specific tissues or in body fluids. Moreover, detection of aberrantly expressed proteins or protein fragments is probative of a disease state. For example, expression of the present polypeptides encoded by the polynucleotides of NSEQ, or a portion thereof, may indicate that the protein is being expressed at an inappropriate rate or at an inappropriate developmental stage. Hence, the present antibodies may be useful for detecting diseases associated with protein expression from NSEQs disclosed herein.

For in vivo detection purposes, antibodies may be those which preferably

recognize an epitope present at the surface of a tumor cell.

A variety of protocols for measuring polypeptides, including ELISAs, RIAs, and FACS, are well known in the art and provide a basis for diagnosing altered or abnormal levels of expression. Standard values for polypeptide expression are established by combining samples taken from healthy subjects, preferably human, with antibody to the polypeptide under conditions for complex formation. The amount of complex formation may be quantified by various methods, such as photometric means. Quantities of polypeptide expressed in disease samples may be compared with standard values. Deviation between standard and subject values may establish the parameters for diagnosing or monitoring disease.

Design of immunoassays is subject to a great deal of variation and a variety of these are known in the art. Immunoassays may use a monoclonal or polyclonal antibody reagent that is directed against one epitope of the antigen being assayed. Alternatively, a combination of monoclonal or polyclonal antibodies may be used which are directed against more than one epitope. Protocols may be based, for example, upon competition where one may use competitive drug screening assays in which neutralizing antibodies capable of binding a polypeptide encoded by the polynucleotides of NSEQ, or a portion thereof, specifically compete with a test compound for binding the polypeptide. Alternatively one may use, direct antigen-antibody reactions or sandwich type assays and protocols may, for example, make use of solid supports or immunoprecipitation. Furthermore, antibodies may be labelled with a reporter molecule for easy detection. Assays that amplify the signal from a bound reagent are also known. Examples include immunoassays that utilize avidin and biotin, or which utilize enzyme-labelled antibody or antigen conjugates, such as ELISA assays.

Kits suitable for immunodiagnosis and containing the appropriate labelled reagents include antibodies directed against the polypeptide protein epitopes or antigenic regions, packaged appropriately with the remaining reagents and materials required for the conduct of the assay, as well as a suitable set of assay instructions.

The present invention therefore provides a kit for specifically detecting a polypeptide described herein, the kit may comprise, for example, an antibody or antibody fragment capable of binding specifically to the polypeptide described herein.

In accordance with the present invention, the kit may be a diagnostic kit, which may comprise:

a) one or more antibodies described herein; and

b) a detection reagent which may comprise a reporter group.

In accordance with the present invention, the antibodies may be immobilized on a solid support. The detection reagent may comprise, for example, an anti-immunoglobulin, protein G, protein A or lectin etc. The reporter group may be selected, without limitation, from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles

Use of NSEQ, PSEQ as a Therapeutic or Therapeutic targets

One of skill in the art will readily appreciate that the NSEQ, PSEQ, expression systems, assays, kits and array discussed above may also be used to evaluate the efficacy of a particular therapeutic treatment regimen, in animal studies, in clinical trials, or to monitor the treatment of an individual subject. Once the presence of disease is established and a treatment protocol is initiated, hybridization or amplification assays may be repeated on a regular basis to determine if the level of mRNA or protein in the patient (patient's blood, tissue, cell etc.) begins to approximate the level observed in a healthy subject. The results obtained from successive assays may be used to show the efficacy of treatment over a period ranging from several days to many years.

In yet another aspect of the invention, NSEQ may be used therapeutically for the purpose of expressing mRNA and polypeptide, or conversely to block transcription and/or translation of the mRNA. Expression vectors may be constructed using elements from retroviruses, adenoviruses, herpes or vaccinia viruses, or bacterial plasmids, and the like. These vectors may be used for delivery of nucleotide sequences to a particular target organ, tissue, or cell population. Methods well known to those skilled in the art may be used to construct vectors to express nucleic acid sequences or their complements.

Alternatively, NSEQ may be used for somatic cell or stem cell gene therapy. Vectors may be introduced *in vivo*, *in vitro*, and *ex vivo*. For *ex vivo* therapy, vectors are introduced into stem cells taken from the subject, and the resulting transgenic cells are clonally propagated for autologous transplant back into that same subject. Delivery of NSEQ by transfection, liposome injections, or polycationic amino polymers may be achieved using methods that are well known in the art. Additionally, endogenous NSEQ expression may be inactivated using homologous recombination methods that insert an inactive gene sequence into the coding region or other targeted region of NSEQ.

Depending on the specific goal to be achieved, vectors containing NSEQ may be introduced into a cell or tissue to express a missing polypeptide or to replace a non-

functional polypeptide. Of course, when one wishes to express PSEQ in a cell or tissue, one may use a NSEQ able to encode such PSEQ for that purpose or may directly administer PSEQ to that cell or tissue.

On the other hand, when one wishes to attenuate or inhibit the expression of PSEQ, one may use a NSEQ (e.g., an inhibitory NSEQ) which is substantially complementary to at least a portion of a NSEQ able to encode such PSEQ.

The expression of an inhibitory NSEQ may be done by cloning the inhibitory NSEQ into a vector and introducing the vector into a cell to down-regulate the expression of a polypeptide encoded by the target NSEQ. Complementary or anti-sense sequences may also comprise an oligonucleotide derived from the transcription initiation site; nucleotides between about positions -10 and +10 from the ATG may be used. Therefore, inhibitory NSEQ may encompass a portion which is substantially complementary to a desired nucleic acid molecule to be inhibited and a portion (sequence) which binds to an untranslated portion of the nucleic acid.

Similarly, inhibition may be achieved using triple helix base-pairing methodology. Triple helix pairing is useful because it causes inhibition of the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors, or regulatory molecules. Recent therapeutic advances using triplex DNA have been described in the literature. (See, e.g., Gee et al. 1994)

Ribozymes, enzymatic RNA molecules, may also be used to catalyze the cleavage of mRNA and decrease the levels of particular mRNAs, such as those comprising the polynucleotide sequences of the invention. Ribozymes may cleave mRNA at specific cleavage sites. Alternatively, ribozymes may cleave mRNAs at locations dictated by flanking regions that form complementary base pairs with the target mRNA. The construction and production of ribozymes is well known in the art.

RNA molecules may be modified to increase intracellular stability and half-life. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends of the molecule, or the use of phosphorothioate or 2' O-methyl rather than phosphodiester linkages within the backbone of the molecule. Alternatively, nontraditional bases such as inosine, queosine, and wybutosine, as well as acetyl-, methyl-, thio-, and similarly modified forms of adenine, cytidine, guanine, thymine, and uridine which are not as easily recognized by endogenous endonucleases, may be included.

Pharmaceutical compositions are also encompassed by the present invention. The pharmaceutical composition may comprise at least one NSEQ or PSEQ and a pharmaceutically acceptable carrier.

As it will be appreciated form those of skill in the art, the specificity of expression NSEQ and/or PSEQ in tumor cells may advantageously be used for inducing an immune response (through their administration) in an individual having, or suspected of having a tumor expressing such sequence. Administration of NSEQ and/or PSEQ in individuals at risk of developping a tumor expressing such sequence is also encompassed herewith.

In addition to the active ingredients, a pharmaceutical composition may contain pharmaceutically acceptable carriers comprising excipients and auxiliaries that facilitate processing of the active compounds into preparations that may be used pharmaceutically.

For any compound, the therapeutically effective dose may be estimated initially either in cell culture assays or in animal models such as mice, rats, rabbits, dogs, or pigs. An animal model may also be used to determine the concentration range and route of administration. Such information may then be used to determine useful doses and routes for administration in humans. These techniques are well known to one skilled in the art and a therapeutically effective dose refers to that amount of active ingredient that ameliorates the symptoms or condition. Therapeutic efficacy and toxicity may be determined by standard pharmaceutical procedures in cell cultures or with experimental animals, such as by calculating and contrasting the ED_{50} (the dose therapeutically effective in 50% of the population) and LD_{50} (the dose lethal to 50% of the population) statistics. Any of the therapeutic compositions described above may be applied to any subject in need of such therapy, including, but not limited to, mammals such as dogs, cats, cows, horses, rabbits, monkeys, and most preferably, humans.

The pharmaceutical compositions utilized in this invention may be administered by any number of routes including, but not limited to, oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, or rectal means.

The term "treatment" for purposes of this disclosure refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented.

Use of NSEQ in General Research

The invention also provides products, compositions, processes and methods

that utilize a NSEQ described herein, a polypeptide encoded by a NSEQ described herein, a PSEQ described herein for research, biological, clinical and therapeutic purposes. For example, to identify splice variants, mutations, and polymorphisms and to generate diagnostic and prognostic tools.

NSEQ may be extended utilizing a partial nucleotide sequence and employing various PCR-based methods known in the art to detect upstream sequences such as promoters and other regulatory elements. Additionally, one may use an XL-PCR kit (PE Biosystems, Foster City Calif.), nested primers, and commercially available cDNA libraries (Life Technologies, Rockville Md.) or genomic libraries (Clontech, Palo Alto Calif.) to extend the sequence.

The polynucleotides (NSEQ) may also be used as targets in a microarray. The microarray may be used to monitor the expression patterns of large numbers of genes simultaneously and to identify splice variants, mutations, and polymorphisms. Information derived from analyses of the expression patterns may be used to determine gene function, to identify a particular cell, cell type or tissue, to understand the genetic basis of a disease, to diagnose a disease, and to develop and monitor the activities of therapeutic agents used to treat a disease. Microarrays may also be used to detect genetic diversity, single nucleotide polymorphisms which may characterize a particular population, at the genomic level.

The polynucleotides (NSEQ) may also be used to generate hybridization probes useful in mapping the naturally occurring genomic sequence. Fluorescent *in situ* hybridization (FISH) may be correlated with other physical chromosome mapping techniques and genetic map data.

It is to be understood herein that a sequence which is upregulated in an ovarian cancer cell (e.g., malignant ovarian cancer cell) may represent a sequence which is involved in or responsible for the growth, development, maligancy and so on, of the cancer cell (referred herein as a positive regulator of ovarian cancer). It is also to be understood that a sequence which is downregulated (unexpressed or expressed at low levels) in a malignant ovarian cancer cell may represent a sequence which is responsible for the maintenance of the normal status (untransformed) of an ovarian cell (referred herein as a negative regulator of ovarian cancer). Therefore, both the presence or absence of some sequences may be indicative of the disease or may be indicative of the disease, probability of having a disease, degree of severity of the disease (staging).

Therefore, the present invention relates in an aspect thereof to an isolated polynucleotide (e.g., exogenous form of) which may comprise a member selected from

the group consisting of;

a) a polynucleotide which may comprise or consist of any one of SEQ ID NO.:1 to SEQ ID NO.49 and SEQ ID NO.169,

b) a polynucleotide which may comprise the open reading frame of any one of SEQ ID NO.:1 to SEQ ID NO.49 and SEQ ID NO.169,

c) a polynucleotide which may comprise a transcribed or transcribable portion of any one of SEQ. ID. NOs:1 to 49 and 169, which may be, for example, free of untranslated or untranslatable portion(s),

d) a polynucleotide which may comprise a translated or translatable portion of any one of SEQ. ID. NOs:1 to 49 and 169 (e.g., coding portion),

e) a polynucleotide which may comprise a sequence substantially identical (e.g., from about 50 to 100%, or about 60 to 100% or about 70 to 100% or about 80 to 100% or about 85, 90, 95 to 100% identical over the entire sequence or portion of sequences) to a), b), c), or d);

f) a polynucleotide which may comprise a sequence substantially complementary (e.g., from about 50 to 100%, or about 60 to 100% or about 70 to 100% or about 80 to 100% or about 85, 90, 95 to 100% complementarity over the entire sequence or portion of sequences) to a), b), c), or d) and;

g) a fragment of any one of a) to f)

including polynucleotides which consist in the above.

More specifically, the present invention relates to expressed polynucleotides which are selected from the group consisting of;

a) a polynucleotide which may comprise or consist of any one of SEQ ID NO.: 1, SEQ ID NO.:14, SEQ ID NO.:16, SEQ ID NO.:19, SEQ ID NO.:20, SEQ ID NO.:22, SEQ ID NO.:28, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46, SEQ ID NO.:47 and SEQ ID NO.:49 and even more specifically those which are selected from the group consisting of SEQ ID NO.: 14, SEQ ID NO.:19, SEQ ID NO.: 22, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46 and SEQ ID NO.:49,

b) a polynucleotide which may comprise the open reading frame of any one of SEQ ID NO.: 1, SEQ ID NO.:14, SEQ ID NO.:16, SEQ ID NO.:19, SEQ ID NO.:20, SEQ ID NO.:22, SEQ ID NO.:28, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46, SEQ ID

NO.:47 and SEQ ID NO.:49 and even more specifically those which are selected from the group consisting of SEQ ID NO.: 14, SEQ ID NO.:19, SEQ ID NO.: 22, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46 and SEQ ID NO.:49,

c) a polynucleotide which may comprise a transcribed or transcribable portion of any one of SEQ ID NO.: 1, SEQ ID NO.:14, SEQ ID NO.:16, SEQ ID NO.:19, SEQ ID NO.:20, SEQ ID NO.:22, SEQ ID NO.:28, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46, SEQ ID NO.:47 and SEQ ID NO.:49 and even more specifically those which are selected from the group consisting of SEQ ID NO.: 14, SEQ ID NO.:19, SEQ ID NO.: 22, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46 and SEQ ID NO.:49, which may be, for example, free of untranslated or untranslatable portion(s),

d) a polynucleotide which may comprise a translated or translatable portion of any one of SEQ ID NO.: 1, SEQ ID NO.:14, SEQ ID NO.:16, SEQ ID NO.:19, SEQ ID NO.:20, SEQ ID NO.:22, SEQ ID NO.:28, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46, SEQ ID NO.:47 and SEQ ID NO.:49 and even more specifically those which are selected from the group consisting of SEQ ID NO.: 14, SEQ ID NO.:19, SEQ ID NO.: 22, SEQ ID NO.:37, SEQ ID NO.:41, SEQ ID NO.:45, SEQ ID NO.:46 and SEQ ID NO.:49, (e.g., coding portion),

e) a polynucleotide which may comprise a sequence substantially identical (e.g., from about 50 to 100%, or about 60 to 100% or about 70 to 100% or about 80 to 100% or about 85, 90, 95 to 100% identical over the entire sequence or portion of sequences) to a), b), c), or d);

f) a polynucleotide which may comprise a sequence substantially complementary (e.g., from about 50 to 100%, or about 60 to 100% or about 70 to 100% or about 80 to 100% or about 85, 90, 95 to 100% complementarity over the entire sequence or portion of sequences) to a), b), c), or d) and;

g) a fragment of any one of a) to f)

including polynucleotides which consist in the above.

Vectors (e.g., a viral vector, a mammalian vector, a plasmid, a cosmid, etc.) which may comprise the polynucleotides described herein are also encompassed by the present invention. The vector may be, for example, an expression vector.

The present invention also provides a library of polynucleotide comprising at least one polynucleotide (e.g., at least two, etc.) described herein (may include SEQ ID NO.:50). The library may be, for example, an expression library. Some or all of the polynucleotides described herein may be contained within an expression vector. The present invention also relates to a polypeptide library which may comprise at least one (e.g., at least two, etc.) polypeptide as described herein.

In another aspect, the present invention provides arrays which may comprise at least one polynucleotide (e.g., at least two, etc.) described herein.

The present invention also provides an isolated cell (e.g., an isolated live cell such as an isolated mammalian cell, a bacterial cell, a yeast cell, an insect cell, etc.) which may comprise the polynucleotide, the vector or the polypeptide described herein.

In yet a further aspect the present invention relates to a composition comprising the polynucleotide and/or polypeptide described herein.

In accordance with the present invention, the composition may be, for example, a pharmaceutical composition which may comprise a polynucleotide and/or a polypeptide described herein and a pharmaceutically acceptable carrier. More specifically, the pharmaceutical composition may be used for the treatment of ovarian cancer and/or for inhibiting the growth of an ovarian cancer cell.

Polynucleotides fragments of those listed above includes polynucleotides comprising at least 10 nucleic acids which may be identical to a corresponding portion of any one of a) to e) and more particularly a coding portion of any one of SEQ ID NO.:1 to 49, 50 or 169.

Another examplary embodiment of polynucleotide fragments encompassed by the present invention includes polynucleotides comprising at least 10 nucleic acids which may be substantially complementary to a corresponding portion of a coding portion of any one of SEQ ID NO.:1 to 49, 50 or 169 and encompasses, for example, fragments selected from the group consisting of any one of SEQ ID NO.: 103 to 150.

These above sequences may represent powerful markers of cancer and more particularly of, ovarian cancer, breast cancer, prostate cancer, leukemia, melanoma, renal cancer, colon cancer, lung cancer, cancer of the central nervous system and any combination thereof.

Based on the results presented herein and upon reading the present description, a person skilled in the art will understand that the appearance of a positive signal upon testing (hybridization, PCR amplification etc.) for the presence of a given sequence amongst those expressed in a cancer cell, indicates that such sequence is specifically expressed in that type of cancer cell. A person skilled in the art will also

understand that, sequences which are specifically expressed in a certain types of cancer cell may be used for developing tools for the detection of this specific type of cancer cell and may also be used as targets in the development of anticancer drugs.

A positive signal may be in the form of a band in a gel following electrophoresis, Northern blot or Western blot, a PCR fragment detected by emission of fluorescence, etc.

As it will be understood, sequences which are particularly useful for the development of tools for the detection of cancer cell may preferably be expressed at lower levels in at least some normal cells (non-cancerous cells).

For example, in Figure 57 and related description, the appearance of a band upon RT-PCR amplification of mRNAs obtained from ovarian cancer cells, renal cancer cells, lung cancer cells, breast cancer cells and melanoma cells indicates that SEQ ID NO.:1 is expressed in such cancer cells and that SEQ ID NO.:1 may therefore represent a valid marker and target for these types of cancer cells. Similar conclusions may be derived from the results obtained from other Figures and related description.

NSEQs chosen among those which are substantially complementary to those listed in Table 2, or to fragments of those of Table 2, may be used for the treatment of cancer.

The present invention therefore relates to a method for identifying a cancer cell. The method may comprise contacting a cell, a cell sample (cell lysate), a body fluid (blood, urine, plasma, saliva etc.) or a tissue with a reagent which may be, for example, capable of specifically binding at least one NSEQ or PSEQ described herein. The method may more particularly comprise contacting a sequence isolated or derived such cell, sample, fluid or tissue. The complex formed may be detected using methods known in the art.

In accordance with the present invention, the presence of the above mentioned complex may be indicative (a positive indication of the presence) of the presence of a cancer cell.

The present invention also relates in an additional aspect thereof to a method for the diagnosis or prognosis of cancer. The method may comprise, for example, detecting, in a cell, tissue, sample, body fluid, etc., at least one NSEQ or PSEQ described herein.

The cell, cell sample, body fluid or tissue may originate, for example, from an individual which has or is suspected of having a cancer and more particularly ovarian

cancer, breast cancer, prostate cancer, leukemia, melanoma, renal cancer, colon cancer, lung cancer and/or cancer of the central nervous system

Any of the above mentioned methods may further comprise comparing the level obtained with at least one reference level or value.

Detection of NSEQ may require an amplification (e.g., PCR) step in order to have sufficient material for detection purposes. ,

In accordance with the present invention, the polynucleotide described herein may comprise, for example, a RNA molecule, a DNA molecule, including those which are partial or complete, single-stranded or double-stranded, hybrids, modified by a group etc.

Other aspects of the present invention which are encompassed herewith comprises the use of at least one NSEQ or PSEQ described herein and derived antibodies in the manufacture of a composition for identification or detection of a cancer cell (e.g., a tumor cell) or for inhibiting or lowering the growth of cancer cell (e.g., for treatment of ovarian cancer or other cancer).

As some NSEQ and PSEQ are expressed at higher levels in malignant ovarian cancer than in LMP detection of such NSEQ or PSEQ in a sample from an individual (or in vivo) one may rule-out a low malignant potential ovarian cancer and may therefore conclude in a diagnostic of a malignant ovarian cancer. Furthermore, detection of the NSEQ or PSEQ in a cell, tissue, sample or body fluid from an individual may also be indicative of a late-stage malignant ovarian cancer. As such, therapies adapted for the treatment of a malignant ovarian cancer or a late-stage malignant ovarian cancer may be commenced.

In accordance with an embodiment of the present invention, the method may also comprise a step of qualitatively or quantitatively comparing the level (amount, presence) of at least one complex present in the test cell, test sample, test fluid or test tissue with the level of complex in a normal cell, a normal cell sample, a normal body fluid, a normal tissue or a reference value (e.g., for a non-cancerous condition).

The normal cell may be any cell which does not substantially express the desired sequence to be detected. Examples of such normal cells are included for example, in the description of the drawings section. A normal cell sample or tissue thus include, for example, a normal (non-cancerous) ovarian cell, a normal breast cell, a normal prostate cell, a normal lymphocyte, a normal skin cell, a normal renal cell, a normal colon cell, a normal lung cell and/or a normal cell of the central nervous system. For comparison purposes , a normal cell may be chosen from those of identical or similar cell type.

Of course, the presence of more than one complex may be performed in order to increase the precision of the diagnostic method. As such, at least two complexes (e.g., formed by a first reagent and a first polynucleotide and a second reagent or a second polynucleotide) or multiple complexes may be detected.

An exemplary embodiment of a reagent which may be used for detecting a NSEQ described herein is a polynucleotide which may comprise a sequence substantially complementary to the NSEQ.

A suitable reference level or value may be, for example, derived from the level of expression of a specified sequence in a low malignant potential ovarian cancer and/or from a normal cell.

It will be understood herein that a higher level of expression measured in a cancer cell, tissue or sample in comparison with a reference value or sample is a indicative of the presence of cancer in the tested individual.

For example, the higher level measured in an ovarian cell, ovarian tissue or a sample of ovarian origin compared to a reference level or value for a normal cell (normal ovarian cell or normal non-ovarian cell) may be indicative of an ovarian cancer. For comparison purpose, the presence or level of expression of a desired NSEQ or PSEQ to be detected or identified may be compared with the presence, level of expression, found in a normal cell which has been shown herein not to express the desired sequence.

Therapeutic uses and methods are also encompassed herewith.

The invention therefore provides polynucleotides which may be able to lower or inhibit the growth of an ovarian cancer cell (e.g., in a mammal or mammalian cell thereof).

The present invention therefore relates in a further aspect to the use of a polynucleotide sequence which may be selected from the group consisting of

a) a polynucleotide which may comprise a sequence substantially complementary to any of SEQ ID NO.:1 to SEQ ID NO.49, 50 or 169

b) a polynucleotide which may comprise a sequence substantially complementary to a transcribed or transcribable portion of any one of SEQ. ID. NOs:1 to 49, 50 or 169,

c) a polynucleotide which may comprise a sequence substantially complementary to a translated or translatable portion of any one of SEQ. ID. NOs:1 to 49, 50 or 169, and;

d) a fragment of any one of a) to c)

for reducing, lowering or inhibiting the growth of a cancer cell.

The polynucleotide may be selected, for example, from the group consisting of polynucleotides which may comprise a sequence of at least 10 nucleotides which is complementary to the nucleic acid sequence of any one of SEQ ID NO.: 1 to 49, 50 and 169 (to a translated portion which may be free, for example, of untranslated portions).

Of course, the present invention encompasses immunizing an individual by administering a NSEQ (e.g., in an expression vector) or a PSEQ.

The present invention also relates to a method of reducing or slowing the growth of an ovarian cancer cell in an individual in need thereof. The method may comprise administering to the individual a polynucleotide sequence which may be selected from the group consisting of

a) a polynucleotide which may comprise a sequence substantially complementary (also including 100% complementary over a portion, e.g., a perfect match) to any of SEQ ID NO.:1 to SEQ ID NO.49 and 169 or 50,

b) a polynucleotide which may comprise a sequence substantially complementary (also including 100% complementary over a portion, e.g., a perfect match) to a transcribed or transcribable portion of any one of SEQ. ID. NOs:1 to 49 and 169 or 50,

c) a polynucleotide which may comprise a sequence substantially complementary (also including 100% complementary over a portion, e.g., a perfect match) to a translated or translatable portion of any one of SEQ. ID. NOs:1 to 49 and 169 or 50, and;

d) a fragment of any one of a) to c).

The present invention therefore provides in yet another aspect thereof, a siRNA or shRNA molecule that is able to lower the expression of a nucleic acid selected from the group consisting of

a) a polynucleotide which may comprise any one of SEQ ID NO.:1 to SEQ ID NO.:49 and SEQ ID NO.:169, or SEQ ID NO.:50,

b) a polynucleotide which may comprise a transcribed or transcribable portion of any one of SEQ. ID. NOs:1 to 49 and 169, or SEQ ID NO.:50,

c) a polynucleotide which may comprise a translated or translatable portion of any one of SEQ. ID. NOs:1 to 49 and 169 or SEQ ID NO.:50, and;

d) a polynucleotide which may comprise a sequence substantially identical to a), b), or c).

Exemplary embodiment of polynucleotides are those which, for example, may be able to inhibit the growth of an ovarian cancer cell, such as, for example, a

polynucleotide having or comprising a sequence selected from the group consisting of any one of SEQ ID NO. 103 to 150. These specific sequences are provided as guidance only and are not intended to limit the scope of the invention.

The present invention also provides a kit for the diagnosis of cancer. The kit may comprise at least one polynucleotide as described herein and/or a reagent capable of specifically binding at least one polynucleotide described herein.

In a further aspect, the present invention relates to an isolated polypeptide encoded by the polynucleotide described herein.

The present invention more particularly provides an isolated polypeptide which may be selected from the group consisting of

a) a polypeptide which may comprise any one of SEQ ID NO.:51 to 88 and 170

b) a polypeptide which may be encoded by any one of the polynucleotide described herein,

c) a fragment of any one of a) or b),

d) a derivative of any one of a) or b) and;

e) an analog of any one of a) or b).

In accordance with the present invention, the analog may comprise, for example, at least one amino acid substitution, deletion or insertion in its amino acid sequence.

The substitution may be conservative or non-conservative. The polypeptide analog may be a biologically active analog or an immunogenic analog which may comprise, for example, at least one amino acid substitution (conservative or non conservative), for example, 1 to 5, 1 to 10, 1 to 15, 1 to 20, 1 to 50 etc. (including any number there between) compared to the original sequence. An immunogenic analog may comprise, for example, at least one amino acid substitution compared to the original sequence and may still be bound by an antibody specific for the original sequence.

In accordance with the present invention, a polypeptide fragment may comprise, for example, at least 6 consecutive amino acids, at least 8 consecutive amino acids or more of an amino acid sequence selected from the group consisting of polypeptides encoded by a polynucleotide selected from the group consisting of SEQ ID NO.: 1 to 49 and 169 or any one of SEQ. ID. NOs:51 to 88 and 170, including variants and analogs thereof. The fragment may be immunogenic and may be used for the purpose, for example, of generating antibodies.

Exemplary embodiments of polypeptide encompassed by the present

invention are those which may be encoded by any one of SEQ ID NO.:1-49 and 169, more particularly those encoded by any one of SEQ ID NO.:1, 14, 16, 19, 20, 22, 28, 37, 41, 45, 46, 47 or 49 and even more particularly those encoded by any one of SEQ ID NO.: 14, 19, 22, 37, 41, 45, 46 or 49.

In a further aspect the present invention relates to a polypeptide which may be encoded by the isolated differentially expressed sequence of the present invention. The present invention as well relates to the polypeptide encoded by the non-human ortholog polynucleotide, analogs, derivatives and fragments thereof.

A person skilled in the art may easily determine the possible peptide sequence encoded by a particular nucleic acid sequence as generally, a maximum of 6 possible open-reading frames exist in a particular coding sequence. The first possible open-reading frame may start at the first nucleotide (5'-3') of the sequence, therefore using in a 5' to 3' direction nucleotides No. 1 to 3 as the first codon, using nucleotides 4 to 6 as the second codon, etc. The second possible open-reading frame may start at the second nucleotide (5'-3') of the sequence, therefore using in a 5' to 3' direction nucleotides No. 2 to 4 as the first codon, using nucleotides 5 to 7 as the second codon, etc. Finally, the third possible open-reading frame may start at the third nucleotide (5'-3') of the sequence, therefore using in a 5' to 3' direction nucleotides No. 3 to 5 as the first codon, using nucleotides 6 to 8 as the second codon, etc. The fourth possible open-reading frame may start at the first nucleotide of the sequence in a 3' to 5' direction, therefore using in 3' to 5' direction, nucleotides No. 1 to 3 as the first codon, using nucleotides 4 to 6 as the second codon, etc. The fifth possible open-reading frame may start at the second nucleotide of the sequence in a 3' to 5' direction, therefore using in a 3' to 5' direction, nucleotides No. 2 to 4 as the first codon, using nucleotides 5 to 7 as the second codon, etc. Finally, the sixth possible open-reading frame may start at the third nucleotide of the sequence in a 3' to 5' direction, therefore using in a 3' to 5' direction nucleotides No. 3 to 5 as the first codon, using nucleotides 6 to 8 as the second codon, etc.

In an additional aspect, the present invention relates to the use of at least one polypeptide in the manufacture of a composition for the identification or detection of a cancer cell (tumor cell). The polypeptide may be used, for example, as a standard in an assay and/or for detecting antibodies specific for the particular polypeptide, etc.

In yet an additional aspect, the present invention relates to the use of at least one polypeptide described herein in the identification or detection of a cancer cell, such as for example, an ovarian cancer cell or any other cancer cell as described herein.

The present invention therefore relates in a further aspect, to the use of at least one polypeptide described herein in the prognosis or diagnosis of cancer, such as, for example, a malignant ovarian cancer or a low malignant potential ovarian cancer.

As such and in accordance with the present invention, detection of the polypeptide in a cell (e.g., ovarian cell), tissue (e.g., ovarian tissue), sample or body fluid from an individual may preferentially be indicative of a malignant ovarian cancer diagnosis over a low malignant potential ovarian cancer diagnosis and therefore may preferentially be indicative of a malignant ovarian cancer rather than a low malignant potential ovarian cancer.

Further in accordance with the present invention, the presence of the polypeptide in a cell, tissue, sample or body fluid from an individual may preferentially be indicative of a late-stage malignant ovarian cancer.

There is also provided by the present invention, methods for identifying a cancer cell, which may comprise, for example, contacting a test cell, a test cell sample (cell lysate), a test body fluid (blood, urine, plasma, saliva etc.) or a test tissue with a reagent which may be capable of specifically binding the polypeptide described herein, and detecting the complex formed by the polypeptide and reagent. The presence of a complex may be indicative (a positive indication of the presence) of a cancer cell such as for example, an ovarian cancer cell, a breast cancer cell, a prostate cancer cell, leukemia, melanoma, a renal cancer cell, a colon cancer cell, a lung cancer cell, a cancer cell of the central nervous system and any combination thereof.

The presence of a complex formed by the polypeptide and the specific reagent may be indicative, for example, of ovarian cancer including, for example, a low malignant potential ovarian cancer or a malignant ovarian cancer.

However, the method is more particularly powerful for the detection of ovarian cancer of the malignant type. Therefore, the presence of a complex may preferentially be indicative of a malignant ovarian cancer relative (rather than) to a low malignant potential ovarian cancer.

Detection of the complex may also be indicative of a late stage malignant ovarian cancer.

In accordance with the present invention, the method may also comprise a step of qualitatively or quantitatively comparing the level (amount, presence) of at least one complex present in a test cell, a test sample, a test fluid or a test tissue with the level of complex in a normal cell, a normal cell sample, a normal body fluid, a normal tissue or a reference value (e.g., for a non-cancerous condition).

Of course, the presence of more than one polypeptide or complex (two complexes or more (multiple complexes)) may be determined, e.g., one formed by a first specific reagent and a first polypeptide and another formed by a second specific reagent and a second polypeptide may be detected. Detection of more than one polypeptide or complex may help in the determination of the tumorigenicity of the cell.

An exemplary embodiment of a reagent, which may be used for the detection of the polypeptide described herein, is an antibody and antibody fragment thereof.

The present invention also relates to a kit which may comprise at least one of the polypeptide described herein and/or a reagent capable of specifically binding to at least one of the polypeptide described herein.

As one skill in the art will understand, compositions which comprises a polypeptide may be used, for example, for generating antibodies against the particular polypeptide, may be used as a reference for assays and kits, etc.

Additional aspects of the invention relates to isolated or purified antibodies (including an antigen-binding fragment thereof) which may be capable of specifically binding to a polypeptide selected from the group consisting of;

a) a polypeptide comprising or consisting of any one of SEQ ID NO.:51 to 89 or 170, and;

b) a polypeptide comprising a polypeptide sequence encoded by any one of the polynucleotide sequence described herein (e.g., a fragment of at least 6 amino acids of the polypeptide).

More particularly, exemplary embodiments of the present invention relates to antibodies which may be capable of specifically binding a polypeptide comprising a polypeptide sequence encoded by any one of SEQ ID NO.: 1, 14, 16, 19, 20, 22, 28, 37, 41, 45, 46, 47 or 49, or a fragment of at least 6 amino acids of the polypeptide.

Even more particular exemplary embodiments of the present invention relates to antibodies which may be capable of specifically binding a polypeptide comprising a polypeptide sequence encoded by any one of SEQ ID NO.: 14, 19, 22, 37, 41, 45, 46 or 49, or a fragment of at least 6 amino acids of the polypeptide.

In yet an additional aspect, the present invention relates to a hybridoma cell which is capable of producing an antibody which may specifically bind to a polypeptide selected from the group consisting of ;

a) a polypeptide which may comprise any one of SEQ ID NO.:51 to 88, 89 and 170, and;

b) a polypeptide which may comprise a polypeptide sequence encoded by any one of the polynucleotide sequence described herein or a fragment of at least 6 amino acids of the polypeptide.

Exemplary hybridoma which are more particularly encompassed by the present invention are those which may produce an antibody which may be capable of specifically binding a polypeptide comprising a polypeptide sequence encoded by any one of SEQ ID NO.: 1, 14, 16, 19, 20, 22, 28, 37, 41, 45, 46, 47 or 49 or a fragment of at least 6 amino acids of the polypeptide.

Exemplary embodiments of hybridoma which are even more particularly encompassed by the present invention are those which may produce an antibody which is capable of specifically binding a polypeptide comprising a polypeptide sequence encoded by any one of SEQ ID NO.: 14, 19, 22, 37, 41, 45, 46 or 49 or a fragment of at least 6 amino acids of the polypeptide.

The present invention also relates to a composition which may comprise an antibody described herein.

In a further aspect the present invention provides a method of making an antibody which may comprise immunizing a non-human animal with an immunogenic fragment (at least 6 amino acids, at least 8 amino acids, etc.) of a polypeptide which may be selected, for example, from the group consisting of ;

a) a polypeptide which may comprise or consist in any one of SEQ ID NO.:51 to 88, 89 and 170 or a fragment thereof, and;

b) a polypeptide which may comprise a polypeptide sequence encoded by any one of the polynucleotide sequence described herein or a portion thereof.

Exemplary polypeptides which may, more particularly, be used for generating antibodies are those which are encoded by any one of SEQ ID NO.: 1, 14, 16, 19, 20, 22, 28, 37, 41, 45, 46, 47 or 49 (and polypeptide comprising a polypeptide fragment of these particular PSEQ). Even more particular polypeptides encompassed by the present invention are those which are encoded by any one of SEQ ID NO.: 14, 19, 22, 37, 41, 45, 46 or 49.

In a further aspect, the present invention relates to a method of identifying a compound which is capable of inhibiting the activity or function of a polypeptide which may be selected, for example from the group consisting of any one of SEQ ID NO.:51 to 88 and 170 or a polypeptide comprising a polypeptide sequence encoded by any one of SEQ ID NO.:1 to 49 and 169 (e.g., a transcribed portion, a translated portion, a fragment, substantially identical and even substantially complementary sequences).

The method may comprise contacting the polypeptide with a putative compound an isolating or identifying a compound which is capable of specifically binding any one of the above mentioned polypeptide. The compound may originate from a combinatorial library.

The method may also further comprise determining whether the activity or function of the polypeptide (e.g., such as a function indicated at Table 2) is affected by the binding of the compound. Those compounds which capable of binding to the polypeptide and which and/or which are capable of altering the function or activity of the polypeptide represents a desirable compound to be used in cancer therapy.

The method may also further comprise a step of determining the effect of the putative compound on the growth of a cancer cell such as an ovarian cancer cell.

The present invention also relates to an assay and method for identifying a nucleic acid sequence and/or protein involved in the growth or development of ovarian cancer. The assay and method may comprise silencing an endogenous gene of a cancer cell such as an ovarian cancer cell and providing the cell with a candidate nucleic acid (or protein). A candidate gene (or protein) positively involved in inducing cancer cell death (e.g., apoptosis) (e.g., ovarian cancer cell) may be identified by its ability to complement the silenced endogenous gene. For example, a candidate nucleic acid involved in ovarian cancer provided to a cell for which an endogenous gene has been silenced, may enable the cell to undergo apoptosis more so in the presence of an inducer of apoptosis.

Alternatively, an assay or method may comprise silencing an endogenous gene (gene expression) corresponding to the candidate nucleic acid or protein sequence to be evaluated and determining the effect of the candidate nucleic acid or protein on cancer growth (e.g., ovarian cancer cell growth). A sequence involved in the promotion or inhibition of cancer growth, development or malignancy may change the viability of the cell, may change the ability of the cell to grow or to form colonies, etc. The activity of a polypeptide may be impaired by targeting such polypeptide with an antibody molecule or any other type of compound. Again, such compound may be identified by screening combinatorial libraries, phage libraries, etc.

The present invention also provides a method for identifying an inhibitory compound (inhibitor, antagonist) able to impair the function (activity) or expression of a polypeptide described herein. The method may comprise, for example, contacting the (substantially purified or isolated) polypeptide or a cell expressing the polypeptide with a candidate compound and measuring the function (activity) or expression of the polypeptide. A reduction in the function or activity of the polypeptide (compared to the

absence of the candidate compound) may thus positively identify a suitable inhibitory compound.

In accordance with the present invention, the impaired function or activity may be associated, for example, with a reduced ability of the polypeptide to reduce growth of an ovarian cancer cell or a reduced enzymatic activity or function identified for example in Table 2.

The cell used to carry the screening test may not naturally (endogenously) express the polypeptide or analogs, or alternatively the expression of a naturally expressed polypeptide analog may be repressed.

As used herein the term " sequence identity" relates to (consecutive) nucleotides of a nucleotide sequence with reference to an original nucleotide sequence which when compared are the same or have a specified percentage of nucleotides which are the same.

The identity may be compared over a region or over the total sequence of a nucleic acid sequence. Thus, "identity" may be compared, for example, over a region of 10, 19, 20 nucleotides or more (and any number therebetween) and more preferably over a longer region or over the entire region of a polynucleotide sequence described at Table 4 (e.g., any one of SEQ ID NO.:1 to 49 and 169). It is to be understood herein that gaps of non-identical nucleotides may be found between identical nucleic acids regions (identical nucleotides). For example, a polynucleotide may have 100% identity with another polynucleotide over a portion thereof. However, when the entire sequence of both polynucleotides is compared, the two polynucleotides may have 50% of their overall (total) sequence identity to one another.

Percent identity may be determined, for example, with n algorithm GAP, BESTFIT™, or FASTA in the Wisconsin Genetics Software Package Release 7.0, using default gap weights.

Polynucleotides of the present invention or portion thereof having from about 50 to about 100% and any range therebetween, or about 60 to about 100% or about 70 to about 100% or about 80 to about 100% or about 85% to about 100%, about 90% to about 100%, about 95% to about 100% sequence identity with an original polynucleotide are encompassed herewith. It is known by those of skill in the art, that a polynucleotide having from about 50% to 100% identity may function (e.g., anneal to a substantially complementary sequence) in a manner similar to an original polynucleotide and therefore may be used in replacement of an original polynucleotide. For example a polynucleotide (a nucleic acid sequence) may comprise or have from about 50% to about 100% identity with an original polynucleotide over a defined region

and may still work as efficiently or sufficiently to achieve the present invention.

The term "substantially identical" used to define the polynucleotides of the present invention refers to polynucleotides which have, for example, from 50% to 100% sequence identity and any range therebetween but preferably at least 80%, at least 85%, at least 90%, at least 95% sequence identity and also include 100% identity with that of an original sequence (including sequences 100% identical over the entire length of the polynucleotide sequence).

"Substantially identical" polynucleotide sequences may be identified by providing a probe of about 10 to about 25, or more or about 10 to about 20 nucleotides long (or longer) based on the sequence of any one of SEQ ID NOs.:1 to 49 and 169 (more particularly, a transcribed and/or translated portion of any one of SEQ ID NOs.: 1 to 49 and 169) and complementary sequence thereof and hybridizing a library of polynucleotide (e.g., cDNA or else) originating from another species, tissue, cell, individual etc. A polynucleotide which hybridizes under highly stringent conditions (e.g., 6XSCC, 65°C) to the probe may be isolated and identified using methods known in the art. A sequence "substantially identical" includes for example, an isolated allelic variant, an isolated splice variant, an isolated non-human ortholog, a modified NSEQ etc.

As used herein the terms " sequence complementarity" refers to (consecutive) nucleotides of a nucleotide sequence which are complementary to a reference (original) nucleotide sequence. The complementarity may be compared over a region or over the total sequence of a nucleic acid sequence.

Polynucleotides of the present invention or portion thereof having from about 50 to about 100%, or about 60 to about 100% or about 70 to about 100% or about 80 to about 100% or about 85%, about 90%, about 95% to about 100% sequence complementarity with an original polynucleotide are thus encompassed herewith. It is known by those of skill in the art, that a polynucleotide having from about 50% to 100% complementarity with an original sequence may anneal to that sequence in a manner sufficient to carry out the present invention (e.g., inhibit expression of the original polynucleotide).

The term "substantially complementary" used to define the polynucleotides of the present invention refers to polynucleotides which have, for example, from 50% to 100% sequence complementarity and any range therebetween but preferably at least 80%, at least 85%, at least 90%, at least 95% sequence complementarity and also include 100% complementarity with that of an original sequence (including sequences 100% complementarity over the entire length of the polynucleotide sequence).

As used herein the term "polynucleotide" generally refers to any polyribonucleotide or polydeoxyribo-nucleotide, which may be unmodified RNA or DNA, or modified RNA or DNA. "Polynucleotides" include, without limitation single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is a mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, "polynucleotide" refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The term polynucleotide also includes DNAs or RNAs containing one or more modified bases and DNAs or RNAs with backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications may be made to DNA and RNA; thus "polynucleotide" embraces chemically, enzymatically or metabolically modified forms of polynucleotides as typically found or not in nature, as well as the chemical forms of DNA and RNA characteristic of viruses and cells. "Polynucleotide" includes but is not limited to linear and end-closed molecules. "Polynucleotide" also embraces relatively short polynucleotides, often referred to as oligonucleotides.

"Polypeptides" refers to any peptide or protein comprising two or more amino acids joined to each other by peptide bonds or modified peptide bonds (i.e., peptide isosteres). "Polypeptide" refers to both short chains, commonly referred as peptides, oligopeptides or oligomers, and to longer chains generally referred to as proteins. As described above, polypeptides may contain amino acids other than the 20 gene-encoded amino acids.

As used herein the term "polypeptide analog" or "analog" relates to mutants, chimeras, fusions, a polypeptide comprising at least one amino acid deletion, a polypeptide comprising at least one amino acid insertion or addition, a polypeptide comprising at least one amino acid substitutions, and any other type of modifications made relative to a given polypeptide.

An "analog" is thus to be understood herein as a molecule having a biological activity and/or chemical structure similar to that of a polypeptide described herein. An "analog" may have sequence similarity with that of an original sequence or a portion of an original sequence and may also have a modification of its structure as discussed herein. For example, an "analog" may have at least 80% or 85% or 90 % sequence similarity with an original sequence or a portion of an original sequence. An "analog" may also have, for example; at least 70 % or even 50 % sequence similarity with an

original sequence or a portion of an original sequence and may function in a suitable manner.

A "derivative" is to be understood herein as a polypeptide originating from an original sequence or from a portion of an original sequence and which may comprise one or more modification; for example, one or more modification in the amino acid sequence (e.g., an amino acid addition, deletion, insertion, substitution etc.), one or more modification in the backbone or side-chain of one or more amino acid, or an addition of a group or another molecule to one or more amino acids (side-chains or backbone). Biologically active derivatives of the carrier described herein are encompassed by the present invention. Also, an "derivative" may have, for example, at least 50 %, 70%, 80%, 90% sequence similarity to an original sequence with a combination of one or more modification in a backbone or side-chain of an amino acid, or an addition of a group or another molecule, etc.

As used herein the term "biologically active" refers to an analog which retains some or all of the biological activity of the original polypeptide, i.e., to have some of the activity or function associated with the polypeptide described at Table 2, or to be able to promote or inhibit the growth ovarian cancer.

Therefore, any polypeptide having a modification compared to an original polypeptide which does not destroy significantly a desired activity, function or immunogenicity is encompassed herein. It is well known in the art, that a number of modifications may be made to the polypeptides of the present invention without deleteriously affecting their biological activity. These modifications may, on the other hand, keep or increase the biological activity of the original polypeptide or may optimize one or more of the particularity (e.g. stability, bioavailability, etc.) of the polypeptides of the present invention which, in some instance might be desirable. Polypeptides of the present invention may comprise for example, those containing amino acid sequences modified either by natural processes, such as posttranslational processing, or by chemical modification techniques which are known in the art. Modifications may occur anywhere in a polypeptide including the polypeptide backbone, the amino acid side-chains and the amino- or carboxy-terminus. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. It is to be understood herein that more than one modification to the polypeptides described herein are encompassed by the present invention to the extent that the biological activity is similar to the original (parent) polypeptide.

As discussed above, polypeptide modification may comprise, for example, amino acid insertion, deletion and substitution (i.e., replacement), either conservative or non-conservative (e.g., D-amino acids, desamino acids) in the polypeptide sequence where such changes do not substantially alter the overall biological activity of the polypeptide.

Example of substitutions may be those, which are conservative (i.e., wherein a residue is replaced by another of the same general type or group) or when wanted, non-conservative (i.e., wherein a residue is replaced by an amino acid of another type). In addition, a non-naturally occurring amino acid may substitute for a naturally occurring amino acid (i.e., non-naturally occurring conservative amino acid substitution or a non-naturally occurring non-conservative amino acid substitution).

As is understood, naturally occurring amino acids may be sub-classified as acidic, basic, neutral and polar, or neutral and non-polar. Furthermore, three of the encoded amino acids are aromatic. It may be of use that encoded polypeptides differing from the determined polypeptide of the present invention contain substituted codons for amino acids, which are from the same type or group as that of the amino acid to be replaced. Thus, in some cases, the basic amino acids Lys, Arg and His may be interchangeable; the acidic amino acids Asp and Glu may be interchangeable; the neutral polar amino acids Ser, Thr, Cys, Gln, and Asn may be interchangeable; the non-polar aliphatic amino acids Gly, Ala, Val, Ile, and Leu are interchangeable but because of size Gly and Ala are more closely related and Val, Ile and Leu are more closely related to each other, and the aromatic amino acids Phe, Trp and Tyr may be interchangeable.

It should be further noted that if the polypeptides are made synthetically, substitutions by amino acids, which are not naturally encoded by DNA (non-naturally occurring or unnatural amino acid) may also be made.

A non-naturally occurring amino acid is to be understood herein as an amino acid which is not naturally produced or found in a mammal. A non-naturally occurring amino acid comprises a D-amino acid, an amino acid having an acetylaminomethyl group attached to a sulfur atom of a cysteine, a pegylated amino acid, etc. The inclusion of a non-naturally occurring amino acid in a defined polypeptide sequence will therefore generate a derivative of the original polypeptide. Non-naturally occurring amino acids (residues) include also the omega amino acids of the formula $NH_2(CH_2)_nCOOH$ wherein n is 2-6, neutral nonpolar amino acids, such as sarcosine, t-butyl alanine, t-butyl glycine, N-methyl isoleucine, norleucine, etc. Phenylglycine may substitute for Trp, Tyr or Phe; citrulline and methionine sulfoxide are neutral nonpolar,

cysteic acid is acidic, and ornithine is basic. Proline may be substituted with hydroxyproline and retain the conformation conferring properties.

It is known in the art that analogs may be generated by substitutional mutagenesis and retain the biological activity of the polypeptides of the present invention. These analogs have at least one amino acid residue in the protein molecule removed and a different residue inserted in its place. For example, one site of interest for substitutional mutagenesis may include but are not restricted to sites identified as the active site(s), or immunological site(s). Other sites of interest may be those, for example, in which particular residues obtained from various species are identical. These positions may be important for biological activity. Examples of substitutions identified as "conservative substitutions" are shown in Table A. If such substitutions result in a change not desired, then other type of substitutions, denominated "exemplary substitutions" in Table A, or as further described herein in reference to amino acid classes, are introduced and the products screened.

In some cases it may be of interest to modify the biological activity of a polypeptide by amino acid substitution, insertion, or deletion. For example, modification of a polypeptide may result in an increase in the polypeptide's biological activity, may modulate its toxicity, may result in changes in bioavailability or in stability, or may modulate its immunological activity or immunological identity. Substantial modifications in function or immunological identity are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation. (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side chain properties:

(1) hydrophobic: norleucine, methionine (Met), Alanine (Ala), Valine (Val), Leucine (Leu), Isoleucine (Ile)

(2) neutral hydrophilic: Cysteine (Cys), Serine (Ser), Threonine (Thr)

(3) acidic: Aspartic acid (Asp), Glutamic acid (Glu)

(4) basic: Asparagine (Asn), Glutamine (Gln), Histidine (His), Lysine (Lys), Arginine (Arg)

(5) residues that influence chain orientation: Glycine (Gly), Proline (Pro); and aromatic: Tryptophan (Trp), Tyrosine (Tyr), Phenylalanine (Phe)

Non-conservative substitutions will entail exchanging a member of one of these classes for another.

TABLE A. Examplary amino acid substitution

Original residue	Exemplary substitution	Conservative substitution
Ala (A)	Val, Leu, Ile	Val
Arg (R)	Lys, Gln, Asn	Lys
Asn (N)	Gln, His, Lys, Arg	Gln
Asp (D)	Glu	Glu
Cys (C)	Ser	Ser
Gln (Q)	Asn	Asn
Glu (E)	Asp	Asp
Gly (G)	Pro	Pro
His (H)	Asn, Gln, Lys, Arg	Arg
Ile (I)	Leu, Val, Met, Ala, Phe, norleucine	Leu
Leu (L)	Norleucine, Ile, Val, Met, Ala, Phe	Ile
Lys (K)	Arg, Gln, Asn	Arg
Met (M)	Leu, Phe, Ile	Leu
Phe (F)	Leu, Val, Ile, Ala	Leu
Pro (P)	Gly	Gly
Ser (S)	Thr	Thr
Thr (T)	Ser	Ser
Trp (W)	Tyr	Tyr
Tyr (Y)	Trp, Phe, Thr, Ser	Phe
Val (V)	Ile, Leu, Met, Phe, Ala, norleucine	Leu

It is to be understood herein, that if a "range" or "group" of substances (e.g. amino acids), substituents" or the like is mentioned or if other types of a particular characteristic (e.g. temperature, pressure, chemical structure, time, etc.) is mentioned, the present invention relates to and explicitly incorporates herein each and every specific member and combination of sub-ranges or sub-groups therein whatsoever. Thus, any specified range or group is to be understood as a shorthand way of referring to each and every member of a range or group individually as well as each and every possible sub-ranges or sub-groups encompassed therein; and similarly with respect to any sub-ranges or sub-groups therein. Thus, for example, with respect to a

percentage (%) of identity of from about 80 to 100%, it is to be understood as specifically incorporating herein each and every individual %, as well as sub-range, such as for example 80%, 81%, 84.78%, 93%, 99% etc. with respect to a length of "about 10 to about 25" it is to be understood as specifically incorporating each and every individual numebr such as for example 10, 11, 12, 13, 14, 15 up to and including 25; and similarly with respect to other parameters such as, concentrations, elements, etc.

BRIEF DESCRIPTION OF THE DRAWINGS

In the appended drawings:

Fig. 1 to Fig. 31, Fig. 33, Fig. 34, Fig. 36, Fig. 37, Fig. 39, Fig. 40, Fig. 42, Fig. 43, Fig. 46, Fig. 47, Fig. 49, Fig. 50 and Fig. 56 are pictures of macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human sequences. Macroarrays were prepared using RAMP amplified RNA from six human LMP samples (A-F 1) and twenty malignant ovarian tumor samples (Table B) (A-F 2 and A-G 3-4), and 30 different normal human tissues (adrenal (A7), breast (B7), jejunum (C7), trachea (D7), liver (E7), placenta (F7), aorta (G7), brain (H7), lung (A8), adrenal cortex (B8), esophagus (C8), colon (D8), ovary (E8), kidney (F8), prostate (G8), thymus (H8), skeletal muscle (A9), vena cava (B9), stomach (C9), small intestine (D9), heart (E9), fallopian tube (F9), spleen (G9), bladder (H9), cervix (A10), pancreas (B10), ileum (C10), duodenum (D10), thyroid (E10) and testicle (F10)). Also included on the RNA macroarray were breast cancer cell lines (MDA (A5), MCF7 (B5) and MCF7+estradiol (C5)) and LCM microdissected prostate normal epithelium (A-C 6) and prostate cancer (D-F 6), prostate cancer cell line, LNCap (G6) and LNCap+androgen (H6). In these figures, the probe labeling reaction was also spiked with a dsDNA sequence for Arabidopsis, which hybridizes to the same sequence spotted on the macroarray (M) in order to serve as a control for the labeling reaction.

Fig. 32, Fig. 35, Fig. 38, Fig. 41, Fig. 44, Fig. 45 and Fig. 48 are pictures of RT-PCR results showing the differential expression data for STAR selected ovarian cancer-related human sequences. Complimentary DNAs were prepared using random hexamers from RAMP amplified RNA from six human LMP samples and at least twenty malignant ovarian tumor samples (Table B) as indicated in the figures. The cDNAs were quantified and used as templates for PCR with gene-specific primers using standard methods known to those skilled in the art.

Fig. 57 to Fig. 105 are pictures of RT-PCR results showing the differential expression data for STAR selected cancer-related human sequences in RNA samples derived from the NCI-60 panel of cancer cell lines. These 59 cell lines are derived from tumors that encompass 9 human cancer types that include leukemia, the central nervous system, breast, colon, lung, melanoma, ovarian, prostate, and renal. Complimentary DNAs were prepared using random hexamers from RAMP amplified RNA from 59 human cancer cell lines (Table C). The cDNAs were quantified and used as templates for PCR with gene-specific primers using standard methods known to those skilled in the art. For each PCR result depicted in Fig. 57 to Fig. 105, equal amounts of template cDNA used in each PCR reaction was confirmed by reamplifying GAPDH with a specific primer pair, OGS 315 (TGAAGGTCGGAGTCAACGGATTTGGT; SEQ. ID. NO. 167) and OGS 316 (CATGTGGGCCATGAGGTCCACCAC; SEQ. ID. NO. 168) for this housekeeping gene.

More particularly,

Fig. 1 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 1. The STAR dsDNA clone representing SEQ. ID. NO. 1 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Expression of this sequence was only observed in one (placenta (F7)) of the 30 normal tissues and the breast cancer cell line, MCF7 (B-C 5);

Fig. 2 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 2. The STAR dsDNA clone representing SEQ. ID. NO. 2 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Expression of this sequence was also evident in

six (breast (B7), placenta (F7), aorta (G7), colon (D8), ovary (E8) and thymus (H8)) of the 30 normal tissues;

Fig. 3 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 3. The STAR dsDNA clone representing SEQ. ID. NO. 3 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1) but overall, only low levels of expression. No significant expression was seen in any of the normal tissues;

Fig. 4 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 4. The STAR dsDNA clone representing SEQ. ID. NO. 4 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Expression of this sequence was also evident in two (esophagus (C8) and fallopian tube (F9)) of the 30 normal tissues;

Fig. 5 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 5. The STAR dsDNA clone representing SEQ. ID. NO. 5 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Weak expression of this sequence similar to that of LMPs was also observed in many of the normal tissues;

Fig. 6 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 6. The STAR dsDNA clone representing SEQ. ID. NO. 6 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Expression of this sequence was also evident in three (liver (E7), placenta (F7) and kidney (F8)) of the 30 normal tissues;

Fig. 7 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 7. The STAR dsDNA clone representing SEQ. ID. NO. 7 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in several malignant ovarian cancer samples (A-F 2 and A-G 3-4)

compared to LMP samples (A-F 1). Expression of this sequence was only evident in one (testicle (F10)) of the 30 normal tissues;

Fig. 8 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 8. The STAR dsDNA clone representing SEQ. ID. NO. 8 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Expression of this sequence was only evident in two (esophagus (C8) and stomach (C9)) of the 30 normal tissues and the breast and prostate cancer cell lines, MDA (A5) and LNCap (G6 and H6), respectively;

Fig. 9 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 9. The STAR dsDNA clone representing SEQ. ID. NO. 9 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Expression of this sequence was only evident in one (placenta (F7)) of the 30 normal tissues, the breast cancer cell line, MCF7 (B-C 5) and LCM microdissected prostate cancer samples (D6 and F6);

Fig. 10 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 10. The STAR dsDNA clone representing SEQ. ID. NO. 10 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Expression of this sequence was only evident in one (testicle (F10)) of the 30 normal tissues, the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5) and prostate cancer cell line, LNCap (G-H 6);

Fig. 11 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 11. The STAR dsDNA clone representing SEQ. ID. NO. 11 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was only evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5);

Fig. 12 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 12. The STAR dsDNA clone representing SEQ. ID. NO. 12 was labeled with ^{32}P

and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in the majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was only evident in one (testicle (F10)) of the 30 normal tissues and the prostate cancer cell line, LNCap (G-H 6). Weaker expression was also observed in normal ovary (E8);

Fig. 13 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 13. The STAR dsDNA clone representing SEQ. ID. NO. 13 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was only evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5). Weaker expression was also observed in some normal tissues and the prostate cancer cell line, LNCap (G-H 6);

Fig. 14 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 14. The STAR dsDNA clone representing SEQ. ID. NO. 14 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Weaker expression of this sequence was only observed in the normal kidney (F8) tissue;.

Fig. 15 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 15. The STAR dsDNA clone representing SEQ. ID. NO. 15 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in the majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Weaker expression of this sequence similar to that of the LMPs was noted in many of the normal tissues as well;

Fig. 16 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 16. The STAR dsDNA clone representing SEQ. ID. NO. 16 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in the majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5). Weaker

expression similar to that of the LMPs was seen in prostate and some normal tissue samples;

Fig. 17 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 17. The STAR dsDNA clone representing SEQ. ID. NO. 17 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in the majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was only evident in two (breast (B7) and bladder (H9)) of the 30 normal tissues;

Fig. 18 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 18. The STAR dsDNA clone representing SEQ. ID. NO. 18 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5), and somewhat lower expression in prostate cancer cell line, LNCap (G-H 6) and eight normal tissues (adrenal (A7), placenta (F7), lung (A8), adrenal cortex (B8), esophagus (C8), colon (D8), ovary (E8) and testicle (F10));

Fig. 19A is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 19. The STAR dsDNA clone representing SEQ. ID. NO. 19 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in several malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also only evident in the breast cancer cell line, MCF7 (B-C 5);

Fig. 19B (panels A and B) is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 19 and KCNMB2 gene belonging to Unigene cluster, Hs.478368. Primer pairs specific to either the STAR clone sequence for SEQ. ID. NO. 19 or the KCNMB2 gene were used to perform RT-PCR on normal ovarian tissue, and benign and different stages/grades of ovarian cancer. As indicated by the expected PCR amplicon product (Fig. 19B, panel A), compared to normal (Lane 1), benign (Lanes 2-3) and LMPs (Lanes 4-7) samples, increased expression of SEQ. ID. NO. 19 mRNA was evident in clear cell carcinoma (Lanes 8-9), late stage endometrioid (Lane 12) and malignant serous (Lanes 15-17). These results confirm the upregulation of the gene expression for SEQ.

ID. NO. 19 in malignant ovarian cancer. However, the expression of KCNMB2 was markedly different from that of SEQ. ID. NO. 19 showing essentially no difference in its expression amongst the different ovarian samples (Fig 19B, panel B);

Fig. 20 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 20. The STAR dsDNA clone representing SEQ. ID. NO. 20 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in several malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the four (jejunum (C7), trachea (D7), colon (D8) and thymus (H8)) of the 30 normal tissues;

Fig. 21 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 21. The STAR dsDNA clone representing SEQ. ID. NO. 21 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the three (adrenal (A7), breast (B7) and aorta (G7)) of the 30 normal tissues;

Fig. 22 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 22. The STAR dsDNA clone representing SEQ. ID. NO. 22 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell line, MCF7 (B-C 5). Weaker expression similar to that of the LMPs was seen in a majority of the normal tissues;

Fig. 23 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 23. The STAR dsDNA clone representing SEQ. ID. NO. 23 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in several malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5) and prostate cancer cell line, LNCap (G-H 6);

Fig. 24 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID.

NO. 24. The STAR dsDNA clone representing SEQ. ID. NO. 24 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in several of the malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell line, MCF7 (B-C 5);

Fig. 25 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 25. The STAR dsDNA clone representing SEQ. ID. NO. 25 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the prostate cancer cell line, LNCap (G-H 6);

Fig. 26 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 26. The STAR dsDNA clone representing SEQ. ID. NO. 26 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5), prostate cancer cell line, LNCap (G-H 6) and one normal tissue, testicle (F10). Weaker expression similar to that of the LMPs was seen in some normal tissues as well;

Fig. 27 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 27. The STAR dsDNA clone representing SEQ. ID. NO. 27 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5), prostate cancer cell line, LNCap (G-H 6). Weaker expression similar to that of the LMPs was seen in seven (adrenal (A7), placenta (F7), lung (A8), esophagus (C8), colon (D8), ovary (E8) and testicle (F10)) of the 30 normal tissues as well;

Fig. 28 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 28. The STAR dsDNA clone representing SEQ. ID. NO. 28 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4)

compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell lines, MDA (A5) and MCF7 (B-C 5). Weaker expression similar to that of LMPs was seen for all other tissues;

Fig. 29 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 29. The STAR dsDNA clone representing SEQ. ID. NO. 29 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell line, MCF7 (B-C 5) and three (breast (B7), esophagus (C8) and fallopian tube (F9)) of the 30 normal tissues;

Fig. 30 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 30. The STAR dsDNA clone representing SEQ. ID. NO. 30 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell line, MCF7 (B-C 5), prostate cancer samples (D-H 6). Weaker expression similar to that of LMPs was seen in only very few normal tissues;

Fig. 31 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 31. The STAR dsDNA clone representing SEQ. ID. NO. 31 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the breast cancer cell line, MCF7 (B-C 5), prostate cancer samples (D-H 6). Weaker expression similar to that of LMPs was seen in only very few normal tissues;

Fig. 32 is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 32. For this gene, the macroarray data was not available. A primer pair, OGS 1077 (GCGTCCGGGCCTGTCTTCAACCT; SEQ. ID. NO. 153) and OGS 1078 (GCCCCACCCTCTACCCCACCACTA; SEQ. ID. NO. 154) for SEQ. ID. NO. 32 was used to perform RT-PCR on normal ovarian tissue, and benign and different stages/grades of ovarian cancer. As indicated by the expected PCR amplicon product, compared to normal (Lane 1) and benign (Lanes 2-3), increased expression of SEQ. ID. NO. 32 mRNA was evident in LMPs (Lanes 4-7), clear cell carcinoma (Lanes 8-9),

late stage endometrioid (Lane 12) and malignant serous (Lanes 15-17). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 32 in malignant ovarian cancer;

Fig. 33 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 33. The STAR dsDNA clone representing SEQ. ID. NO. 33 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the prostate cancer samples (B-F 6). Weaker expression was seen in many normal tissues and strong expression was seen trachea (D7), colon (D8), small intestine (D9), thymus (H8) and spleen (G9). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 33 in malignant ovarian cancer;

Fig. 34 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 34. The STAR dsDNA clone representing SEQ. ID. NO. 34 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the prostate cancer samples (B-F 6). Weaker expression was seen in many normal tissues and strong expression was seen trachea (D7), colon (D8), small intestine (D9), thymus (H8) and spleen (G9). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 34 in malignant ovarian cancer;

Fig. 35 is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 35. For this gene, the macroarray data was not available. A primer pair, OGS 1141 (GAGATCCTGATCAAGGTGCAGG; SEQ. ID. NO. 155) and OGS 1142 (TGCACGCTCACAGCAGTCAGG; SEQ. ID. NO. 156) for SEQ. ID. NO. 35 was used to perform RT-PCR on LMP samples, different stages/grades of ovarian cancer and normal human tissue samples. As indicated by the expected PCR amplicon product (indicated as AB-0201), increased expression of SEQ. ID. NO. 35 mRNA was evident in some ovarian cancer lanes (lanes 10, 11, 14, 18, 28 and 29) and the mRNA was not expressed in LMP samples. Expression was observed in only one normal tissue sample, ileum (lane 27). Equal amounts of template cDNA used in each PCR reaction was confirmed by reamplifying GAPDH with a specific primer pair, OGS 315 (TGAAGGTCGGAGTCAACGGATTTGGT; SEQ. ID. NO. 167) and OGS 316

(CATGTGGGCCATGAGGTCCACCAC; SEQ. ID. NO. 168) for this housekeeping gene. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 35 in malignant ovarian cancer;

Fig. 36 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 36. The STAR dsDNA clone representing SEQ. ID. NO. 36 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a few of the malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). No expression was seen in other cancer types nor in normal human tissues. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 36 in malignant ovarian cancer;

Fig. 37 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 37. The STAR dsDNA clone representing SEQ. ID. NO. 37 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Weak expression of this sequence was also evident in the prostate cancer samples (B-F 6). Weaker expression was seen in some normal tissues. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 37 in malignant ovarian cancer;

Fig. 38 is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 38. For this gene, the macroarray data was not available. A primer pair, OGS 1202 (AACATGACTAAGATGCCCAACC; SEQ. ID. NO. 157) and OGS 1203 (AATCTCCTTCACCTCCACTACTG; SEQ. ID. NO. 158) for SEQ. ID. NO. 38 was used to perform RT-PCR on LMP samples, different stages/grades of ovarian cancer and normal human tissue samples. As indicated by the expected PCR amplicon product (indicated as AB-0332), increased expression of SEQ. ID. NO. 38 mRNA was evident in approximately half of the ovarian cancer lanes and weaker expression was seen in LMP samples. Expression was observed in many normal tissue samples. Equal amounts of template cDNA used in each PCR reaction was confirmed by reamplifying GAPDH with a specific primer pair, OGS 315 (TGAAGGTCGGAGTCAACGGATTTGGT; SEQ. ID. NO. 167) and OGS 316 (CATGTGGGCCATGAGGTCCACCAC; SEQ. ID. NO. 168) for this housekeeping gene. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 38 in malignant ovarian cancer;

Fig. 39 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 39. The STAR dsDNA clone representing SEQ. ID. NO. 39 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Strong expression was also observed in breast cancer samples (A-C 5) and weak expression in prostate cancer samples (A-H 6). Weaker expression was seen in a few normal tissues with strong expression in testes (F 10). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 39 in malignant ovarian cancer;

Fig. 40 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 40. The STAR dsDNA clone representing SEQ. ID. NO. 40 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Weak expression was seen in a few normal tissues with strong expression in kidney (F 8). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 40 in malignant ovarian cancer;

Fig. 41 is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 41. For this gene, the macroarray data was not available. A primer pair, OGS 1212 (AAGCATAGCCATAGGTGATTGG; SEQ. ID. NO. 159) and OGS 1213 (ACAGGTATCAGACAAGGGAGCAG; SEQ. ID. NO. 160) for SEQ. ID. NO. 41 was used to perform RT-PCR on LMP samples, different stages/grades of ovarian cancer and normal human tissue samples. As indicated by the expected PCR amplicon product (indicated as AB-0532), increased expression of SEQ. ID. NO. 41 mRNA was evident in a large majority of the ovarian cancer lanes and weaker expression was seen in LMP samples. Expression was observed in a few normal tissue samples such as kidney, thymus and spleen (lanes 14, 16 and 23, respectively). Equal amounts of template cDNA used in each PCR reaction was confirmed by reamplifying GAPDH with a specific primer pair, OGS 315 (TGAAGGTCGGAGTCAACGGATTTGGT; SEQ. ID. NO. 167) and OGS 316 (CATGTGGGCCATGAGGTCCACCAC; SEQ. ID. NO. 168) for this housekeeping gene. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 41 in malignant ovarian cancer;

Fig. 42 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID.

NO. 42. The STAR dsDNA clone representing SEQ. ID. NO. 42 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained showed its expression in both malignant ovarian cancer samples (A-F 2 and A-G 3-4) and LMP samples (A-F 1). Weak expression was also observed in breast cancer samples (A-C 5). Weak expression was seen in a few normal tissues with moderate expression in placenta (F 7). These results confirm the expression for SEQ. ID. NO. 42 in malignant ovarian cancer;

Fig. 43 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 43. The STAR dsDNA clone representing SEQ. ID. NO. 43 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Strong expression was also observed in breast cancer samples (A-C 5) and weak expression in prostate cancer samples (A-H 6). Weaker expression was seen in normal tissues with strong expression in testes (F 10). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 43 in malignant ovarian cancer;

Fig. 44 is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 44. For this gene, the macroarray data was not available. A primer pair, OGS 1171 (TTACGACCTATTTCTCCGTGG; SEQ. ID. NO. 161) and OGS 1172 (AATGCAATAATTGGCCACTGC; SEQ. ID. NO. 162) for SEQ. ID. NO. 44 was used to perform RT-PCR on LMP samples, different stages/grades of ovarian cancer and normal human tissue samples. As indicated by the expected PCR amplicon product (indicated as AB-0795), increased expression of SEQ. ID. NO. 44 mRNA was evident in a large majority of the ovarian cancer lanes and weaker expression was seen in LMP samples. Expression was observed in several normal tissue samples such as aorta, skeletal muscle, small intestine and spleen (lanes 7, 17, 20 and 23, respectively). Equal amounts of template cDNA used in each PCR reaction was confirmed by reamplifying GAPDH with a specific primer pair, OGS 315 (TGAAGGTCGGAGTCAACGGATTTGGT; SEQ. ID. NO. 167) and OGS 316 (CATGTGGGCCATGAGGTCCACCAC; SEQ. ID. NO. 168) for this housekeeping gene. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 44 in malignant ovarian cancer;

Fig. 45 is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 45. For this gene, the

macroarray data was not available. A primer pair, OGS 1175 (ACACATCAAACTGCTTATCCAGG; SEQ. ID. NO. 163) and OGS 1176 (ACTGATGTGAAAATGCACATCC; SEQ. ID. NO. 164) for SEQ. ID. NO. 45 was used to perform RT-PCR on LMP samples, different stages/grades of ovarian cancer and normal human tissue samples. As indicated by the expected PCR amplicon product (indicated as AB-0846), increased expression of SEQ. ID. NO. 45 mRNA was evident in half of the ovarian cancer lanes and weaker expression was seen in LMP samples. Expression was observed in only a few normal tissue samples such as kidney, fallopian tube and testes (lanes 14, 22 and 30, respectively). Equal amounts of template cDNA used in each PCR reaction was confirmed by reamplifying GAPDH with a specific primer pair, OGS 315 (TGAAGGTCGGAGTCAACGGATTTGGT; SEQ. ID. NO. 167) and OGS 316 (CATGTGGGCCATGAGGTCCACCAC; SEQ. ID. NO. 168) for this housekeeping gene. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 45 in malignant ovarian cancer;

Fig. 46 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 46. The STAR dsDNA clone representing SEQ. ID. NO. 46 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Weak expression was also observed in prostate cancer samples (A-H 6). Weaker expression was seen in a few normal tissues with moderate expression in breast (B 7) and ovary (E 8). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 46 in malignant ovarian cancer;

Fig. 47 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 47. The STAR dsDNA clone representing SEQ. ID. NO. 47 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the prostate cancer samples (B-F 6). Weaker expression was seen in many normal tissues and strong expression was seen trachea (D7), colon (D8), small intestine (D9), thymus (H8) and spleen (G9). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 47 in malignant ovarian cancer;

Fig. 48 is a picture of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 48. For this gene, the macroarray data was not available. A primer pair, OGS 1282

(ATGGCTCATACAGCACTCAGG; SEQ. ID. NO. 165) and OGS 1283 (GAACTGTCACTCCGGAAAGCCT; SEQ. ID. NO. 166) for SEQ. ID. NO. 48 was used to perform RT-PCR on LMP samples, different stages/grades of ovarian cancer and normal human tissue samples. As indicated by the expected PCR amplicon product (indicated as AB-1120), increased expression of SEQ. ID. NO. 48 mRNA was evident in a majority of the ovarian cancer lanes and weaker expression was seen in LMP samples. Expression was eveident in virtually all normal tissues. Equal amounts of template cDNA used in each PCR reaction was confirmed by reamplifying GAPDH with a specific primer pair, OGS 315 (TGAAGGTCGGAGTCAACGGATTTGGT; SEQ. ID. NO. 167) and OGS 316 (CATGTGGGCCATGAGGTCCACCAC; SEQ. ID. NO. 168) for this housekeeping gene. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 48 in malignant ovarian cancer;

Fig. 49 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 49. The STAR dsDNA clone representing SEQ. ID. NO. 49 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Strong expression was also observed in breast cancer samples (A-C 5) and weak expression in prostate cancer samples (A-H 6). Weaker expression was seen in normal tissues. These results confirm the upregulation of the gene expression for SEQ. ID. NO. 49 in malignant ovarian cancer;

Fig. 50 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 50. The STAR dsDNA clone representing SEQ. ID. NO. 50 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in a majority of malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Significant expression of this sequence was also evident in the seven (adrenal (A7), breast (B7), trachea (D7), placenta (F7), lung (A8), kidney (F8) and fallopian tube (F9)) of the 30 normal tissues;

Fig. 51 is a picture showing an example of STAR subtraction for the ovarian cancer samples. The housekeeping genes, GAPDH (Panel A) and ß-actin (Panel B) were nicely subtracted for both LMP minus Malignant (SL133 to SL137) and Malignant minus LMP (SL123 to SL127) whereas, a known differentially expressed upregulated gene, CCNE1 (Panel C) in malignant ovarian tumors was not subtracted in Malignant minus LMP STAR libraries but instead, enriched (Lanes SL123 to SL127 compared to Lanes 6 to 10);

Fig. 52 is a picture showing the effect of shRNAs on the expression of endogenous genes encoded by SEQ.ID Nos. 1 and 3 in transfected TOV-21G cells. Two shRNAs per SEQ.ID. were transfected in TOV-21G ovarian cancer cell lines and monitored by RT-PCR using gene-specific primers. In each case, both shRNAs attenuated the expression of the genes;

Fig. 53 is a picture showing the effect of SEQ.ID.-specific shRNAs on the proliferation of TOV-21G cells. Decreased proliferation is indicative of a gene that, when attenuated, is required for normal growth of the cancer cells. The cells were stably transfected with two separate shRNA expression vectors and the proliferation of the cells was measured in an MTT assay. The positive control plasmid expresses a shRNA that has homology to no known gene in humans;

Fig. 54 is a picture showing SEQ.ID.-specific shRNAs on the survival of TOV-21G cells. Less staining is indicative of a gene that, when attenuated, is required for survival of the cancer cells in this assay. The cells were transiently transfected with two separate shRNA expression vectors and the remaining colonies were stained with crystal violet and photographed. The positive control plasmid expresses a shRNA that has homology to no known gene in humans;

Fig. 55A and 55B are pictures of RT-PCR data showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 01, 09, 12, 15, 17, 19, 20 and 24. To further demonstrate that the STAR SEQ. ID. NOs. selected after macroarray analysis were upregulated in malignant ovarian cancer samples compared to LMPs and normal ovarian samples, semi-quantitative RT-PCR was performed for 25 cycles using HotStarTaq™ polymerase according to the supplier instructions (Qiagen). Furthermore, these results serve to demonstrate the utility of these sequences as potential diagnostic, prognostic or theranostic markers for ovarian cancer. For SEQ. ID. NOs. 01, 09, 12, 15, 17, 19, 20 and 24, a specific primer pair for each was used. The differential expression results obtained for each SEQ. ID. NO. tested are shown in Figure 55A and 55B. As indicated by the expected PCR amplicon product for each SEQ. ID. NO., there is a clear tendency towards increased expression of the mRNAs corresponding to SEQ. ID. NOs. 01, 09, 12, 15, 17, 19, 20 and 24 in clear cell carcinoma (Lanes 8-9), late stage endometrioid (Lane 12) and different stages of malignant serous (Lanes 15-17) compared to normal (Lane 1), benign (Lanes 2-3) and LMPs (Lanes 4-7) ovarian samples. These results confirm the upregulation of the gene expression for SEQ. ID. NOs. 01, 09, 12, 15, 17, 19, 20 and 24 in the different stages of malignant ovarian cancer as was observed using the macroarrays;

Fig. 56 is a picture of the macroarray hybridization results showing the differential expression data for STAR selected ovarian cancer-related human SEQ. ID. NO. 169. The STAR dsDNA clone representing SEQ. ID. NO. 169 was labeled with ^{32}P and hybridized to the macroarray. The hybridization results obtained confirm its upregulation in malignant ovarian cancer samples (A-F 2 and A-G 3-4) compared to LMP samples (A-F 1). Weaker expression was seen in some normal tissues and strong expression was seen liver (E7) and aorta (G7). These results confirm the upregulation of the gene expression for SEQ. ID. NO. 169 in malignant ovarian cancer;

Fig. 57 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 1 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1136 (GCTTAAAAGAGTCCTCCTGTGGC; SEQ. ID. NO. 171) and OGS 1044 (TGGACATTGTTCTTAAAGTGTGG; SEQ. ID. NO. 172) for SEQ. ID. NO. 1 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 1 mRNA was evident in ovarian, renal, lung, colon, breast cancers and weaker expression was seen in melanoma samples;

Fig. 58 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 2 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1250 (AGGTTTTATGGCCACCGTCAG; SEQ. ID. NO. 173) and OGS 1251 (ATCCTATACCGCTCGGTTATGC; SEQ. ID. NO. 174) for SEQ. ID. NO. 2 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 2 mRNA was evident in all nine cancer types but weaker expression was seen in melanoma and leukemia samples;

Fig. 59 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 3 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1049 (GGGCGGCGGCTCTTTCCTCCTC; SEQ. ID. NO. 175) and OGS 1050 (GCTAGCGGCCCCATACTCG; SEQ. ID. NO. 176) for SEQ. ID. NO. 3 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 3 mRNA was evident in eight cancer types and absent in the leukemia samples;

Fig. 60 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 4 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1051 (ACACTGGATGCCCTGAATGACACA; SEQ. ID. NO. 177) and OGS 1052

(GCTTTGGCCCTTTTTGCTAA; SEQ. ID. NO. 178) for SEQ. ID. NO. 4 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 4 mRNA was evident in melanoma, ovarian, CNS, and lung cancers and weakly expressd in the leukemia samples;

Fig. 61 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 5 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1252 (CCCACTTCTGTCTTACTGCATC; SEQ. ID. NO. 179) and OGS 1253 (CATAGTACTCCAGGGCTTATTC; SEQ. ID. NO. 180) for SEQ. ID. NO. 4 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 5 mRNA was evident all cancer types;

Fig. 62 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 6 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1083 (AACGATTGCCCGGATTGATGACA; SEQ. ID. NO. 181) and OGS 1084 (TACTTGAGGCTGGGGTGGGAGATG; SEQ. ID. NO. 182) for SEQ. ID. NO. 6 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 6 mRNA was evident all cancer types;

Fig. 63 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 7 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1053 (CACTACGCCAGGCACCCCCAAAAC; SEQ. ID. NO. 183) and OGS 1054 (CGAGGCGCACGGCAGTCT; SEQ. ID. NO. 184) for SEQ. ID. NO. 7 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 7 mRNA was evident only in ovarian cancer samples;

Fig. 64 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 8 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1037 (ATCCGTTGCTGCAGCTCGTTCCTC; SEQ. ID. NO. 185) and OGS 1038 (ACCCTGCTGACCTTCTTCCATTCC; SEQ. ID. NO. 186) for SEQ. ID. NO. 8 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 8 mRNA was evident in all cancer types;

Fig. 65 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 9 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1045 (TCGGAGGAGGGCTGGCTGGTGTTT; SEQ. ID. NO. 187) and OGS 1046

(CTTGGGCGTCTTGGAGCGGTTCTG; SEQ. ID. NO. 188) for SEQ. ID. NO. 9 was used to perform RT-PCR. As indicated by the expected PCR amplicon, (lower band on the gel; the top band is an artifact of the PCR reaction) increased expression of SEQ. ID. NO. 9 mRNA was evident in ovarian, lung, colon, breast cancer, and melanoma and weakly expressed in leukemia and CNS cancer;

Fig. 66 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 10 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1240 (AGAGCCTATTGAAGATGAACAG; SEQ. ID. NO. 189) and OGS 1241 (TGATTGCCCCGGATCCTCTTAGG; SEQ. ID. NO. 190) for SEQ. ID. NO. 10 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 10 mRNA was evident in all cancer types;

Fig. 67 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 11 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1304 (GGACAAATACGACGACGAGG; SEQ. ID. NO. 191) and OGS 1305 (GGTTTCTTGGGTAGTGGGC; SEQ. ID. NO. 192) for SEQ. ID. NO. 11 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 11 mRNA was evident in all cancer types;

Fig. 68 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 12 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1039 (CCCCGGAGAAGGAAGAGCAGTA; SEQ. ID. NO. 193) and OGS 1040 (CGAAAGCCGGCAGTTAGTTATTGA; SEQ. ID. NO. 194) for SEQ. ID. NO. 12 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 12 mRNA was evident in all cancer types but weakly in CNS cancer and leukemia;

Fig. 69 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 13 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1095 (GGCGGGCAACGAATTCCAGGTGTC; SEQ. ID. NO. 195) and OGS 1096 (TCAGAGGTTCGTCGCATTTGTCCA; SEQ. ID. NO. 196) for SEQ. ID. NO. 13 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 13 mRNA was evident in all cancer types;

Fig. 70 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 15 in RNA

samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1284 (CAACAGTCATGATGTGTGGATG; SEQ. ID. NO. 197) and OGS 1285 (ACTGCACCTTGTCCGTGTTGAC; SEQ. ID. NO. 198) for SEQ. ID. NO. 15 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 15 mRNA was evident in ovarian, prostate, lung, colon, and breast cancer;

Fig. 71 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 16 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1063 (CCGGCTGGCTGCTTTGTTTA; SEQ. ID. NO. 199) and OGS 1064 (ATGATCAGCAGGTTCGTTGGTAGG; SEQ. ID. NO. 200) for SEQ. ID. NO. 16 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 16 mRNA was evident in ovarian, lung, colon, and breast cancer;

Fig. 72 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 17 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1031 (ATGCCGGAAGTGAATGTGG; SEQ. ID. NO. 201) and OGS 1032 (GGTGACTCCGCCTTTTGAT; SEQ. ID. NO. 202) for SEQ. ID. NO. 17 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 17 mRNA was evident in ovarian, renal, lung, colon, and breast cancer but weakly in CNS cancer;

Fig. 73 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 18 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1308 (ACATTCGCTTCTCCATCTGG; SEQ. ID. NO. 203) and OGS 1309 (TGTCACGGAAGGGAACCAGG; SEQ. ID. NO. 204) for SEQ. ID. NO. 18 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 18 mRNA was evident in all cancer types;

Fig. 74 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 19 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1069 (ACGCTGCCTCTGGGTCACTT; SEQ. ID. NO. 205) and OGS 1070 (TTGGCAAATCAATGGCTTGTAAT; SEQ. ID. NO. 206) for SEQ. ID. NO. 19 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 19 mRNA was evident in all cancer types;

Fig. 75 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 20 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1061 (ATGGCTTGGGTCATCAGGAC; SEQ. ID. NO. 207) and OGS 1062 (GTGTCACTGGGCGTAAGATACTG; SEQ. ID. NO. 208) for SEQ. ID. NO. 20 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 20 mRNA was evident in all cancer types but weakly in breast and colon cancer;

Fig. 76 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 21 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1097 (CACCAAATCAGCTGCTACTACTCC; SEQ. ID. NO. 209) and OGS 1098 (GATAAACCCCAAAGCAGAAAGATT; SEQ. ID. NO. 210) for SEQ. ID. NO. 21 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 21 mRNA was evident in all cancer types but weakly in leukemia;

Fig. 77 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 22 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1075 (CGAGATTCCGTGGGCGTAGG; SEQ. ID. NO. 211) and OGS 1076 (TGAGTGGGAGCTTCGTAGG; SEQ. ID. NO. 212) for SEQ. ID. NO. 22 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 22 mRNA was evident in ovarian, lung, breast, and CNS cancer. Another larger transcript was weakly expressed in colon and renal cancer ion addition to melanoma;

Fig. 78 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 23 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1232 (TCAGAGTGGACGTTGGATTAC; SEQ. ID. NO. 213) and OGS 1233 (TGCTTGAAATGTAGGAGAACA; SEQ. ID. NO. 214) for SEQ. ID. NO. 23 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 23 mRNA was evident in all cancer types;

Fig. 79 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 24 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1067 (GAGGGGCATCAATCACACCGAGAA; SEQ. ID. NO. 215) and OGS 1068

(CCCCACCGCCCACCCATTTAGG; SEQ. ID. NO. 216) for SEQ. ID. NO. 24 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 24 mRNA was evident in ovarian, renal, lung, colon, breast cancer, and melanoma but weakly in CNS cancer and leukemia;

Fig. 80 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 25 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1099 (GGGGGCACCAGAGGCAGTAA; SEQ. ID. NO. 217) and OGS 1100 (GGTTGTGGCGGGGGCAGTTGTG; SEQ. ID. NO. 218) for SEQ. ID. NO. 25 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 25 mRNA was evident in all cancer types but weakly in leukemia;

Fig. 81 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 26 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1246 (ACAGACTCCTGTACTGCAAACC; SEQ. ID. NO. 219) and OGS 1247 (TACCGGTTCGTCCTCTTCCTC; SEQ. ID. NO. 220) for SEQ. ID. NO. 26 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 26 mRNA was evident in all cancer types;

Fig. 82 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 27 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1093 (GAAGTTCCTCACGCCCTGCTATC; SEQ. ID. NO. 221) and OGS 1094 (CTGGCTGGTGACCTGCTTTGAGTA; SEQ. ID. NO. 222) for SEQ. ID. NO. 27 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 27 mRNA was evident in all cancer types;

Fig. 83 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 28 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1332 (TAGGCGCGCCTGACATACAGCAATGCCAGTT; SEQ. ID. NO. 223) and OGS 1333 (TAAGAATGCGGCCGCGCCACATCTTGAACACTTTGC ; SEQ. ID. NO. 224) for SEQ. ID. NO. 28 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 28 mRNA was evident in ovarian, prostate, and renal cancer but weakly in all other types;

Fig. 84 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 29 in RNA

samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1101 (TGGGGAGGAGTTTGAGGAGCAGAC; SEQ. ID. NO. 225) and OGS 1102 (GTGGGACGGAGGGGGCAGTGAAG; SEQ. ID. NO. 226) for SEQ. ID. NO. 29 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 29 mRNA was evident in ovarian, renal, lung, colon, and breast cancer but weakly in CNS cancer and melanoma;

Fig. 85 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 30 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1300 (GCAACTATTCGGAGCGCGTG; SEQ. ID. NO. 227) and OGS 1301 (CCAGCAGCTTGTTGAGCTCC; SEQ. ID. NO. 228) for SEQ. ID. NO. 30 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 30 mRNA was evident in all cancer types;

Fig. 86 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 31 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1302 (GGAGGAGCTAAGCGTCATCGC; SEQ. ID. NO. 229) and OGS 1303 (TCGCTTCAGCGCGTAGACC; SEQ. ID. NO. 230) for SEQ. ID. NO. 31 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 31 mRNA was evident in all cancer types;

Fig. 87 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 32 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1077 (GCGTCCGGGCCTGTCTTCAACCT; SEQ. ID. NO. 153) and OGS 1078 (GCCCCACCCTCTACCCCACCACTA; SEQ. ID. NO. 154) for SEQ. ID. NO. 32 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 32 mRNA was evident in ovarian cancer and melanoma but weaker expression was detectable in CNS, breast, colon, lung, and renal cancer;

Fig. 88 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 33 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1292 (TATTAGTTGGGATGGTGGTAGCAC; SEQ. ID. NO. 231) and OGS 1294 (GAGAATTCGAGTCGACGATGAC; SEQ. ID. NO. 232) for SEQ. ID. NO. 33 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 33 mRNA was evident only in ovarian cancer samples;

Fig. 89 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 34 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1242 (GAAATTGTGTTGACGCAGTCTCC; SEQ. ID. NO. 233) and OGS 1243 (AGGCACACAACAGAGGCAGTTC; SEQ. ID. NO. 234) for SEQ. ID. NO. 34 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 34 mRNA was evident only in ovarian cancer samples;

Fig. 90 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 35 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1141 (GAGATCCTGATCAAGGTGCAGG; SEQ. ID. NO. 155) and OGS 1142 (TGCACGCTCACAGCAGTCAGG; SEQ. ID. NO. 156) for SEQ. ID. NO. 35 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 35 mRNA was evident in ovarian, lung and breast cancer, but weakly in colon and CNS cancer;

Fig. 91 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 36 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1280 (GTACATCAACCTCCTGCTGTCC; SEQ. ID. NO. 235) and OGS 1281 (GACATCTCCAAGTCCCAGCATG; SEQ. ID. NO. 236) for SEQ. ID. NO. 36 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 36 mRNA was evident in all cancer types;

Fig. 92 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 37 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1159 (AGTCTCTCACTGTGCCTTATGCC; SEQ. ID. NO. 237) and OGS 1160 (AGTCCTAAGAACTGTAAACG; SEQ. ID. NO. 238) for SEQ. ID. NO. 37 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 37 mRNA was evident only in ovarian and renal cancer;

Fig. 93 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 38 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1202 (AACATGACTAAGATGCCCAACC; SEQ. ID. NO. 157) and OGS 1203 (AATCTCCTTCACCTCCACTACTG; SEQ. ID. NO. 158) for SEQ. ID. NO. 38 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 38 mRNA was evident in all cancer types;

Fig. 94 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 39 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1310 (CATCTATACGTGGATTGAGGA; SEQ. ID. NO. 239) and OGS 1311 (ATAGGTACCAGGTATGAGCTG; SEQ. ID. NO. 240) for SEQ. ID. NO. 39 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 39 mRNA was evident in all cancer types;

Fig. 95 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 40 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1155 (TGTCCACATCATCATCGTCATCC; SEQ. ID. NO. 241) and OGS 1156 (TGTCACTGGTCGGTCGCTGAGG; SEQ. ID. NO. 242) for SEQ. ID. NO. 39 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 39 mRNA was evident in all cancer types;

Fig. 96 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 41 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1212 (AAGCATAGCCATAGGTGATTGG; SEQ. ID. NO. 159) and OGS 1213 (ACAGGTATCAGACAAGGGAGCAG; SEQ. ID. NO. 160) for SEQ. ID. NO. 41 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 41 mRNA was evident only in ovarian and renal cancer and leukemia;

Fig. 97 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 42 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1316 (CATGGGGCTTAAGATGTC; SEQ. ID. NO. 243) and OGS 1317 (GTCGATTTCTCCATCATCTG; SEQ. ID. NO. 244) for SEQ. ID. NO. 42 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 42 mRNA was evident in all cancer types;

Fig. 98 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 43 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1306 (AAGAGGCGCTCTACTAGCCG; SEQ. ID. NO. 245) and OGS 1307 (CTTTCCACATGGAACACAGG; SEQ. ID. NO. 246) for SEQ. ID. NO. 43 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 43 mRNA was evident in all cancer types;

Fig. 99 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 44 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1171 (TTACGACCTATTTCTCCGTGG; SEQ. ID. NO. 161) and OGS 1172 (AATGCAATAATTGGCCACTGC; SEQ. ID. NO. 162) for SEQ. ID. NO. 44 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 44 mRNA was evident in all cancer types;

Fig. 100 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 45 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1175 (ACACATCAAACTGCTTATCCAGG; SEQ. ID. NO. 163) and OGS 1176 (ACTGATGTGAAAATGCACATCC; SEQ. ID. NO. 164) for SEQ. ID. NO. 45 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 45 mRNA was evident only in ovarian cancer samples;

Fig. 101 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 46 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1286 (CATTTTCCTGGAATTTGATACAG; SEQ. ID. NO. 247) and OGS 1287 (GTAGAGAGTTTATTTGGGCCAAG; SEQ. ID. NO. 248) for SEQ. ID. NO. 46 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 46 mRNA was evident in all cancer types;

Fig. 102 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 47 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1244 (CATCTATGGTAACTACAATCG; SEQ. ID. NO. 249) and OGS 1245 (GTAGAAGTCACTGATCAGACAC; SEQ. ID. NO. 250) for SEQ. ID. NO. 47 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 47 mRNA was evident only in ovarian cancer;

Fig. 103 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 48 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1282 (ATGGCTCATACAGCACTCAGG; SEQ. ID. NO. 165) and OGS 1283 (GAACTGTCACTCCGGAAAGCCT; SEQ. ID. NO. 166) for SEQ. ID. NO. 48 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 48 mRNA was evident in all cancer types;

Fig. 104 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 50 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1035 (CTGCCTGCCAACCTTTCCATTTCT; SEQ. ID. NO. 251) and OGS 1036 (TGAGCAGCCACAGCAGCATTAGG; SEQ. ID. NO. 252) for SEQ. ID. NO. 50 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 50 mRNA was evident in all cancer types but weak in CNS cancer and leukemia, and;

Fig. 105 is a picture of RT-PCR data showing the differential expression data for the STAR selected ovarian cancer-related human SEQ. ID. NO. 169 in RNA samples derived from the NCI-60 panel of cancer cell lines. A primer pair, OGS 1248 (CACCTGATCAGGTGGATAAGG; SEQ. ID. NO. 253) and OGS 1249 (TCCCAGGTAGAAGGTGGAATCC; SEQ. ID. NO. 254) for SEQ. ID. NO. 169 was used to perform RT-PCR. As indicated by the expected PCR amplicon, increased expression of SEQ. ID. NO. 169 mRNA was evident in ovarian, renal, and lung cancer but weak in CNS cancer.

DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

The applicant employed a carefully planned strategy to identify and isolate genetic sequences involved in ovarian cancer. The process involved the following steps: 1) preparation of highly representative cDNA libraries using mRNA isolated from LMPs and malignant ovarian cancer samples of human origin; 2) isolation of sequences upregulated in the malignant ovarian cancer samples; 3) identification and characterization of upregulated sequences; 4) selection of upregulated sequences for tissue specificity; 5) determination of knock-down effects on ovarian cancer cell line proliferation and migration; and 6) determination of the expression pattern of each upregulated sequence in samples derived from nine different cancer types. The results discussed in this disclosure demonstrate the advantage of targeting ovarian cancer-related genes that are highly specific to this differentiated cell type compared to normal tissues and provide a more efficient screening method when studying the genetic basis of diseases and disorders. Polynucleotide and/or polypeptide sequences that are known but have not had a role assigned to them until the present disclosure have also been isolated and shown to have a critical role in ovarian cancer cell line proliferation and migration. Finally, novel polynucleotide and/or polypeptide sequences have been identified that play a role as well.

The present invention is illustrated in further details below in a non-limiting

fashion.

A- Material and Methods

Commercially available reagents referred to in the present disclosure were used according to supplier's instructions unless otherwise indicated. Throughout the present disclosure certain starting materials were prepared as follows:

B - Preparation of LMP and malignant ovarian cancer cells

LMP and malignant ovarian tumor samples were selected based on histopathology to identify the respective stage and grade (Table B) . LMP was choosen instead of normal ovarian tissue to avoid genes that associated with proliferation due to ovulation. Also very few cells would have been recovered and stromal cells would have been a major contaminant. LMP and serous (most common) ovarian tumors represent the extremes of tumorigenicity, differentiation and invasion. Once the sample were selected, total RNA was extracted with Trizol™ (InVitrogen, Grand Island, NY) after the tissues were homogenized. The quality of the RNA was assessed using a 2100 Bioanalyzer (Agilent Technologies, Palo Alto, CA)

Table B: shows the pathologies including grade and stage of the different ovarian cancer samples used on the macroarrays.

MF Code No.	Pathologies	Symbol	Stage	Grade	Position on Macroarray
15	Borderline serous	B	1b	B	A1
16	Borderline serous	B	2a	B	B1
17	Borderline/carcinoma serous	B/CS	3c	1	F1
18	Borderline serous	B	3c	B	C1
19	Borderline serous	B	1b	B	D1
20	Borderline serous	B	1a	B	E1
42	Carcinoma serous of the surface	CSS	3a	3	A4
22	Carcinoma serous	CS	1b	3	A2
30	Carcinoma serous	CS	2c	3	E2
23	Carcinoma serous	CS	3c	3	F2
25	Carcinoma serous	CS	3c	3	B2
26	Carcinoma serous	CS	3c	3	A3
27	Carcinoma serous	CS	3c	3	C2
28	Carcinoma serous	CS	3c	3	D2
43	Carcinoma serous	CS	3c	3	B4
45	Carcinoma serous	CS	3c	3	D4
49	Carcinoma serous	CS	3c	2	F4
41	Carcinoma endometrioide	CE	3b	3	G3
40	Carcinoma endometrioide	CE	3c	3	F3
44	Carcinoma endometrioide	CE	3c	3	C4
39	Carcinoma endometrioide	CE	3c	2	E3
50	Carcinoma endometrioide	CE	1c	1	G4
46	Carcinoma endometrioide	CE	1a	2	E4

MF Code No.	Pathologies	Symbol	Stage	Grade	Position on Macroarray
34	Clear cell carcinoma	CCC	3c	2	B3
38	Clear cell carcinoma	CCC	3c	3	D3
37	Clear cell carcinoma	CCC	1c	2	C3

C- Method of Isolating Differentially Expressed mRNA

Key to the discovery of differentially expressed sequences unique to malignant ovarian cancer is the use of the applicant's patented STAR technology (Subtractive Transcription-based Amplification of mRNA; U.S. Patent No. 5,712,127 Malek et al., 1998). Based on this procedure, mRNA isolated from malignant ovarian tumor sample is used to prepare "tester RNA", which is hybridized to complementary single-stranded "driver DNA" prepared from mRNA from LMP sample and only the un-hybridized "tester RNA" is recovered, and used to create cloned cDNA libraries, termed "subtracted libraries". Thus, the "subtracted libraries" are enriched for differentially expressed sequences inclusive of rare and novel mRNAs often missed by micro-array hybridization analysis. These rare and novel mRNA are thought to be representative of important gene targets for the development of better diagnostic and therapeutic strategies.

The clones contained in the enriched "subtracted libraries" are identified by DNA sequence analysis and their potential function assessed by acquiring information available in public databases (NCBI and GeneCard). The non-redundant clones are then used to prepare DNA micro-arrays, which are used to quantify their relative differential expression patterns by hybridization to fluorescent cDNA probes. Two classes of cDNA probes may be used, those which are generated from either RNA transcripts prepared from the same subtracted libraries (subtracted probes) or from mRNA isolated from different ovarian LMP and malignant samples (standard probes). The use of subtracted probes provides increased sensitivity for detecting the low abundance mRNA sequences that are preserved and enriched by STAR. Furthermore, the specificity of the differentially expressed sequences to malignant ovarian cancer is measured by hybridizing radio-labeled probes prepared from each selected sequence to macroarrays containing RNA from different LMP and malignant ovarian cancer samples and different normal human tissues.

A major challenge in gene expression profiling is the limited quantities of RNA available for molecular analysis. The amount of RNA isolated from many human specimens (needle aspiration, laser capture micro-dissection (LCM) samples and transfected cultured cells) is often insufficient for preparing: 1) conventional tester and

driver materials for STAR; 2) standard cDNA probes for DNA micro-array analysis; 3) RNA macroarrays for testing the specificity of expression; 4) Northern blots and; 5) full-length cDNA clones for further biological validation and characterization etc. Thus, the applicant has developed a proprietary technology called RAMP (RNA Amplification Procedure) (U.S. Patent Application No. 11/000,958 published under No. US 2005/0153333A1 on July 14, 2005 and entitled "Selective Terminal Tagging of Nucleic Acids"), which linearly amplifies the mRNA contained in total RNA samples yielding microgram quantities of amplified RNA sufficient for the various analytical applications. The RAMP RNA produced is largely full-length mRNA-like sequences as a result of the proprietary method for adding a terminal sequence tag to the 3'-ends of single-stranded cDNA molecules, for use in linear transcription amplification. Greater than 99.5% of the sequences amplified in RAMP reactions show <2-fold variability and thus, RAMP provides unbiased RNA samples in quantities sufficient to enable the discovery of the unique mRNA sequences involved in ovarian cancer.

D- Preparation of Human Malignant Ovarian Cancer Subtracted Library

Total RNA from five human ovarian LMP samples (MF-15, -16, -18, -19 and –20) (Table B) and five malignant ovarian cancer samples (MF-22, -25, -27, -28 and –30) (Table B) (CHUM, Montreal, QC) were prepared as described above. Following a slight modification of the teachings of Malek et al., 1998 (U.S. Patent No. 5,712,127) i.e., preparation of the cDNA libraries on the paramagnetic beads as described below), 1 µg of total RNA from each sample were used to prepare highly representative cDNA libraries on streptavidin-coated paramagnetic beads (InVitrogen, Grand Island, NY) for preparing tester and driver materials. In each case, first-strand cDNA was synthesized using an oligo dT_{11} primer with 3' locking nucleotides (e.g., A, G or C), a 5'-biotin moiety and containing a Not I recognition site (OGS 364: SEQ. ID. NO. 90) Next, second-strand cDNA synthesis was performed according to the manufacturer's procedure for double-stranded cDNA synthesis (Invitrogen, Burlington, ON) and the resulting double-stranded cDNA ligated to linkers containing an Asc I recognition site (New England Biolabs, Pickering, ON). The double-stranded cDNAs were then digested with Asc I and Not I restriction enzymes (New England Biolabs, Pickering, ON), purified from the excess linkers using the cDNA fractionation column from Invitrogen (Burlington, ON) as specified by the manufacturer. Each sample was equally divided and ligated separately to specialized oligonucleotide promoter tags, TAG1 (OGS 594 and 595: SEQ. ID. NO: 91 and SEQ. ID. NO:92) and TAG2 (OGS458 and 459: SEQ. ID. NO:93 and SEQ. ID. NO:94) used for preparing tester and driver

materials, respectively. Thereafter, each ligated cDNA was purified by capturing on the streptavidin beads as described by the supplier (InVitrogen, Grand Island, NY), and transcribed *in vitro* with T7 RNA polymerase (Ambion, Austin, TX).

Next, in order to prepare 3'-represented tester and driver libraries, a 10-µg aliquot of each of the in vitro synthesized RNA was converted to double-stranded cDNA by performing first-strand cDNA synthesis as described above followed by primer-directed (primer OGS 494 (SEQ. ID. NO:95) for TAG1 and primer OGS 302 (SEQ. ID. NO:96) for TAG2) second-strand DNA synthesis using Advantage™-2 Taq polymerase (BD Biosciences Clontech, Mississauga, ON). The double-stranded cDNA was purified using Qiaquick™ columns and quantified at A_{260}nm. Thereafter, 6x 1-µg aliquots of each double-stranded cDNA was digested individually with one of the following 4-base recognition restriction enzymes Rsa I, Sau3A1, Mse I, Msp I, HinPI I and Bsh 1236I (MBI Fermentas, Burlington, ON), yielding up to six possible 3'-fragments for each RNA species contained in the cDNA library. Following digestion, the restriction enzymes were inactivated with phenol and the set of six reactions pooled. The restriction enzymes sites were then blunted with T4 DNA polymerase and ligated to linkers containing an Asc I recognition site. Each linker-adapted pooled DNA sample was digested with Asc I and Not I restriction enzymes, desalted and ligated to specialized oligonucleotide promoter tags, TAG1 (OGS 594 and 595) for the original TAG1-derived materials to generate tester RNA and TAG2-related OGS 621 and 622 (SEQ. ID. NO:97 and SEQ. ID. NO:98) with only the promoter sequence for the original TAG2-derived materials for generating driver DNA. The promoter-ligated materials were purified using the streptavidin beads, which were then transcribed *in vitro* with either T7 RNA polymerase (Ambion, Austin, TX), purified and quantified at A_{260nm}. The resulting TAG1 3'-represented RNA was used directly as "tester RNA" whereas, the TAG2 3'-represented RNA was used to synthesize first-strand cDNA, which then served as single-stranded "driver DNA". Each "driver DNA" reaction was treated with RNase A and RNase H to remove the RNA, phenol extracted and purified before use. An equivalent amount of each driver RNA for the five LMP samples were pooled before synthesis of the single-stranded driver DNA.

The following 3'-represented libraries were prepared:

Tester 1 (MF-22) - human malignant ovarian cancer donor 1

Tester 2 (MF-25) - human malignant ovarian cancer donor 2

Tester 3 (MF-27) - human malignant ovarian cancer donor 3

Tester 4 (MF-28) - human malignant ovarian cancer donor 4

Tester 5 (MF-30) - human malignant ovarian cancer donor 5

Driver 1 (MF-15) - human ovarian LMP donor 1

Driver 2 (MF-16) - human ovarian LMP donor 2

Driver 3 (MF-18) - human ovarian LMP donor 3

Driver 4 (MF-19) - human ovarian LMP donor 4

Driver 5 (MF-20) - human ovarian LMP donor 5

Each tester RNA sample was subtracted following the teachings of U.S. patent No. 5,712,127 with the pooled driver DNA (MF-15, -16, -18, -19 and –20) in a ratio of 1:100 for 2-rounds following the teachings of Malek et al., 1998 (U.S. Patent No. 5,712,127). Additionally, control reactions containing tester RNA and no driver DNA, and tester RNA plus driver DNA but no RNase H were prepared. The tester RNA remaining in each reaction after subtraction was converted to double-stranded DNA, and a volume of 5% removed and amplified in a standard PCR reaction for 30-cycles for analytical purposes. The remaining 95% of only the tester-driver plus RNase H subtracted samples after 2-rounds were amplified for 4-cycles in PCR, digested with Asc I and Not I restriction enzymes, and one half ligated into the pCATRMAN (SEQ. ID. NO:99) plasmid vector and the other half, into the p20 (SEQ. ID. NO:100) plasmid vector. The ligated materials were transformed into E. coli DH10B and individual clones contained in the pCATRMAN libraries were picked for further analysis (DNA sequencing and hybridization) whereas, clones contained in each p20 library were pooled for use as subtracted probes. Each 4-cycles amplified cloned subtracted library contained between 15,000 and 25,000 colonies. Additionally, in order to prepare subtracted cDNA probes, reciprocal subtraction for 2-rounds was performed using instead, the pooled driver RNA as “tester” and each of the malignant tester RNA as “driver”. The materials remaining after subtraction for each were similarly amplified for 4-cycles in PCR, digested with Asc I and Not I restriction enzymes, and one half ligated into the p20 plasmid vector.

The following cloned subtracted libraries were prepared:

SL123 - Tester 1 (MF-22) minus Pooled Driver (MF-15, -16, -18, -19 and –20)

SL124 - Tester 2 (MF-25) minus Pooled Driver (MF-15, -16, -18, -19 and –20)

SL125 - Tester 3 (MF-27) minus Pooled Driver (MF-15, -16, -18, -19 and –20)

SL126 - Tester 4 (MF-28) minus Pooled Driver (MF-15, -16, -18, -19 and –20)

SL127 - Tester 5 (MF-30) minus Pooled Driver (MF-15, -16, -18, -19 and –20)

SL133 - Pooled Driver (MF-15, -16, -18, -19 and –20) minus Tester 1 (MF-22)

SL134 - Pooled Driver (MF-15, -16, -18, -19 and –20) minus Tester 2 (MF-25)

SL135 - Pooled Driver (MF-15, -16, -18, -19 and –20) minus Tester 3 (MF-27)

SL136 - Pooled Driver (MF-15, -16, -18, -19 and –20) minus Tester 4 (MF-28)

SL137 - Pooled Driver (MF-15, -16, -18, -19 and –20) minus Tester 5 (MF-30)

A 5-µL aliquot of the 30-cycles PCR amplified subtracted and non-subtracted materials were visualized on a 1.5% agarose gel containing ethidium bromide and then transferred to Hybond™ N+ (Amersham Biosciences, Piscataway, NJ) nylon membrane for Southern blot analysis. Using radiolabeled probes specific for GAPDH (glyceraldehyde-3-phosphate dehydrogenase; Accession #M32599.1) and β-actin (Accession #X00351), which are typically non-differentially expressed house-keeping genes, it was evident that there was subtraction of both GAPDH and β-actin (Fig. 51, Panels A and B). Yet, at the same time, a probe specific for CCNE1 (Accession # NM_001238, a gene known to be upregulated in malignant ovarian cancer, indicated that it was not subtracted (Fig. 51, Panel C). Based on these results, it was anticipated that the subtracted libraries would be enriched for differentially expressed upregulated sequences.

E - Sequence identification and annotation of clones contained in the subtracted libraries:

Approximately ~5300 individual colonies contained in the pCATRMAN subtracted libraries (SL123 to SL127) described above were randomly picked using a Qbot (Genetix Inc., Boston, MA) into 60 µL of autoclaved water. Then, 42 µL of each was used in a 100-µL standard PCR reaction containing oligonucleotide primers, OGS 1 and OGS 142 and amplified for 40-cycles (94°C for 10 minutes, 40x (94 °C for 40 seconds, 55 °C for 30 seconds and 72 °C for 2 minutes) followed by 72 °C for 7 minutes) in 96-wells microtitre plates using HotStartTM Taq polymerase (Qiagen, Mississauga, ON). The completed PCR reactions were desalted using the 96-well filter plates (Corning) and the amplicons recovered in 100 µL 10mM Tris (pH 8.0). A 5-µL aliquot of each PCR reaction was visualized on a 1.5% agarose gel containing ethidium bromide and only those reactions containing a single amplified product were selected for DNA sequence analysis using standard DNA sequencing performed on an ABI 3100 instrument (Applied Biosystems, Foster City, CA). Each DNA sequence obtained was given a Sequence Identification Number and entered into a database for subsequent tracking and annotation.

Each sequence was selected for BLAST analysis of public databases (e.g. NCBI). Absent from these sequences were the standard housekeeping genes (GAPDH, actin, most ribosomal proteins etc.), which was a good indication that the subtracted library was depleted of at least the relatively abundant non-differentially expressed sequences.

Once sequencing and annotation of the selected clones were completed, the next step involved identifying those sequences that were actually upregulated in the malignant ovarian cancer samples compared to the LMP samples.

F - Hybridization analysis for identifying upregulated sequences

The PCR amplicons representing the annotated sequences from the pCATRMAN libraries described above were used to prepare DNA microarrays. The purified PCR amplicons contained in 70 µL of the PCR reactions prepared in the previous section was lyophilized and each reconstituted in 20 µL of spotting solution comprising 3xSSC and 0.1% sarkosyl. DNA micro-arrays of each amplicon in triplicate were then prepared using CMT-GAP2 slides (Corning, Corning, NY) and the GMS 417 spotter (Affymetrix, Santa Clara, CA).

The DNA micro-arrays were then hybridized with either standard or subtracted cy3 and cy5 labelled cDNA probes as recommended by the supplier (Amersham Biosciences, Piscataway, NJ). The standard cDNA probes were synthesized using RAMP amplified RNA prepared from the different human ovarian LMP and malignant samples. It is well known to the skilled artisan that standard cDNA probes only provide limited sensitivity of detection and consequently, low abundance sequences contained in the cDNA probes are usually missed. Thus, the hybridization analysis was also performed using cy3 and cy5 labelled subtracted cDNA probes prepared from *in vitro* transcribed RNA generated from subtracted libraries (SLP123 to SLP127 and SLP133 to SLP137) cloned into the p20 plasmid vector and represent the different tester and driver materials. These subtracted libraries may be enriched for low abundance sequences as a result of following the teachings of Malek et al., 1998 (U.S. Patent No. 5,712,127), and therefore, may provide increased detection sensitivity.

All hybridization reactions were performed using the dye-swap procedure as recommended by the supplier (Amersham Biosciences, Piscataway, NJ) and approximately 750 putatively differentially expressed upregulated (>2-fold) sequences were selected for further analysis.

G - Determining malignant ovarian cancer specificity of the differentially expressed sequences identified:

The differentially expressed sequences identified in Section F for the different human malignant ovarian cancer subtracted libraries (SL123 to SL127) were tested for specificity by hybridization to nylon membrane-based macroarrays. The macroarrays were prepared using RAMP amplified RNA from 6 LMP and 20 malignant human

ovarian samples, and 30 normal human tissues (adrenal, liver, lung, ovary, skeletal muscle, heart, cervix, thyroid, breast, placenta, adrenal cortex, kidney, vena cava, fallopian tube, pancreas, testicle, jejunum, aorta, esophagus, prostate, stomach, spleen, ileum, trachea, brain, colon, thymus, small intestine, bladder and duodenum) purchased commercially (Ambion, Austin, TX). In addition, RAMP RNA prepared from breast cancer cell lines, MDA and MCF7, prostate cancer cell line, LNCap, and a normal and prostate cancer LCM microdissected sample. Because of the limited quantities of mRNA available for many of these samples, it was necessary to first amplify the mRNA using the RAMP methodology. Each amplified RNA sample was reconstituted to a final concentration of 250 ng/μL in 3xSSC and 0.1% sarkosyl in a 96-well microtitre plate and 1 μL spotted onto Hybond™ N+ nylon membranes using the specialized MULTI-PRINT™ apparatus (VP Scientific, San Diego, CA), air dried and UV-cross linked. Of the ~750 different sequences selected from SL123 to SL127 for macroarray analysis, only 250 sequences were individually radiolabeled with α-^{32}P-dCTP using the random priming procedure recommended by the supplier (Amersham, Piscataway, NJ) and used as probes on the macroarrays thus far. Hybridization and washing steps were performed following standard procedures well known to those skilled in the art.

Occasionally, the results obtained from the macroarray methodology were inconclusive. For example, probing the membranes with certain STAR clones resulted in patterns where all the RNA samples appeared to express equal levels of the message or in patterns where there was no signal. This suggested that not all STAR clones were useful tools to verify the expression of their respective genes. To circumvent this problem, RT-PCR was used to determine the specificity of expression. Using the same RAMP RNA samples that were spotted on the macroarrays, 500 μg of RNA was converted to single-stranded cDNA with Thermoscript™ RT (Invitrogen, Burlington, ON) as described by the manufacturer. The cDNA reaction was diluted so that 1/200 of the reaction was used for each PCR experiment. After trial PCR reactions with gene-specific primers designed against each SEQ. ID NOs. to be tested, the linear range of the reaction was determined and applied to all samples, PCR was conducted in 96-well plates using HotStarTaq™ Polymerase from Qiagen (Mississauga, ON) in a DNA Engine Tetrad™ from MJ Research. Half of the reaction mixture was loaded on a 1.2% agarose/ethidium bromide gel and the amplicons visualized with UV light.

Of the 250 sequences tested, approximately 55% were found to be upregulated in many of the malignant samples compared to the LMPs. However, many

of these sequences were also readily detected in a majority of the different normal human tissues. Based on these results, those sequences that were detected in many of the other human tissues at significantly elevated levels were eliminated. Consequently, only 49 sequences, which appeared to be upregulated and highly malignant ovarian cancer-specific, were selected for biological validation studies. This subset of 49 sequences include some genes previously reported in the literature to be upregulated in ovarian cancer but without demonstration of their relative expression in normal tissues. The macroarray data for FOLR1 (SEQ. ID. NO.50) is included to exemplify the hybridization pattern and specificity of a gene that is already known to be involved in the development of ovarian cancer.

Fig. 1-49 and 51 show the macroarray hybridization signal patterns and RT-PCR amplification data for the malignant ovarian cancer and normal human tissues relative to LMPs for the 50 sequences isolated and selected for biological validation. Amongst the 50 selected sequences, 27 were associated with genes having functional annotation 15 were associated with genes with no functional annotation and 8 were novel sequences (genomic hits). The identification of gene products involved in regulating the development of ovarian cancer has thus led to the discovery of highly specific, including novel targets, for the development of new therapeutic strategies for ovarian cancer management. Representative sequences summarized in Table 2 are presented below and corresponding sequences are illustrated in Table 4.

The present invention thus relates in one aspect thereof to a method of representatively identifying a differentially expressed sequence involved in ovarian cancer. The sequence may be, for example, differentially expressed in a malignant ovarian cancer cell compared to a LMP ovarian cancer cell or normal ovarian cells. The sequence may be, for example, differentially expressed in a malignant ovarian cancer cell and a LMP ovarian cancer cell compared to a normal ovarian cell.

The method of the present invention may comprise the following steps or some of the following steps;

a) separately providing total messenger RNA from malignant and LMP ovarian cancer cells, and normal ovarian cells, the total messenger RNA may comprise, for example, at least one endogeneously differentially expressed sequence,

b) generating (e.g., single copy) of a) single-stranded cDNA from each messenger RNA of malignant ovarian cancer cell and (e.g., randomly) tagging the 3'-end of the single-stranded cDNA with a RNA polymerase promoter sequence and a first sequence tag;

c) generating (e.g., single copy) of a) single-stranded cDNA from each messenger RNA of LMP ovarian cancer cells or normal ovarian cell and (e.g., randomly) tagging the 3'-end of the single-stranded cDNA with a RNA polymerase promoter sequence and a second sequence tag;

d) separately generating partially or completely double-stranded 5'-tagged-DNA from each of b) and c), the double-stranded 5'-tagged-DNA may thus comprise in a 5' to 3' direction, a double-stranded RNA polymerase promoter, a first or second sequence tag and an expressed nucleic acid sequence,

e) separately linearly amplifying a first and second tagged sense RNA from each of d) with a RNA polymerase enzyme (which may be selected based on the promoter used for tagging),

f) generating single-stranded complementary first or second tagged DNA from one of e),

g) hybridizing the single-stranded complementary first or second tagged DNA of f) with the other linearly amplified sense RNA of e),

h) recovering unhybridized RNA with the help of the first or second sequence tag (for example by PCR or hybridization), and;

i) identifying (determining) the nucleotide sequence of unhybridized RNA.

The method may further comprise the step of comparatively determining the presence of the identified differentially expressed sequence in a cancer cell relative to a normal cell (e.g., a normal ovarian cell, a normal prostate cell, a normal breast cell etc.) or relative to a standard value.

The method may be used to preferentially identify a sequence which is upregulated in malignant ovarian cancer cell compared to a cell from a low malignancy potential ovarian cancer and/or compared to a normal cell.

In accordance with the present invention, a sequence may be further selected based on a reduced, lowered or substantially absent expression in a subset of other normal cell (e.g., a normal ovarian cell) or tissue, therefore representing a candidate sequence specifically involved in ovarian cancer.

The method may also further comprise a step of determining the complete sequence of the nucleotide sequence and may also comprise determining the coding sequence of the nucleotide sequence.

A sequence may also be selected for its specificity to other types of tumor cells, thus identifying a sequence having a more generalized involvement in the

development of cancer. These types of sequence may therefore represent desirable candidates having a more universal utility in the treatment and/or detection of cancer.

The present invention also relates in a further aspect, to the isolated differentially expressed sequence (polynucleotide and polypeptide) identified by the method of the present invention.

SEQ. ID. NO:1:

The candidate STAR sequence for SEQ. ID. NO:1 maps to a genomic hit and est hits according to NCBI's nr and est databases (see Table 2). Although, the matching ests are clustered into a new Unigene identifier number, Hs.555871, the STAR sequence does not map to any of the known mRNA sequences listed in this cluster, which codes for guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 1 (GNGT1). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 1), which have not been previously reported. Thus, it is believed that the gene comprising this STAR sequence or a related gene member as is outlined in the Unigene cluster may be required for ovarian cancer tumorigenesis.

SEQ. ID. NO:2:

The candidate protein encoded by the isolated SEQ. ID. NO:2 is associated with a previously identified gene that encodes a predicted polypeptide, interferon-induced protein 44-like (IFI44L) with an unknown function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 2), which have not been previously reported. Thus, it is believed that expression of this gene may be required for or involved for ovarian cancer tumorigenesis.

SEQ. ID. NO:3:

The candidate protein encoded by the isolated SEQ. ID. NO:3 is associated with a previously identified gene that encodes a known polypeptide, HOX D1, which contains a homeobox DNA-binding domain. This gene is a member of the Antp homeobox family and is nuclear sequence-specific transcription factor that is previously known to be involved in differentiation and limb development (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in

malignant ovarian cancer samples compared to ovarian LMP samples and the normal human tissues (Figure 3), which have not been previously reported. Thus, it is believed that the gene may be required for, or involved in ovarian cancer tumorigenesis as well.

SEQ. ID. NO:4:

The candidate protein encoded by the isolated SEQ. ID. NO:4 is associated with a previously identified gene that encodes a hypothetical polypeptide, LOC92196, similar to death-associated protein with an unknown function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 4), which have not been previously reported. Thus, it is believed that expression of this gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:5

The candidate protein encoded by the isolated SEQ. ID. NO:5 is associated with a previously identified gene that encodes a predicted polypeptide, interferon-induced protein with tetratricopeptide repeats 1 (IFIT1), with unknown function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 5), which have not been previously reported. Thus, it is believed that expression of this gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:6:

The candidate protein encoded by the isolated SEQ. ID. NO:6 is associated with a previously identified gene that encodes a known protein, glycine dehydrogenase (GLDC) (decarboxylating; glycine decarboxylase, glycine cleavage system protein P), which is a mitochondrial enzyme that catalyzes the degradation of glycine (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 6), which have not been previously reported. Thus, it is believed that expression of this gene may be required for, or involved in ovarian cancer tumorigenesis. The GLDC activity may be detected, for example, by measuring the degradation of glycine into urea.

SEQ. ID. NO:7:

The candidate protein encoded by the isolated SEQ. ID. NO:7 is associated with a previously identified gene that encodes a protein, dipeptidase 3 (DPEP3), which has membrane dipeptidase (proteolysis and peptidolysis) activity (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 7), which have not been previously reported. Thus, it is believed that expression of this gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:8

The candidate protein encoded by the isolated SEQ. ID. NO:8 is associated with a previously identified gene that encodes a protein, neuromedin U (NMU), which is a neuropeptide with potent activity on smooth muscle (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 8), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:9

The candidate protein encoded by the isolated SEQ. ID. NO:9 is associated with a previously identified gene that encodes a protein, bone morphogenetic protein 7 (BMP7), which plays a role in calcium regulation and bone homeostasis (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 9), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:10

The candidate protein encoded by the isolated SEQ. ID. NO:10 is associated with a previously identified gene that encodes a protein, cyclin-dependent kinase inhibitor 3 (CDKN3) (CDK2-associated dual specificity phosphatase), which is expressed at the G1 to S transition of the cell cycle (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant

ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 10), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:11

The candidate protein encoded by the isolated SEQ. ID. NO:11 is associated with a previously identified gene that encodes a protein, CDC28 protein kinase regulatory subunit 1B (CKS1B), which has cyclin-dependent protein kinase activity in cell cycle regulation (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 11), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:12

The candidate protein encoded by the isolated SEQ. ID. NO:12 is associated with a previously identified gene that encodes a protein, preferentially expressed antigen in melanoma (PRAME), which has no known function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 12), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:13

The candidate protein encoded by the isolated SEQ. ID. NO:13 is associated with a previously identified gene that encodes a protein, ISG15 ubiquitin-like modifier (ISG15), which is associated with ubiquitin-dependent protein catabolism (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 13), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:14

The candidate STAR sequence represented by the isolated SEQ. ID. NO:14 is associated with a previously identified partial gene sequence related to Accession # AI922121.1 (see Table 2), which codes for a yet unknown protein. We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 14), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynucleotide sequences comprising the STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:15

The candidate protein encoded by the isolated SEQ. ID. NO:15 is associated with a previously identified gene that encodes a hypothetical protein, FLJ33790, which has no known function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 15), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:16

The STAR sequence represented by the isolated SEQ. ID. NO:16 maps to a previously identified est, BG213598 that is from a transcribed genomic locus contained in the Unigene cluster, Hs.334302, which encodes a yet unknown protein (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 16), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynucleotides comprising this STAR sequence) or a related gene member as is outlined in the Unigene cluster may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:17

The candidate protein encoded by the isoalted SEQ. ID. NO:17 is associated with a previously identified gene that encodes a protein, V-set domain containing T cell activation inhibitor 1 (VTCN1), which has no known function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant

ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 17), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:18

The candidate protein encoded by the isolated SEQ. ID. NO:18 is associated with a previously identified gene that encodes a protein, kinesin family member 20A (KIF20A), which is involved in cell division in and membrane traffic within the Golgi apparatus (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 18), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:19

The STAR sequence represented by the isolated SEQ. ID. NO:19 maps to a genomic hit, Accession #AY769439 and to a group of ests represented by Accession # AA744939. The ests are clustered into Unigene identifier, Hs.478368 representing the protein, potassium large conductance calcium-activated channel, subfamily M, beta member 2 (KCNMB2). However, the STAR sequence does not overlap with any of the mRNA sequences listed thus far in the Hs.478368 Unigene cluster (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 19A), which have not been previously reported. In addition, performing RT-PCR using primers specific to either the STAR clone sequence for SEQ. ID. NO. 19 or the KCNMB2 sequence represented by Accession No. NM_005832, the amplification profiles were not the same across a number of ovarian samples tested (Figure 19B). It was obvious that KCNMB2 was expressed in essentially all ovarian samples including the normal at similar levels whereas, PCR amplicons for SEQ. ID. NO. 19 was observed at higher levels in the malignant ovarian tumor samples compared to the LMPs and normal ovarian samples (Figure 19B). Thus, it is believed that the expression of the gene corresponding to this STAR sequence (and polynucleotide sequences comprising the STAR sequence) or a related gene member may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:20

The STAR sequence represented by the isolated SEQ. ID. NO:20 maps to a previously identified est, BU595315 belonging to a group of ests that is from a transcribed genomic locus contained in the Unigene cluster, Hs.603908, which encodes a yet unknown protein (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 20), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynucleotide sequences comprising this STAR sequence) or a related gene member as is outlined in the Unigene cluster may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:21

The candidate protein encoded by the isolated SEQ. ID. NO:21 is a previously identified gene that encodes a protein, chemokine (C-X-C motif) ligand 10 (CXCL10), which has chemokine activity (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 21), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:22

The STAR sequence represented by the isolated SEQ. ID. NO:22 maps to chromosome 14, and may represent a portion of an unknown gene sequence (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 22), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynuclotides comprising this STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:23

The candidate protein encoded by the isolated SEQ. ID. NO:23 is a previously identified gene that encodes a protein, asparagine-linked glycosylation 8 homolog (yeast, alpha-1,3-glucosyltransferase) (ALG8), which catalyzes the addition of the second glucose residue to the lipid-linked oligosaccharide precursor for N-linked

glycosylation of proteins (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 23), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:24

The candidate protein encoded by the isolated SEQ. ID. NO:24 is a previously identified gene that encodes a protein, kidney associated antigen 1 (KAAG1), which has no known function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 24), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:25

The candidate protein encoded by the isolated SEQ. ID. NO:25 is a previously identified gene that encodes a protein, cyclin-dependent kinase inhibitor 2A (CDKN2A), which is involved in cell cycle control, G1/S Checkpoint (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 25), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:26

The candidate protein encoded by the isolated SEQ. ID. NO:26 is a previously identified gene that encodes a protein, microtubule-associated protein homolog (Xenopus laevis) (TPX2), which is involved in cell proliferation from the transition G1/S until the end of cytokinesis (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 26), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:27

The candidate protein encoded by the isolated SEQ. ID. NO:27 is a previously identified gene that encodes a protein, ubiquitin-conjugating enzyme E2C (UBE2C), which is required for the destruction of mitotic cyclins and for cell cycle progression (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 27), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:28

The STAR sequence represented by the isolated SEQ. ID. NO:28 maps to cDNA FLJ35538 fis, clone SPLEN2002463 of Unigene cluster, Hs.590469 and may represent a portion of an unknown gene sequence (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 28), which have not been previously reported. Thus, it is believed that expression of the gene correspondong to this STAR sequence (and polynucleotides comprising this STAR sequence) or a related gene member as is outlined in the Unigene cluster may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:29

The candidate protein encoded by the isolated SEQ. ID. NO:29 is a previously identified gene that encodes a protein, cellular retinoic acid binding protein 2 (CRABP2), whose function has not been precisely determined but this isoform is important in retinoic acid-mediated regulation of human skin growth and differentiation (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 29), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:30

The candidate protein encoded by the isolated SEQ. ID. NO:30 is a previously identified gene that encodes a protein, Histone 3, H2a (HIST3H2A), which is involved in nucleosome formation (see Table 2). We have demonstrated that expression of this

gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 30), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:31

The candidate protein encoded by the isolated SEQ. ID. NO:31 is a previously identified gene that encodes a protein, Histone 1, H4h (HIST1H4H), which is involved in nucleosome formation (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 30), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:32

The candidate protein encoded by the isolated SEQ. ID. NO:32 is a previously identified gene that encodes a hypothetical protein, Homeo box D3 (HOXD3), which is a nuclear transcription factor involved in development and differentiation (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 32), which have not been previously reported. Thus, it is believed that expression of the gene may be required for ovarian cancer tumorigenesis.

SEQ. ID. NO:33

The candidate protein encoded by the isolated SEQ. ID. NO:33 is a previously identified gene that encodes a member of the immunoglobulin gene family, immunoglobulin constant gamma 1 (IGHG1), which probably plays a role in immune response and antigen binding (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 33), which have not been previously reported. The expression pattern of this gene is similar to two other genes disclosed here, SEQ. ID. NO. 34 and SEQ. ID. NO. 47, which also encode immunoglobulins. This type of clustered immunoglobulin expression in ovarian cancer has not been previously described. Thus, it is believed that expression of the gene may be required for ovarian cancer tumorigenesis.

SEQ. ID. NO:34

The candidate protein encoded by the isolated SEQ. ID. NO:34 is a previously identified gene that encodes a member of the immunoglobulin gene family, immunoglobulin kappa constant (IGKC), which probably plays a role in immune response and antigen biinding (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 34), which have not been previously reported. The expression pattern of this gene is similar to two other genes disclosed here, SEQ. ID. NO. 33 and SEQ. ID. NO. 47, which also encode immunoglobulins. This type of clustered immunoglobulin expression in ovarian cancer has not been previously described. Thus, it is believed that expression of the gene may be required for ovarian cancer tumorigenesis.

SEQ. ID. NO:35

The candidate protein encoded by the isolated SEQ. ID. NO:35 is a gene located on chromosome 10 that encodes an open reading frame of unknown function. (see Table 2). The gene may encode a protein termed astroprincin that was found to be expressed in a critical region in DiGeorge syndrome. We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 35), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:36

The candidate protein encoded by the isolated SEQ. ID. NO:36 is a previously identified gene that encodes a protein, histocompatibility (minor) 13 (HM13), which has no known function (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 36), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:37

The STAR sequence represented by the isolated SEQ. ID. NO:37 maps to chromosome 13, and may represent a portion of an unknown gene sequence (see

Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 37), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynuclotides comprising this STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:38

The candidate protein encoded by the isolated SEQ. ID. NO:38 is a previously identified gene that encodes a protein, frizzled-related protein (FRZB), which is associated with symptomatic osteoarthritis and may play a role in skeletal morphogenesis (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 38), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:39

The candidate protein encoded by the isolated SEQ. ID. NO:39 is a previously identified gene that encodes a protein, forkhead box M1 (FOXM1), which is a transcription factor that regulates genes involved in cell proliferation (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 39), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:40

The candidate protein encoded by the isolated SEQ. ID. NO:40 is a gene located on chromosome 20 that encodes an open reading frame of unknown function. (see Table 2). The gene is predicted to encode a membrane protein. We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 40), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:41

The STAR sequence represented by the isolated SEQ. ID. NO:41 maps to chromosome 1, and may represent a portion of an unknown gene sequence (see Table 2). Weak homology has been found between SEQ. ID. NO. 41 and the envelop proteins present at the surface of human endogenous retroviruses. We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 41), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynuclotides comprising this STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:42

The candidate protein encoded by the isolated SEQ. ID. NO:42 is a gene located on chromosome 16 that encodes an open reading frame of unknown function. (see Table 2). The gene is predicted to encode a membrane protein. We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 42), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:43

The candidate protein encoded by the isolated SEQ. ID. NO:43 is a previously identified gene that encodes a protein, Rac GTPase activating protein 1 (RACGAP1), which is a GTPase that interacts with Rho GTPases to control many cellular processes (see Table 2). These types of proteins are important effector molecules for the downstream signaling of Rho GTPases. We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 43), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:44

The candidate protein encoded by the isolated SEQ. ID. NO:44 is a gene that

encodes transmembrane protein 19 (TMEM19) that has no known function. (see Table 2). The gene is predicted to encode a membrane protein. We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 44), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:45

The STAR sequence represented by the isolated SEQ. ID. NO:45 maps to chromosome 4, and may represent a portion of an unknown gene sequence (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 45), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynuclotides comprising this STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:46

The STAR sequence represented by the isolated SEQ. ID. NO:46 maps to chromosome 1, and may represent a portion of an unknown gene sequence (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 46), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynuclotides comprising this STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:47

The candidate protein encoded by the isolated SEQ. ID. NO:47 is a previously identified gene with the Unigene cluster, Hs.449585, and may represent a portion immunoglobulin lambda locus (IGLV@), which probably plays a role in immune response and antigen biinding (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 47), which have not been previously reported. The expression pattern of this gene is similar to two other genes disclosed here, SEQ. ID. NO. 33 and SEQ. ID. NO. 34, which also encode

immunoglobulins. This type of clustered immunoglobulin expression in ovarian cancer has not been previously described. Thus, it is believed that expression of the gene may be required for ovarian cancer tumorigenesis.

SEQ. ID. NO:48

The candidate protein encoded by the isolated SEQ. ID. NO:48 is a previously identified gene that encodes a protein, secretory carrier membrane protein 3 (SCAMP3), which functions as a cell surface carrier protein during vesicular transport (see Table 2). We have demonstrated that expression of this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples but it is also expressed in a majority of normal human tissues (Figure 48), which have not been previously reported. Thus, it is believed that expression of the gene may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:49

The STAR sequence represented by the isolated SEQ. ID. NO:49 maps to chromosome 2, and may represent a portion of an unknown gene sequence (see Table 2). We have demonstrated that this STAR clone sequence is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 49), which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynuclotides comprising this STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

SEQ. ID. NO:50

The candidate protein encoded by the isolated SEQ. ID. NO:50 is a previously identified gene that encodes a protein, Folate receptor 1 (adult) (FOLR1), with members of this gene family having a high affinity for folic acid and for several reduced folic acid derivatives, and mediate delivery of 5-methyltetrahydrofolate to the interior of cells (see Table 2). We have demonstrated that this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 50). The potential role of FOLR1 in ovarian cancer therapeutics has been previously documented (Leamon and Low, 2001 and Jhaveri et al., 2006, United States Patent 7,030,236). By way of example of the FOLR1 gene target, similar genes described herein with upregulation in malignant ovarian tumors and limited or no expression in a majority of normal tissues may also serve as potential

therapeutic targets for ovarian cancer.

SEQ. ID. NO:169

The candidate protein encoded by the isolated SEQ. ID. NO:169 is a previously identified gene that encodes a protein, ceruloplasmin (CP), that binds most of the copper in plasma and is involved in the peroxidation of Fe(II)transferrin. The deficiency of this metalloprotein, termed aceruloplasminemia, leads to iron accumulation and tissue damage, and is associated diabetes and neurologic diseases (see Table 2). We have demonstrated that this gene is markedly upregulated in malignant ovarian cancer samples compared to ovarian LMP samples and a majority of normal human tissues (Figure 56) which have not been previously reported. Thus, it is believed that expression of the gene corresponding to this STAR sequence (and polynuclotides comprising this STAR sequence) may be required for, or involved in ovarian cancer tumorigenesis.

H- RNA Interference Studies

RNA interference is a recently discovered gene regulation mechanism that involves the sequence-specific decrease in a gene's expression by targeting the mRNA for degradation and although originally described in plants, it has been discovered across many animal kingdoms from protozoans and invertebrates to higher eukaryotes (reviewed in Agrawal et al., 2003). In physiological settings, the mechanism of RNA interference is triggered by the presence of double-stranded RNA molecules that are cleaved by an RNAse III-like protein active in cells, called Dicer, which releases the 21-23 bp siRNAs. The siRNA, in a homology-driven manner, complexes into a RNA-protein amalgamation termed RISC (RNA-induced silencing complex) in the presence of mRNA to cause degradation resulting in attenuation of that mRNA's expression (Agrawal et al., 2003).

Current approaches to studying the function of genes, such as gene knockout mice and dominant negatives, are often inefficient, and generally expensive, and time-consuming. RNA interference is proving to be a method of choice for the analysis of a large number of genes in a quick and relatively inexpensive manner. Although transfection of synthetic siRNAs is an efficient method, the effects are often transient at best (Hannon G.J., 2002). Delivery of plasmids expressing short hairpin RNAs by stable transfection has been successful in allowing for the analysis of RNA interference in longer-term studies (Brummelkamp et al., 2002; Elbashir et al., 2001).

I- Determination of knockdown effects on the proliferation of ovarian cancer cell lines

In order to determine which ovarian cancer-specific genes participate in the proliferation of ovarian cancer cells, an assay was developed using stably transfected cell lines that contain attenuated (i.e., knocked down) levels of the specific gene being investigated. Two human ovarian cancer cell lines derived from chemotherapy-naïve patients were utilized that have been previously characterized in terms of their morphology, tumorigenicity, and global expression profiles. In addition, these analyses revealed that these cell lines were excellent models for in vivo behavior of ovarian tumors in humans (Provencher et al., 2000 and Samouelian et al., 2004). These cell lines are designated TOV-21G and TOV-112D.

The design and subcloning of individual shRNA expression cassettes and the procedure utilized for the characterisation of each nucleotide sequence is described below. Selection of polynucleotides were chosen based on their upregulation in ovarian tumors and the selective nature of their expression in these tumors compared to other tissues as described above. The design of shRNA sequences was performed using web-based software that is freely available to those skilled in the art (Qiagen for example). These chosen sequences, usually 19-mers, were included in two complementary oligonucleotides that form the template for the shRNAs, i.e. the 19-nt sense sequence, a 9-nt linker region (loop), the 19-nt antisense sequence followed by a 5-6 poly-T tract for termination of the RNA polymerase III. Appropriate restriction sites were inserted at the ends of these oligonucleotides to facilitate proper positioning of the inserts so that the transcriptional start point is at a precise location downstream of the hU6 promoter. The plasmid utilized in all RNA interference studies, pSilencer 2.0 (SEQ. ID. NO. 101), was purchase from a commercial supplier (Ambion, Austin, TX). For each sequence selected, at least two different shRNA expression vectors were constructed to increase the chance of observing RNA interference.

TOV-21G or TOV-112D cells were seeded in 6-well plates in OSE (Samouelian et al., 2004) containing 10% fetal bovine serum at a density of 600 000 cells/well, allowed to plate overnight and transfected with 1 µg of pSil-shRNA plasmid (Figure 53, sh-1 and sh-2) using the Fugene™ 6 reagent (Roche, Laval, QC). After 16h of incubation, fresh medium was added containing 2 µg/ml puromycin (Sigma, St. Louis, Mo) to select for stable transfectants. Control cells were transfected with a control pSil (sh-scr (SEQ. ID. NO. 102) that contains a scrambled shRNA sequence that displays homology to no known human gene. After approximately 4-5 days, pools

and/or individual clones of cells were isolated and expanded for further analyses. The effectiveness of attenuation was verified in all shRNA cells lines. Total RNA was prepared by standard methods using Trizol™ reagent from cells grown in 6-well plates and expression of the target gene was determined by RT-PCR using gene-specific primers. First strand cDNA was generated using Thermoscript™ (Invitrogen, Burlington, ON) and semi-quantitative PCR was performed by standard methods (Qiagen, Mississauga, ON). 100% expression levels for a given gene was assigned to those found in the cell lines transfected with the control pSil plasmid (sh-scr). Figure 52 shows representative results from the attenuation of two candidate genes, SEQ. ID. NO. 1 and SEQ. ID. NO. 3. When RT-PCR was performed using total RNA from the control cell lines (Figure 52, pSil-scr), a single band of expected size was observed. When the total RNA from the cell line containing shRNAs to SEQ. ID. NO. 1 (0094) (sh-1: SEQ. ID. NO. 103 and sh-2: SEQ. ID. NO. 104) or SEQ. ID. NO. 3 (0671) (sh-1: SEQ. ID. NO. 107 and sh-2: SEQ. ID. NO. 108) was amplified under identical conditions, significant reduction in the levels of expression of these genes were observed. These results indicate that the shRNAs that were expressed in the TOV-21G stable transfectants were successful in attenuating the expression of their target genes. As a control for equal quantities of RNA in all reactions, the expression of glyceraldehyde-3-phosphate dehydrogenase (Figure 52, GAPDH) was monitored and found to be expressed at equal levels in all samples used.

The proliferative ability of each shRNA-expressing cell line was determined and compared to cells expressing the scrambled shRNA (control). Cell number was determined spectrophotometrically by MTT assay at 570 nm (Mosmann, 1983). After selection of stably shRNA expressing pools and expansion of the lines, 5 000 cells/well of each cell lines was plated in 48-well plates in triplicate and incubated for 4 days under standard growth conditions. Representative data from 2 experiments ±SEM is displayed and experiments were typically repeated at least three times to confirm the results observed. Figure 53 shows representative results that were obtained when the proliferation assay was applied to stable TOV-21G cells lines. The cell number after 4 days in the control cell line expressing the scrambled shRNA (Figure 53, sh scr) was arbitrarily set to 100%. TOV-21G cell lines containing shRNA against SEQ. ID. NO. 1 (sh-1: SEQ. ID. NO. 103 and sh-2: SEQ. ID. NO. 104), SEQ. ID. NO. 3 (sh-1: SEQ. ID. NO. 107 and sh-2: SEQ. ID. NO. 108) and SEQ. ID. NO. 8 (0065) (sh-1: SEQ. ID. NO. 117 and sh-2: SEQ. ID. NO. 118) exhibited less than 50% proliferation for at least one shRNA compared to the control cell line (Figure 53, sh-1 and sh-2 for each). The proliferation of TOV-21G cell lines containing shRNA against SEQ. ID. NO. 2 (0478)

(sh-1: SEQ. ID. NO. 105 and sh-2: SEQ. ID. NO. 106) and SEQ. ID. NO. 7 (1096) (sh-1: SEQ. ID. NO. 115 and sh-2: SEQ. ID. NO. 116) was not affected to the same extent but significant inhibition of growth was still observed nevertheless. These results indicate that attenuation of these genes causes retardation in the growth of this ovarian cancer cell line. Several of these shRNA expression vectors were also transfected into the TOV-112D cell line and similar results were obtained (data not shown). This suggested that these genes are important for proliferation of ovarian cancer cells.

The gene encoding the folate receptor 1, SEQ. ID. NO. 50 (0967A) (Figure 53, 0967A), which has been documented as being an important marker for ovarian cancer (Leamon and Low, 2001), was also attenuated in TOV-21G cells, and marked growth inhibition was observed in the presence of the shRNAs (sh-1: SEQ. ID. NO. 151 and sh-2: SEQ. ID. NO. 152). This gives credibility to the approach used to validate the genes presented in this patent and substantiated their functional importance in the proliferation of ovarian cancer cells.

Table 1 below lists all of the genes tested and the average growth inhibition (n=3-4) that was observed in TOV-21G cells. Differences of less than 20% (see Table 1, <20) compared to the control cell lines represent cells where statistically significant reduction in proliferation was measured within a range of 5 – 20%.

Table 1 – List of genes tested in cell proliferation assay and results

Gene SEQ . ID. NO.	Alethia's Gene Code	shRNA SEQ. ID. NO.	Average Growth inhibition in TOV-21G cells (%) (n=3-4)
Control		SEQ. ID. NO. 102	0
SEQ. ID. NO. 1	0094	SEQ. ID. NOs. 103 and 104	47.9
SEQ. ID. NO. 2	0478	SEQ. ID. NOs. 105 and 106	41.7
SEQ. ID. NO. 3	0671	SEQ. ID. NOs. 107 and 108	65.7
SEQ. ID. NO. 4	0851	SEQ. ID. NOs. 109 and 110	21.5
SEQ. ID. NO. 5	0713	SEQ. ID. NOs. 111 and 112	42.3
SEQ. ID. NO. 6	1064	SEQ. ID. NOs. 113 and 114	28.9
SEQ. ID. NO. 7	1096	SEQ. ID. NOs. 115 and 116	25.8
SEQ. ID. NO. 8	0065	SEQ. ID. NOs. 117 and 118	32.5
SEQ. ID. NO. 9	1313	SEQ. ID. NOs. 119 and 120	50.5
SEQ. ID. NO. 10	0059	SEQ. ID. NOs. 121 and 122	52.4
SEQ. ID. NO. 11	0239	SEQ. ID. NOs. 123 and 124	22.8
SEQ. ID. NO. 12	0291	SEQ. ID. NOs. 125 and 126	<20
SEQ. ID. NO. 13	0972	SEQ. ID. NOs. 127 and 128	<20
SEQ. ID. NO. 14	0875	SEQ. ID. NOs. 129 and 130	<20
SEQ. ID. NO. 15	0420	SEQ. ID. NOs. 131 and 132	<20
SEQ. ID. NO. 16	0125	SEQ. ID. NOs. 133 and 134	<20
SEQ. ID. NO. 17	0531	SEQ. ID. NOs. 135 and 136	0
SEQ. ID. NO. 18	0967B	SEQ. ID. NOs. 137 and 138	0
SEQ. ID. NO. 19	0889	SEQ. ID. NOs. 139 and 140	<20
SEQ. ID. NO. 20	0313	SEQ. ID. NOs. 141 and 142	<20

Gene SEQ . ID. NO.	Alethia's Gene Code	shRNA SEQ. ID. NO.	Average Growth inhibition in TOV-21G cells (%) (n=3-4)
SEQ. ID. NO. 21	1134	SEQ. ID. NOs. 143 and 144	<20
SEQ. ID. NO. 22	0488	SEQ. ID. NOs. 145 and 146	0
SEQ. ID. NO. 23	0216	SEQ. ID. NOs. 147 and 148	<20
SEQ. ID. NO. 24	0447	SEQ. ID. NOs. 149 and 150	0
SEQ. ID. NO. 50	0967A	SEQ. ID. NOs. 151 and 152	47.4

J- A method for determining the requirement for specifc genes in the survival of ovarian cancer cells

As a means of complementing the growth inhibition data that was generated with the stable TOV-21G cell lines, a colony survival assay was used to determine the requirement of the selected genes in the survival of the cancer cells. The 'colony formation assay' or 'clonogenic assay' is a classical test to evaluate cell growth after treatment. The assay is widespread in oncological research areas where it is used to test the proliferating power of cancer cell lines after radiation and/or treatment with anticancer agents. It was expected that the results obtained when analyzing the genes that were functionally important in ovarian cancer would correlate between the growth inhibition study and the colony survival assay.

TOV-21G cells were seeded in 12-well plates at a density of 50 000 cells/well and transfected 24h later with 1 µg of pSil-shRNA vector, the same plasmids used in the previous assay. The next day, fresh medium was applied containing 2 µg/ml puromycin and the selection of the cells was carried out for 3 days. The cells were washed and fresh medium without puromycin was added and growth continued for another 5 days. To visualize the remaining colonies, the cells were washed in PBS and fixed and stained simultaneously in 1% crystal violet/10% ethanol in PBS for 15 minutes at room temperature. Following extensive washing in PBS, the dried plates were scanned for photographic analysis.

As shown in Figure 37 and as exemplified by SEQ. ID. NO. 1 (0094), SEQ. ID. NO. 3 (0671), and SEQ. ID. NO. 9 (1313), the amount of TOV-21G-derived colonies that survived correlated with the growth inhibition data. For example, the growth inhibition in the proliferation assay (Figure 53) and cell death in the colony assay (Figure 54) was greater in TOV-21G cells containing shRNA-2 compared to shRNA-1 for SEQ. ID. NO. 1 (0094) (0094-sh2 stronger than 0094-sh1) and SEQ. ID. NO. 3 (0671) (0671-sh2 stronger than 0671-sh1) whereas, for SEQ. ID. NO. 9 (1313), the 1313-sh1 was stronger than 1313-sh2. Similar convergence was observed with several other genes that were analyzed using these two assays (data not shown).

Therefore, these results implied that a phenotypic manifestation in both assays was indicative of important genes that are functionally required in ovarian cancer cells and suggest that inhibition of the proteins they encode could be serve as important targets to develop new anticancer drugs.

K- A method for broadening the scope of intervention to other oncology indications

One skilled in the art will recognize that the sequences described in this invention have utilities in not only ovarian cancer, but these applications can also be expanded to other oncology indications where the genes are expressed. To address this, a PCR-based method was adapted to determine the expression pattern of all sequences described above in cancer cell lines isolated from nine types of cancer. The cancer types represented by the cell lines are leukemia, central nervous sytem, breast, colon, lung, melanoma, ovarian, prostate, and renal cancer (see Table C). These RNA samples were obtained from the Developmental Therapeutics Program at the NCI/NIH. Using the same RAMP RNA samples that amplified from the total RNA samples obtained from the NCI, 500 μg of RNA was converted to single-stranded cDNA with Thermoscript™ RT (Invitrogen, Burlington, ON) as described by the manufacturer. The cDNA reaction was diluted so that 1/200 of the reaction was used for each PCR experiment. After trial PCR reactions with gene-specific primers designed against each SEQ. ID NOs. to be tested, the linear range of the reaction was determined and applied to all samples, PCR was conducted in 96-well plates using HotStarTaq™ Polymerase from Qiagen (Mississauga, ON) in a DNA Engine Tetrad™ from MJ Research. Half of the reaction mixture was loaded on a 1.2% agarose/ethidium bromide gel and the amplicons visualized with UV light. To verify that equal quantities of RNA was used in each reaction, the level of RNA was monitored with GAPDH expression.

Table C – List of cancer cell lines from the NCI-60 panel

Cell line	Cancer type
K-562	leukemia
MOLT-4	leukemia
CCRF-CEM	leukemia
RPMI-8226	leukemia
HL-60(TB)	leukemia
SR	leukemia
SF-268	CNS
SF-295	CNS
SF-539	CNS

Cell line	Cancer type
SNB-19	CNS
SNB-75	CNS
U251	CNS
BT-549	breast
HS 578T	breast
MCF7	breast
NCI/ADR-RES	breast
MDA-MB-231	breast
MDA-MB-435	breast
T-47D	breast
COLO 205	colon
HCC-2998	colon
HCT-116	colon
HCT-15	colon
HT29	colon
KM12	colon
SW-620	colon
A549/ATCC	non-small cell lung
EKVX	non-small cell lung
HOP-62	non-small cell lung
HOP-92	non-small cell lung
NCI-H322M	non-small cell lung
NCI-H226	non-small cell lung
NCI-H23	non-small cell lung
NCI-H460	non-small cell lung
NCI-H522	non-small cell lung
LOX IMVI	melanoma
M14	melanoma
MALME-3M	melanoma
SK-MEL-2	melanoma
SK-MEL-28	melanoma
SK-MEL-5	melanoma
UACC-257	melanoma
UACC-62	melanoma
IGROV-1	ovarian
OVCAR-3	ovarian
OVCAR-4	ovarian
OVCAR-5	ovarian
OVCAR-8	ovarian
SK-OV-3	ovarian
DU-145	prostate
PC-3	prostate
786-O	renal
A498	renal
ACHN	renal
CAKI-1	renal
RXF-393	renal
SN-12C	renal

Cell line	Cancer type
TK-10	renal
UO-31	renal

One of skill in the art will readily recognize that orthologues for all mammals maybe identified and verified using well-established techniques in the art, and that this disclosure is in no way limited to one mammal. The term "mammal(s)" for purposes of this disclosure refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, goats, rabbits, etc. Preferably, the mammal is human.

The sequences in the experiments discussed above are representative of the NSEQ being claimed and in no way limit the scope of the invention. The disclosure of the roles of the NSEQs in proliferation of ovarian cancer cells satisfies a need in the art to better understand ovarian cancer disease, providing new compositions that are useful for the diagnosis, prognosis, treatment, prevention and evaluation of therapies for ovarian cancer and other cancers where said genes are expressed as well.

The art of genetic manipulation, molecular biology and pharmaceutical target development have advanced considerably in the last two decades. It will be readily apparent to those skilled in the art that newly identified functions for genetic sequences and corresponding protein sequences allows those sequences, variants and derivatives to be used directly or indirectly in real world applications for the development of research tools, diagnostic tools, therapies and treatments for disorders or disease states in which the genetic sequences have been implicated.

TABLE 2 – Differentially expressed sequences found in malignant ovarian cancer.

Nucleotide Sequence No.	NCBI Unigene #/Gene Symbol/Gene ID	Accession Number	ORF Nucleotide Positions/ Polypeptide sequence No.	Function
SEQ ID NO. 1	STAR clone but possibly belonging to cluster Hs.555871	BX094904 NM_021955 for Hs.555871	Unknown 149-373 for Hs.555871 encoding SEQ ID NO.: 51	Transcribed locus guanine nucleotide binding protein (G protein), gamma transducing activity polypeptide 1
SEQ ID NO. 2	Hs.389724	NM_006820	242-1483	interferon-induced protein

Nucleotide Sequence No.	NCBI Unigene #/Gene Symbol/Gene ID	Accession Number	ORF Nucleotide Positions/ Polypeptide sequence No.	Function
	/ IFI44L / 10964		encoding SEQ ID NO.: 52	44-like ; function unknown
SEQ ID NO. 3	Hs.83465 / HOXD1 / 3231	NM_024501	224-1210 encoding SEQ ID NO.: 53	homeobox D1; sequence-specific transcription factor that is involved in differentiation and limb development
SEQ ID NO. 4	Hs.59761 / LOC92196 / 92196	NM_001017920	45-368 encoding SEQ ID NO.: 54	hypothetical protein LOC92196 ; function unknown
SEQ ID NO. 5	Hs.20315 / IFIT1 / 3434	NM_001001887	93-1529 encoding SEQ ID NO.: 55	interferon-induced protein with tetratricopeptide repeats 1 ; function unknown
SEQ ID NO. 6	Hs.584238 / GLDC / 2731	NM_000170	151-3213 encoding SEQ ID NO.: 56	glycine dehydrogenase (decarboxylating; glycine decarboxylase, glycine cleavage system protein P); mitochondrial glycine cleavage system catalyzes the degradation of glycine
SEQ ID NO. 7	Hs.302028 / DPEP3 / 64180	NM_022357	9-1550 encoding SEQ ID NO.: 57	dipeptidase 3; proteolysis and peptidolysis
SEQ ID NO. 8	Hs.418367 / NMU / 10874	NM_006681	106..630 encoding SEQ ID NO.: 58	neuromedin U (NMU); neuropeptide signaling pathway, regulation of smooth muscle contraction
SEQ ID NO. 9	Hs.473163 / BMP7 / 655	NM_001719	123-1418 encoding SEQ ID NO.: 59	bone morphogenetic protein 7; cell growth and/or maintenance, growth, skeletal development, cytokine activity, growth factor activity
SEQ ID NO. 10	Hs.84113 / CDKN3 / 1033	NM_005192	62-700 encoding SEQ ID NO.: 60	cyclin-dependent kinase inhibitor 3; a cyclin-dependent kinase inhibitor, as well as, dephosphorylate CDK2 kinase which prevent the activation of CDK2 kinase
SEQ ID NO. 11	Hs.374378	NM_001826	10-249	CDC28 protein kinase

Nucleotide Sequence No.	NCBI Unigene #/Gene Symbol/Gene ID	Accession Number	ORF Nucleotide Positions/ Polypeptide sequence No.	Function
	/ CKS1B / 1163		encoding SEQ ID NO.: 61	regulatory subunit 1B ; cell cycle, cytokinesis, cyclin-dependent protein kinase activity
SEQ ID NO. 12	Hs.30743 / PRAME / 23532	NM_006115	250-1779 encoding SEQ ID NO.: 62	preferentially expressed antigen in melanoma ; function unknown
SEQ ID NO. 13	Hs.458485 / ISG15 / 9636	NM_005101	76-573 encoding SEQ ID NO.: 63	ISG15 ubiquitin-like modifier ; protein binding
SEQ ID NO. 14	STAR clone	AI922121.1		Novel genomic hit
SEQ ID NO. 15	Hs.292451 / FLJ33790 / 283212	NM_001039548	220-1311 encoding SEQ ID NO.: 64	hypothetical protein LOC283212 ; function unknown
SEQ ID NO. 16	Hs.334302	BG213598		Transcribed locus; function unknown
SEQ ID NO. 17	Hs.546434 / VTCN1 / 79679	NM_024626	71-919 encoding SEQ ID NO.: 65	V-set domain containing T cell activation inhibitor 1 ; function unknown
SEQ ID NO. 18	Hs.73625 / KIF20A / 10112	NM_005733	28..2700 encoding SEQ ID NO.: 66	kinesin family member 20A ; kinesin family, interacts with guanosine triphosphate (GTP)-bound forms of RAB6A and RAB6B
SEQ ID NO. 19	STAR clone but a possibly of it belonging to cluster Hs.478368 according to NCBI	AC117457 NM_005832 for Hs.478368	300-1007 encoding SEQ ID NO.: 67	novel genomic hit potassium large conductance calcium-activated channel, subfamily M, beta member 2 for Hs.478368
SEQ ID NO. 20	Hs.603908	BU595315		Transcribed locus; function unknown
SEQ ID NO. 21	Hs.632586	NM_001565	67-363	chemokine (C-X-C motif)

Nucleotide Sequence No.	NCBI Unigene #/Gene Symbol/Gene ID	Accession Number	ORF Nucleotide Positions/ Polypeptide sequence No.	Function
	/ CXCL10 / 3627		encoding SEQ ID NO.: 68	ligand 10 ; chemokine
SEQ ID NO. 22	STAR clone	AL583809		Novel genomic hit
SEQ ID NO. 23	Hs.503368 / ALG8 / 79053	NM_001007027	66-1469 encoding SEQ ID NO.: 69	asparagine-linked glycosylation 8 homolog (S. cerevisiae, alpha-1,3-glucosyltransferase) ; catalyzes the addition of the second glucose residue to the lipid-linked oligosaccharide precursor for N-linked glycosylation of proteins
SEQ ID NO. 24	Hs.591801 / KAAG1	NM_181337	738-992 encoding SEQ ID NO.: 70	kidney associated antigen 1 ; fumction unknown
SEQ ID NO. 25	Hs.512599 / CDKN2A / 1029	NM_000077	213-683 encoding SEQ ID NO.: 71	cyclin-dependent kinase inhibitor 2A ; cell cycle G1 control
SEQ ID NO. 26	Hs.244580 / TPX2 / 22974	NM_012112	699-2942 encoding SEQ ID NO.: 72	TPX2, microtubule-associated, homolog (Xenopus laevis) ; involve in cell proliferation
SEQ ID NO. 27	Hs.93002 / UBE2C / 11065	NM_007019	81-620 encoding SEQ ID NO.: 73	ubiquitin-conjugating enzyme E2C ; required for the destruction of mitotic cyclins and for cell cycle progression
SEQ ID NO. 28	Hs.590469	AK092857		cDNA FLJ35538 fis, clone SPLEN2002463; function unknown
SEQ ID NO. 29	Hs.405662 / CRABP2 / 1382	NM_001878	138-554 encoding SEQ ID NO.: 74	cellular retinoic acid binding protein 2 ; function unknown but may be involved in human skin growth and differentiation
SEQ ID NO. 30	Hs.26331 / HIST3H2A / 92815	NM_033445	43-435 encoding SEQ ID NO.: 75	histone 3, H2a ; nucleosome formation
SEQ ID NO. 31	Hs.591790 / HIST1H4H / 8365	NM_003543	1-312 encoding SEQ ID NO.: 76	histone 1, H4h ; nucleosome formation
SEQ ID NO. 32	Hs.93574	NM_006898	177-1475	homeobox D3; may play a

Nucleotide Sequence No.	NCBI Unigene #/Gene Symbol/Gene ID	Accession Number	ORF Nucleotide Positions/ Polypeptide sequence No.	Function
	/ HOXD3 / 3232		encoding SEQ ID NO.: 77	role in the regulation of cell adhesion processes
SEQ ID NO. 33	Hs.525641 / IGHG1 / 3500	BC092518	61-1470 encoding SEQ ID NO.: 78	Immunoglobulin heavy constant gamma 1; may play a role in immune response and antigen binding
SEQ ID NO. 34	Hs.592988 / IGKC /3514	BC073793	10-717 encoding SEQ ID NO.: 79	Immunoglobulin kappa constant; may play a role in immune response and antigen binding
SEQ ID NO. 35	Hs.66762	AY683003	55-2727 encoding SEQ ID NO.: 80	Chromosome 10 ORF 38; unknown function
SEQ ID NO. 36	Hs.373741 / SPP / 81502	NM_178580	115-1299 encoding SEQ ID NO.: 81	Histocompatibility (minor) 13; unknown function
SEQ ID NO. 37	STAR clone	AL157931		Novel genomic hit
SEQ ID NO. 38	Hs.128453 / FRZB / 2487	NM_001463	219-1196 encoding SEQ ID NO.: 82	Frizzled-related protein; Wnt receptor signaling pathway, development, skeletal, transmembrane receptor activity
SEQ ID NO. 39	Hs.239 / FOXM1 / 2305	NM_202003	266-2512 encoding SEQ ID NO.: 83	Forkhead box M1; transcriptional regulation
SEQ ID NO. 40	Hs.46627	NM_152864	89-715 encoding SEQ ID NO.: 84	Chromosome 20 ORF 58; unknown function
SEQ ID NO. 41	STAR clone	AK092936		Novel genomic hit
SEQ ID NO. 42	Gene ID 404550	BC009078	552-746 encoding SEQ ID NO.: 85	Chromosome 16 ORF 74; unknown function
SEQ ID NO. 43	Hs.645513 / RACGAP1 / 29127	NM_013277	225-2123 encoding SEQ ID NO.: 86	Rac GTPase activating protein 1; electron transport, intracellular signaling cascade; iron ion binding
SEQ ID NO. 44	Hs.645522 / TMEM19 / 55266	NM_018279	584-1594 encoding SEQ ID NO.: 87	Transmembrane protein 19; unknown function
SEQ ID NO. 45	STAR clone	AC109350		Novel genomic hit

Nucleotide Sequence No.	NCBI Unigene #/Gene Symbol/Gene ID	Accession Number	ORF Nucleotide Positions/ Polypeptide sequence No.	Function
SEQ ID NO. 46	STAR clone	AC104837		Novel genomic hit
SEQ ID NO. 47	STAR clone	AC002060		Immunoglobulin lambda variable group @; may play a role in antigen binding
SEQ ID NO. 48	Hs.200600 / SCAMP3 / 10067	NM_005698	254-1297 encoding SEQ ID NO.: 88	Secretory carrier membrane protein 3; post-Golgi transport, protein transport
SEQ ID NO. 49	STAR clone	AC068288		
SEQ ID NO. 50	Hs.73769 / FOLR1 / 2348	NM_000802	26-799 encoding SEQ ID NO.: 89	folate receptor 1 (adult) ;·mediate delivery of 5-methyltetrahydrofolate to the interior of cells
SEQ ID NO. 169	Hs.558314 / CP / 1356	NM_000096	251-3448 encoding SEQ ID NO.: 170	Ceruloplasmin; secreted protein; copper ion binding or transport

TABLE 3 – List of additional sequences identification of plasmids, oligonucleotides and shRNA oligonucleotides

Sequence Identification	name	Description
SEQ. ID. NO. 90	OGS 364	Oligo dT_{11} +Not 1+biotin
SEQ. ID. NO. 91	OGS 594	Oligonucleotide promoter tag 1
SEQ. ID. NO. 92	OGS 595	Oligonucleotide promoter tag 1
SEQ. ID. NO. 93	OGS 458	Oligonucleotide promoter tag 2
SEQ. ID. NO. 94	OGS 459	Oligonucleotide promoter tag 2
SEQ. ID. NO. 95	OGS 494	Primer for second-strand synthesis from tag 1
SEQ. ID. NO. 96	OGS 302	Primer for second-strand synthesis from tag 2
SEQ. ID. NO. 97	OGS 621	Oligonucleotide promoter
SEQ. ID. NO. 98	OGS 622	Oligonucleotide promoter

Sequence Identification	name	Description
SEQ. ID. NO. 99	pCATRMAN	Vector for STAR
SEQ. ID. NO. 100	p20	Vector for STAR
SEQ. ID. NO: 101	pSilencer2.0 vector	Vector for shRNA
SEQ. ID. NO: 102	sh-scr	Control shRNA (Ambion)
SEQ. ID. NO: 103	sh-1 0094	shRNA sequence for SEQ. ID. NO. 1
SEQ. ID. NO: 104	sh-2 0094	shRNA sequence for SEQ. ID. NO. 1
SEQ. ID. NO: 105	sh-1 0478	shRNA sequence for SEQ. ID. NO. 2
SEQ. ID. NO: 106	sh-2 0478	shRNA sequence for SEQ ID NO. 2
SEQ. ID. NO: 107	sh-1 0671	shRNA sequence for SEQ. ID. NO. 3
SEQ. ID. NO: 108	sh-2 0671	shRNA sequence for SEQ. ID. NO. 3
SEQ. ID. NO: 109	sh-1 0851	shRNA sequence for SEQ. ID. NO. 4
SEQ. ID. NO: 110	sh-2 0851	shRNA sequence for SEQ ID NO. 4
SEQ. ID. NO: 111	sh-1 0713	shRNA sequence for SEQ. ID. NO. 5
SEQ. ID. NO: 112	sh-2 0713	shRNA sequence for SEQ. ID. NO. 5
SEQ. ID. NO: 113	sh-1 1064	shRNA sequence for SEQ. ID. NO. 5
SEQ. ID. NO: 114	sh-2 1064	shRNA sequence for SEQ ID NO. 6
SEQ. ID. NO: 115	sh-1 1096	shRNA sequence for SEQ. ID. NO. 7
SEQ. ID. NO: 116	sh-2 1096	shRNA sequence for SEQ. ID. NO. 7
SEQ. ID. NO: 117	sh-1 0065	shRNA sequence for SEQ. ID. NO. 8
SEQ. ID. NO: 118	sh-2 0065	shRNA sequence for SEQ ID NO. 8
SEQ. ID. NO: 119	sh-1 1313	shRNA sequence for SEQ. ID. NO. 9
SEQ. ID. NO: 120	sh-2 1313	shRNA sequence for SEQ ID NO. 9
SEQ. ID. NO: 121	sh-1 0059	shRNA sequence for SEQ. ID. NO. 10
SEQ. ID. NO: 122	sh-2 0059	shRNA sequence for SEQ ID NO. 10
SEQ. ID. NO: 123	sh-1 0239	shRNA sequence for SEQ. ID. NO. 11
SEQ. ID. NO: 124	sh-2 0239	shRNA sequence for SEQ ID NO. 11
SEQ. ID. NO: 125	sh-1 0291	shRNA sequence for SEQ. ID. NO. 12
SEQ. ID. NO: 126	sh-2 0291	shRNA sequence for SEQ ID NO. 12
SEQ. ID. NO: 127	sh-1 0972	shRNA sequence for SEQ. ID. NO. 13
SEQ. ID. NO: 128	sh-2 0972	shRNA sequence for SEQ ID NO. 13
SEQ. ID. NO: 129	sh-1 0875	shRNA sequence for SEQ. ID. NO. 14

Sequence Identification	name	Description
SEQ. ID. NO: 130	sh-2 0875	shRNA sequence for SEQ ID NO. 14
SEQ. ID. NO: 131	sh-1 0420	shRNA sequence for SEQ. ID. NO. 15
SEQ. ID. NO: 132	sh-2 0420	shRNA sequence for SEQ ID NO. 15
SEQ. ID. NO: 133	sh-1 0125	shRNA sequence for SEQ. ID. NO. 16
SEQ. ID. NO: 134	sh-2 0125	shRNA sequence for SEQ ID NO. 16
SEQ. ID. NO: 135	sh-1 0531	shRNA sequence for SEQ. ID. NO. 17
SEQ. ID. NO: 136	sh-2 0531	shRNA sequence for SEQ ID NO. 17
SEQ. ID. NO: 137	sh-1 0967B	shRNA sequence for SEQ. ID. NO. 18
SEQ. ID. NO: 138	sh-2 0967B	shRNA sequence for SEQ ID NO. 18
SEQ. ID. NO: 139	sh-1 0889	shRNA sequence for SEQ. ID. NO. 19
SEQ. ID. NO: 140	sh-2 0889	shRNA sequence for SEQ ID NO. 19
SEQ. ID. NO: 141	sh-1 0313	shRNA sequence for SEQ. ID. NO. 20
SEQ. ID. NO: 142	sh-2 0313	shRNA sequence for SEQ ID NO. 20
SEQ. ID. NO: 143	sh-1 1134	shRNA sequence for SEQ. ID. NO. 21
SEQ. ID. NO: 144	sh-2 1134	shRNA sequence for SEQ ID NO. 21
SEQ. ID. NO: 145	sh-1 0488	shRNA sequence for SEQ. ID. NO. 22
SEQ. ID. NO: 146	sh-2 0488	shRNA sequence for SEQ ID NO. 22
SEQ. ID. NO: 147	sh-1 0216	shRNA sequence for SEQ. ID. NO. 23
SEQ. ID. NO: 148	sh-2 0216	shRNA sequence for SEQ ID NO. 23
SEQ. ID. NO: 149	sh-1 0447	shRNA sequence for SEQ. ID. NO. 24
SEQ. ID. NO: 150	sh-2 0447	shRNA sequence for SEQ ID NO. 24
SEQ. ID. NO: 151	sh-1 0967	shRNA sequence for SEQ. ID. NO. 50
SEQ. ID. NO: 152	sh-2 0967	shRNA sequence for SEQ ID NO. 50
SEQ. ID. NO: 153	OGS 1077	Forward primer for SEQ ID NO. 32
SEQ. ID. NO: 154	OGS 1078	Reverse primer for SEQ ID NO. 32
SEQ. ID. NO: 155	OGS 1141	Forward primer for SEQ ID NO. 35
SEQ. ID. NO: 156	OGS 1142	Reverse primer for SEQ ID NO. 35
SEQ. ID. NO: 157	OGS 1202	Forward primer for SEQ ID NO. 38
SEQ. ID. NO: 158	OGS 1203	Reverse primer for SEQ ID NO. 38
SEQ. ID. NO: 159	OGS 1212	Forward primer for SEQ ID NO. 41
SEQ. ID. NO: 160	OGS 1213	Reverse primer for SEQ ID NO. 41
SEQ. ID. NO: 161	OGS 1171	Forward primer for SEQ ID NO. 44

Sequence Identification	name	Description
SEQ. ID. NO: 162	OGS 1172	Reverse primer for SEQ ID NO. 44
SEQ. ID. NO: 163	OGS 1175	Forward primer for SEQ ID NO. 45
SEQ. ID. NO: 164	OGS 1176	Reverse primer for SEQ ID NO. 45
SEQ. ID. NO: 165	OGS 1282	Forward primer for SEQ ID NO. 48
SEQ. ID. NO: 166	OGS 1283	Reverse primer for SEQ ID NO. 48
SEQ. ID. NO: 167	OGS 315	Forward primer for human GAPDH
SEQ. ID. NO: 168	OGS 316	Reverse primer for human GAPDH
SEQ. ID NO. 171	OGS 1136	Forward primer for SEQ ID NO. 1
SEQ. ID NO. 172	OGS 1044	Reverse primer for SEQ ID NO. 1
SEQ. ID NO. 173	OGS 1250	Forward primer for SEQ ID NO. 2
SEQ. ID NO. 174	OGS 1251	Reverse primer for SEQ ID NO. 2
SEQ. ID NO. 175	OGS 1049	Forward primer for SEQ ID NO. 3
SEQ. ID NO. 176	OGS 1050	Reverse primer for SEQ ID NO. 3
SEQ. ID NO. 177	OGS 1051	Forward primer for SEQ ID NO. 4
SEQ. ID NO. 178	OGS 1052	Reverse primer for SEQ ID NO. 4
SEQ. ID NO. 179	OGS 1252	Forward primer for SEQ ID NO. 5
SEQ. ID NO. 180	OGS 1253	Reverse primer for SEQ ID NO. 5
SEQ. ID NO. 181	OGS 1083	Forward primer for SEQ ID NO. 6
SEQ. ID NO. 182	OGS 1084	Reverse primer for SEQ ID NO. 6
SEQ. ID NO. 183	OGS 1053	Forward primer for SEQ ID NO. 7
SEQ. ID NO. 184	OGS 1054	Reverse primer for SEQ ID NO. 7
SEQ. ID NO. 185	OGS 1037	Forward primer for SEQ ID NO. 8
SEQ. ID NO. 186	OGS 1038	Reverse primer for SEQ ID NO. 8
SEQ. ID NO. 187	OGS 1045	Forward primer for SEQ ID NO. 9
SEQ. ID NO. 188	OGS 1046	Reverse primer for SEQ ID NO. 9
SEQ. ID NO. 189	OGS 1240	Forward primer for SEQ ID NO. 10
SEQ. ID NO. 190	OGS 1241	Reverse primer for SEQ ID NO. 10
SEQ. ID NO. 191	OGS 1304	Forward primer for SEQ ID NO. 11
SEQ. ID NO. 192	OGS 1305	Reverse primer for SEQ ID NO. 11
SEQ. ID NO. 193	OGS 1039	Forward primer for SEQ ID NO. 12
SEQ. ID NO. 194	OGS 1040	Reverse primer for SEQ ID NO. 12
SEQ. ID NO. 195	OGS 1095	Forward primer for SEQ ID NO. 13

Sequence Identification	name	Description
SEQ. ID NO. 196	OGS 1096	Reverse primer for SEQ ID NO. 13
SEQ. ID NO. 197	OGS 1284	Forward primer for SEQ ID NO. 15
SEQ. ID NO. 198	OGS 1285	Reverse primer for SEQ ID NO. 15
SEQ. ID NO. 199	OGS 1063	Forward primer for SEQ ID NO. 16
SEQ. ID NO. 200	OGS 1064	Reverse primer for SEQ ID NO. 16
SEQ. ID NO. 201	OGS 1031	Forward primer for SEQ ID NO. 17
SEQ. ID NO. 202	OGS 1032	Reverse primer for SEQ ID NO. 17
SEQ. ID NO. 203	OGS 1308	Forward primer for SEQ ID NO. 18
SEQ. ID NO. 204	OGS 1309	Reverse primer for SEQ ID NO. 18
SEQ. ID NO. 205	OGS 1069	Forward primer for SEQ ID NO. 19
SEQ. ID NO. 206	OGS 1070	Reverse primer for SEQ ID NO. 19
SEQ. ID NO. 207	OGS 1061	Forward primer for SEQ ID NO. 20
SEQ. ID NO. 208	OGS 1062	Reverse primer for SEQ ID NO. 20
SEQ. ID NO. 209	OGS 1097	Forward primer for SEQ ID NO. 21
SEQ. ID NO. 210	OGS 1098	Reverse primer for SEQ ID NO. 21
SEQ. ID NO. 211	OGS 1075	Forward primer for SEQ ID NO. 22
SEQ. ID NO. 212	OGS 1076	Reverse primer for SEQ ID NO. 22
SEQ. ID NO. 213	OGS 1232	Forward primer for SEQ ID NO. 23
SEQ. ID NO. 214	OGS 1233	Reverse primer for SEQ ID NO. 23
SEQ. ID NO. 215	OGS 1067	Forward primer for SEQ ID NO. 24
SEQ. ID NO. 216	OGS 1068	Reverse primer for SEQ ID NO. 24
SEQ. ID NO. 217	OGS 1099	Forward primer for SEQ ID NO. 25
SEQ. ID NO. 218	OGS 1100	Reverse primer for SEQ ID NO. 25
SEQ. ID NO. 219	OGS 1246	Forward primer for SEQ ID NO. 26
SEQ. ID NO. 220	OGS 1247	Reverse primer for SEQ ID NO. 26
SEQ. ID NO. 221	OGS 1093	Forward primer for SEQ ID NO. 27
SEQ. ID NO. 222	OGS 1094	Reverse primer for SEQ ID NO. 27
SEQ. ID NO. 223	OGS 1332	Forward primer for SEQ ID NO. 28
SEQ. ID NO. 224	OGS 1333	Reverse primer for SEQ ID NO. 28
SEQ. ID NO. 225	OGS 1101	Forward primer for SEQ ID NO. 29
SEQ. ID NO. 226	OGS 1102	Reverse primer for SEQ ID NO. 29
SEQ. ID NO. 227	OGS 1300	Forward primer for SEQ ID NO. 30

Sequence Identification	name	Description
SEQ. ID NO. 228	OGS 1301	Reverse primer for SEQ ID NO. 30
SEQ. ID NO. 229	OGS 1302	Forward primer for SEQ ID NO. 31
SEQ. ID NO. 230	OGS 1303	Reverse primer for SEQ ID NO. 31
SEQ. ID NO. 231	OGS 1292	Forward primer for SEQ ID NO. 33
SEQ. ID NO. 232	OGS 1294	Reverse primer for SEQ ID NO. 33
SEQ. ID NO. 233	OGS 1242	Forward primer for SEQ ID NO. 34
SEQ. ID NO. 234	OGS 1243	Reverse primer for SEQ ID NO. 34
SEQ. ID NO. 235	OGS 1280	Forward primer for SEQ ID NO. 36
SEQ. ID NO. 236	OGS 1281	Reverse primer for SEQ ID NO. 36
SEQ. ID NO. 237	OGS 1159	Forward primer for SEQ ID NO. 37
SEQ. ID NO. 238	OGS 1160	Reverse primer for SEQ ID NO. 37
SEQ. ID NO. 239	OGS 1310	Forward primer for SEQ ID NO. 39
SEQ. ID NO. 240	OGS 1311	Reverse primer for SEQ ID NO. 39
SEQ. ID NO. 241	OGS 1155	Forward primer for SEQ ID NO. 40
SEQ. ID NO. 242	OGS 1156	Reverse primer for SEQ ID NO. 40
SEQ. ID NO. 243	OGS 1316	Forward primer for SEQ ID NO. 42
SEQ. ID NO. 244	OGS 1317	Reverse primer for SEQ ID NO. 42
SEQ. ID NO. 245	OGS 1306	Forward primer for SEQ ID NO. 43
SEQ. ID NO. 246	OGS 1307	Reverse primer for SEQ ID NO. 43
SEQ. ID NO. 247	OGS 1286	Forward primer for SEQ ID NO. 46
SEQ. ID NO. 248	OGS 1287	Reverse primer for SEQ ID NO. 46
SEQ. ID NO. 249	OGS 1244	Forward primer for SEQ ID NO. 47
SEQ. ID NO. 250	OGS 1245	Reverse primer for SEQ ID NO. 47
SEQ. ID NO. 251	OGS 1035	Forward primer for SEQ ID NO. 50
SEQ. ID NO. 252	OGS 1036	Reverse primer for SEQ ID NO. 50
SEQ. ID NO. 253	OGS 1248	Forward primer for SEQ ID NO. 51
SEQ. ID NO. 254	OGS 1249	Reverse primer for SEQ ID NO. 51

TABLE 4 – Nucleotide and amino acid sequences of the SEQ.ID NOs.

NucleotideSequence (5'-3')	ORFs
SEQ.ID NO.1 **STAR clone:** CTGGAAGCTGAAGAATCACCGGCTTCAGTGACATGGAACCCAGCGATTTGATTTTTGACGAGTATCGGGTGACTTTGAGG TGGTCAAGAAACCACACTTTAAGAACAATGTCCA **NM_021955:** AATCATATTAGTGAAGATTAGGAAGAAGCTTTAAAATCCCAAGGCTAGTGTGCATTGCTAGAATTGTTAAGAGAGAGAGC TCATATGAAATTGGTTATCGTGGGATATTTAAAATAAAACAAAGAACAGTTTACTTTCAGGCAAAAAGATGCCAGTAATC AATATTGAGGACCTGACAGAAAAGGACAAATTGAAGATGGAAGTTGACCAGCTCAAGAAAGAAGTGACACTGGAAAGAAT GCTAGTTTCCAAATGTTGTGAAGAAGTAAGAGATTACGTTGAAGAACGATCTGGCGAGGATCCACTGGTAAAGGGCATCC CAGAGGACAAAAATCCCTTCAAGGAGCTCAAAGGAGGCTGTGTGATTTCATAATACAAACAAAAAGAAAAAAAATTAAAC AAATTCTTGGAAATATCTCAAATGTTAATAACAATATGAATTTTTCTCATGCATACTATTACTACTAAGCATGTACGTGA ATTTTTAAATTTATAGATGTAAACTTTTAATAAAAATTGGGGTGTGGTAACCCATCATTCTATGTTTTTCTTAACATAGC TGGCACAGGGTTTAACACATAATTGCCAATAAATATTGCTTAAAGTTCTTTAAAAAGAACTATGTTTT	SEQ.ID NO.51 MPVINIEDLTEKDKLKMEVDQLKKEVTLERM LVSKCCEEVRDYVEERSGEDPLVKGIPEDKN PFKELKGG CVIS
SEQ.ID NO.2 GCACGAGGAAGCCACAGATCTCTTAAGAACTTTCTGTCTCCAAACCGTGGCTGCTCGATAAATCAGACAGAACAGTTAAT CCTCAATTTAAGCCTGATCTAACCCCTAGAAACAGATATAGAACAATGGAAGTGACAACAAGATTGACATGGAATGATGA AAATCATCTGCGCAACTGCTTGGAAATGTTTCTTTGAGTCTTCTCTATAAGTCTAGTGTTCATGGAGGTAGCATTGAAGA TATGGTTGAAAGATGCAGCCGTCAGGGATGTACTATAACAATGGCTTACATTGATTACAATATGATTGTAGCCTTTATGC TTGGAAATTATATTAATTTACGTGAAAGTTCTACAGAGCCAAATGATTCCCTATGGTTTTCACTTCAAAAGAAAAATGAC ACCACTGAAATAGAAACTTTACTCTTAAATACAGCACCAAAAATTATTGATGAGCAACTGGTGTGTCGTTTATCGAAAAC GGATATTTTCATTATATGTCGAGATAATAAAATTTATCTAGATAAAATGATAACAAGAAACTTGAAACTAAGGTTTTATG GCCACCGTCAGTATTTGGAATGTGAAGTTTTTCGAGTTGAAGGAATTAAGGATAACCTAGACGACATAAAGAGGATAATT AAAGCCAGAGAGCACAGAAATAGGCTTCTAGCAGACATCAGAGACTATAGGCCCTATGCAGACTTGGTTTCAGAAATTCG TATTCTTTTGGTGGGTCCAGTTGGGTCTGGAAAGTCCAGTTTTTTCAATTCAGTCAAGTCTATTTTTCATGGCCATGTGA CTGGCCAAGCCGTAGTGGGGTCTGATACCACCAGCATAACCGAGCGGTATAGGATATATTCTGTTAAAGATGGAAAAAAT GGAAAATCTCTGCCATTTATGTTGTGTGACACTATGGGGCTAGATGGGGCAGAAGGAGCAGGACTGTGCATGGATGACAT TCCCCACATCTTAAAAGGTTGTATGCCAGACAGATATCAGTTTAATTCCCGTAAACCAATTACACCTGAGCATTCTACTT	SEQ.ID NO.52 MVERCSRQGCTITMAYIDYNMIVAFMLGNYI NLRESSTEPNDSLWFSLQKKNDTTEIETLLL NTAPKIIDEQLVCRLSKTDIFIICRDNKIYL DKMITRNLKLRFYGHRQYLECEVFRVEGIKD NLDDIKRIIKAREHRNRLLADIRDYRPYADL VSEIRILLVGPVGSGKSSFFNSVKSIFHGHV TGQAVVGSDTTSITERYRIYSVKDGKNGKSL PFMLCDTMGLDGAEGAGLCMDDIPHILKGCM PDRYQFNSRKPITPEHSTFITSPSLKDRIHC VAYVLDINSIDNLYSKMLAKVKQVHKEVLNC GIAYVALLTKVDDCSEVLQDNFLNMSRSMTS QSRVMNVHKMLGIPISNILMVGNYASDLELD PMKDILILSALRQMLRAADDFLEDLPLEETG

CA 02655933 2008-12-16

TTATCACCTCTCCATCTCTGAAGGACAGGATTCACTGTGTGGCTTATGTCTTAGACATCAACTCTATTGACAATCTCTAC TCTAAAATGTTGGCAAAAGTGAAGCAAGTTCACAAAGAAGTATTAAACTGTGGTATAGCATATGTGGCCTTGCTTACTAA AGTGGATGATTGCAGTGAGGTTCTTCAAGACAACTTTTTAAACATGAGTAGATCTATGACTTCTCAAAGCCGGGTCATGA ATGTCCATAAAATGCTAGGCATTCCTATTTCCAATATTTTGATGGTTGGAAATTATGCTTCAGATTTGGAACTGGACCCC ATGAAGGATATTCTCATCCTCTCTGCACTGAGGCAGATGCTGCGGGCTGCAGATGATTTTTTAGAAGATTTGCCTCTTGA GGAAACTGGTGCAATTGAGAGAGCGTTACAGCCCTGCATTTGAGATAAGTTGCCTTGATTCTGACATTTGGCCCAGCCTG TACTGGTGTGCCGCAATGAGAGTCAATCTCTATTGACAGCCTGCTTCAGATTTTGCTTTTGTTCGTTTTGCCTTCTGTCC TTGGAACAGTCATATCTCAAGTTCAAAGGCCAAAACCTGAGAAGCGGTGGGCTAAGATAGGTCCTACTGCAAACCACCCC TCCATATTTCCGTACCATTTACAATTCAGTTTCTGTGACATCTTTTTAAACCACTGGAGGAAAAATGAGATATTCTCTAA TTTATTCTTCTATAACACTCTATATAGAGCTATGTGAGTACTAATCACATTGAATAATAGTTATAAAATTATTGTATAGA CATCTGCTTCTTAAACAGATTGTGAGTTCTTTGAGAAACAGCGTGGATTTTACTTATCTGTGTATTCACAGAGCTTAGCA CAGTGCCTGGTAATGAGCAAGCATACTTGCCATTACTTTTCCTTCCCACTCTCTCCAACATCACATTCACTTTAAATTTT TCTGTATATAGAAAGGAAAACTAGCCTGGGCAACATGATGAAACCCCATCTCCACTGC	AIERALQPCI
SEQ.ID NO.3 GCCGAGCGGAGAGGCCGCCCATTGGCCGGCCAGCGCCACGTGGCCGCCCCCGCCGGTATATTAGGCCACTATTTACCTCC GGCTCACTCGCCATGGGTTGGAGAGGGCAGCTCGGGTAGAGAGGGCTGGCGGAGCGGCGCAGACGGCGGCAGTCCTGCTC AGCCTCTGCCCGGCTCCGTACTCCGGCCCCGGCCTGCGCCCTCAGAAAGGTGGGGCCCGAACCATGAGCTCCTACCTGGA GTACGTGTCATGCAGCAGCAGCGGCGGGGTCGGCGGCGACGTGCTCAGCTTGGCACCCAAGTTCTGCCGCTCCGACGCCC GGCCCGTGGCTCTGCAGCCCGCCTTCCCTCTGGGCAACGGCGACGGCGCCTTCGTCAGCTGTCTGCCCCTGGCCGCCGCC CGACCCTCGCCTTCGCCCCCGGCCGCCCCCGCGCGGCCGTCCGTACCGCCTCCGGCCGCGCCCCAGTACGCGCAGTGCAC CCTGGAGGGGGCCTACGAACCTGGTGCCGCACCTGCCGCGGCAGCTGGGGGCGCGGACTACGGCTTCCTGGGGTCCGGGC CGGCGTACGACTTCCCGGGCGTGCTGGGGCGGGCGGCCGACGACGGCGGGTCTCACGTCCACTACGCCACCTCGGCCGTC TTCTCGGGCGGCGGCTCTTTCCTCCTCAGCGGCCAGGTGGATTACGCGGCCTTCGGCGAACCCGGCCCTTTTCCGGCTTG TCTCAAAGCGTCAGCCGACGGCCACCCTGGTGCTTTCCAGACCGCATCCCCGGCCCCAGGCACCTACCCCAAGTCCGTCT CTCCCGCCTCCGGCCTCCCTGCCGCCTTCAGCACGTTCGAGTGGATGAAAGTGAAGAGGAATGCCTCTAAGAAAGGTAAA CTCGCCGAGTATGGGGCCGCTAGCCCCTCCAGCGCGATCCGCACGAATTTCAGCACCAAGCAACTGACAGAACTGGAAAA AGAGTTTCATTTCAATAAGTACTTAACTCGAGCCCGGCGCATCGAGATAGCCAACTGCTTGCACCTGAATGACACGCAAG TCAAAATCTGGTTCCAGAACCGCAGGATGAAACAGAAGAAAAGGGAACGAGAAGGGCTTCTGGCCACGGCCATTCCTGTG GCTCCCCTCCAACTTCCCCTCTCTGGAACAACCCCCACTAAGTTTATCAAGAACCCCGGCAGCCCTTCTCAGTCCCAAGA GCCTTCGTGAGGCCGGTACTTGGGGCCGAAAAACTGTGGCCTGCAGAAGTCCCAGGCGACCCCCATCCCTATCTAGACTT AGGAGCTCAGTTTGGGATGGAGGTGGGAGAACAAAAATGAATAGGGATTTCACTTGGGAAATGAAGTACTTTAGTTGGCT TCCGAGTTCCAGACTATATGTCCAGATATTAATTGACTGTCTTGTAAGCCACTTGTTTGGTTATGATTTGTGTCTTATCA GGGAAAAGGTGCCCAGCTGCCAGCCCAGCTCCGCTGCTATCTTTGCCTCACTTAGTCATGTGCAATTCGCGTTGCAGAGT GGCAGACCATTAGTTGCTGAGTTCTGTCAGCACTCTGATGTGCTCAGAAGAGCACCTGCCCAAAGTTTTTCTGGTTTTAA	SEQ.ID NO.53 MSSYLEYVSCSSSGGVGGDVLSLAPKFCRSD ARPVALQPAFPLGNGDGAFVSCLPLAAARPS PSPPAAPARPSVPPPAAPQYAQCTLEGAYEP GAAPAAAAGGADYGFLGSGPAYDFPGVLGRA ADDGGSHVHYATSAVFSGGGSFLLSGQVDYA AFGEPGPFPACLKASADGHPGAFQTASPAPG TYPKSVSPASGLPAAFSTFEWMKVKRNASKK GKLAEYGAASPSSAIRTNFSTKQLTELEKEF HFNKYLTRARRIEIANCLHLNDTQVKIWFQN RRMKQKKREREGLLATAIPVAPLQLPLSGTT PTKFIKNPGSPSQSQEPS

TTTAAAGGACAAGGCTACATATATTCAGCTTTTTGAGATGACCAAAGCTAGTTAGGGTCTCCTTGATGTAGCTAAGCTGC TTCAGTGATCTTCACATTTGCACTCCAGTTTTTTTTTCTTTAAAAAAGCGGTTTCTACCTCTCTATGTGCCTGAGTGATG ATACAATCGCTGTTTAGTTACTAGATGAACAAATCCACAGAATGGGTAAAGAGTAGAATCTGAACTATATCTTGACAAAT ATTATTCAAACTTGAATGTAAATATATACAGTATGTATATTTTTTAAAAAGATTTGCTTGCAATGACCTTATAAGTGACA TTTAATGTCATAGCATGTAAAGGGTTTTTTTTGTAATAAAAATTATAGAATCTGCAAAAAAAAAAAAAAAA	
SEQ.ID NO.4 CAGCCTCCAGAGCACCAGCACTGGCACTGGCACTGGCACACGCTATGGCAAATGAAGTGCAAGACCTGCTCTCCCCTCGG AAAGGGGGACATCCTCCTGCAGTAAAAGCTGGAGGAATGAGAATTTCCAAAAAACAAGAAATTGGCACCTTGGAAAGACA TACCAAAAAAAACAGGATTCGAGAAAACAAGTGCCATTGCAAATGTTGCCAAAATACAGACACTGGATGCCCTGAATGACA CACTGGAGAAGCTCAACTATAAATTTCCAGCAACAGTGCACATGGCACATCAAAAACCCACACCTGCTCTGGAAAAGGTT GTTCCACTGAAAAGGATCTACATTATTCAGCAGCCTCGAAAATGTTAAGCCTGGATTTAAAACACAGCCGTCTGGCCAGC TGCCTCGAATATCTGACAGCTTAGCAAAAAGGGCCAAAGCTTTCCATAGGCGTGCTGCACTTGCTTGGTAAATTAAACAG CTTTTGTATCTTCCCCTTTGACTTTAGGTAATAAAGCATCCAAACTTGTAAAAAAAAAA	SEQ.ID NO.54 MANEVQDLLSPRKGGHPPAVKAGGMRISKKQ EIGTLERHTKKTGFEKTSAIANVAKIQTLDA LNDTLEKLNYKFPATVHMAHQKPTPALEKVV PLKRIYIIQQPRKC
SEQ.ID NO.5 GTAACTGAAAATCCACAAGACAGAATAGCCAGATCTCAGAGGAGCCTGGCTAAGCAAAACCCTGCAGAACGGCTGCCTAA TTTACAGCAACCATGAGTACAAATGGTGATGATCATCAGGTCAAGGATAGTCTGGAGCAATTGAGATGTCACTTTACATG GGAGTTATCCATTGATGACGATGAAATGCCTGATTTAGAAAACAGAGTCTTGGATCAGATTGAATTCCTAGACACCAAAT ACAGTGTGGGAATACACAACCTACTAGCCTATGTGAAACACCTGAAAGGCCAGAATGAGGAAGCCCTGAAGAGCTTAAAA GAAGCTGAAAACTTAATGCAGGAAGAACATGACAACCAAGCAAATGTGAGGAGTCTGGTGACCTGGGGCAACTTTGCCTG GATGTATTACCACATGGGCAGACTGGCAGAAGCCCAGACTTACCTGGACAAGGTGGAGAACATTTGCAAGAAGCTTTCAA ATCCCTTCCGCTATAGAATGGAGTGTCCAGAAATAGACTGTGAGGAAGGATGGGCCTTGCTGAAGTGTGGAGGAAAGAAT TATGAACGGGCCAAGGCCTGCTTTGAAAAGGTGCTTGAAGTGGACCCTGAAAACCCTGAATCCAGCGCTGGGTATGCGAT CTCTGCCTATCGCCTGGATGGCTTTAAATTAGCCACAAAAAATCACAAGCCATTTTCTTTGCTTCCCCTAAGGCAGGCTG TCCGCTTAAATCCAGACAATGGATATATTAAGGTTCTCCTTGCCCTGAAGCTTCAGGATGAAGGACAGGAAGCTGAAGGA GAAAAGTACATTGAAGAAGCTCTAGCCAACATGTCCTCACAGACCTATGTCTTTCGATATGCAGCCAAGTTTTACCGAAG AAAAGGCTCTGTGGATAAAGCTCTTGAGTTATTAAAAAAGGCCTTGCAGGAAACACCCACTTCTGTCTTACTGCATCACC AGATAGGGCTTTGCTACAAGGCACAAATGATCCAAATCAAGGAGGCTACAAAAGGGCAGCCTAGAGGGCAGAACAGAGAA AAGCTAGACAAAATGATAAGATCAGCCATATTTCATTTTGAATCTGCAGTGGAAAAAAAGCCCACATTTGAGGTGGCTCA TCTAGACCTGGCAAGAATGTATATAGAAGCAGGCAATCACAGAAAAGCTGAAGAGAATTTTCAAAAATTGTTATGCATGA AACCAGTGGTAGAAGAAACAATGCAAGACATACATTTCCACTATGGTCGGTTTCAGGAATTTCAAAAGAAATCTGACGTC AATGCAATTATCCATTATTTAAAAGCTATAAAAATAGAACAGGCATCATTAACAAGGGATAAAAGTATCAATTCTTTGAA	SEQ.ID NO.55 MSTNGDDHQVKDSLEQLRCHFTWELSIDDDE MPDLENRVLDQIEFLDTKYSVGIHNLLAYVK HLKGQNEEALKSLKEAENLMQEEHDNQANVR SLVTWGNFAWMYYHMGRLAEAQTYLDKVENI CKKLSNPFRYRMECPEIDCEEGWALLKCGGK NYERAKACFEKVLEVDPENPESSAGYAISAY RLDGFKLATKNHKPFSLLPLRQAVRLNPDNG YIKVLLALKLQDEGQEAEGEKYIEEALANMS SQTYVFRYAAKFYRRKGSVDKALELLKKALQ ETPTSVLLHHQIGLCYKAQMIQIKEATKGQP RGQNREKLDKMIRSAIFHFESAVEKKPTFEV AHLDLARMYIEAGNHRKAEENFQKLLCMKPV VEETMQDIHFHYGRFQEFQKKSDVNAIIHYL KAIKIEQASLTRDKSINSLKKLVLRKLRRKA LDLESLSLLGFVYKLEGNMNEALEYYERALR LAADFENSVRQGP

GAAATTGGTTTTAAGGAAACTTCGGAGAAAGGCATTAGATCTGGAAAGCTTGAGCCTCCTTGGGTTCGTCTACAAATTGG AAGGAAATATGAATGAAGCCCTGGAGTACTATGAGCGGGCCCTGAGACTGGCTGCTGACTTTGAGAACTCTGTGAGACAA GGTCCTTAGGCACCCAGATATCAGCCACTTTCACATTTCATTTCATTTTATGCTAACATTTACTAATCATCTTTTCTGCT TACTGTTTTCAGAAACATTATAATTCACTGTAATGATGTAATTCTTGAATAATAAATCTGACAAAAAAAAAAAAAAAAAA AAAAAAAAAA	
SEQ.ID NO.6 CCCGCGAGCGTCCATCCATCTGTCCGGCCGACTGTCCAGCGAAAGGGGCTCCAGGCCGGGCGCACGTCGACCCGGGGGAC CGAGGCCAGGAGAGGGGCCAAGAGCGCGGCTGACCCTTGCGGGCCGGGGCAGGGGACGGTGGCCGCGGCCATGCAGTCCT GTGCCAGGGCGTGGGGGCTGCGCCTGGGCCGCGGGGTCGGGGGCGGCCGCCGCCTGGCTGGGGGATCGGGGCCGTGCTGG GCGCCGCGGAGCCGGGACAGCAGCAGTGGCGGCGGGGACAGCGCCGCGGCTGGGGCCTCGCGCCTCCTGGAGCGCCTTCT GCCCAGACACGACGACTTCGCTCGGAGGCACATCGGCCCTGGGGACAAAGACCAGAGAGAGATGCTGCAGACCTTGGGGC TGGCGAGCATTGATGAATTGATCGAGAAGACGGTCCCTGCCAACATCCGTTTGAAAAGACCCTTGAAAATGGAAGACCCT GTTTGTGAAAATGAAATCCTTGCAACTCTGCATGCCATTTCAAGCAAAAACCAGATCTGGAGATCGTATATTGGCATGGG CTATTATAACTGCTCAGTGCCACAGACGATTTTGCGGAACTTACTGGAGAACTCAGGATGGATCACCCAGTATACTCCAT ACCAGCCTGAGGTGTCTCAGGGGAGGCTGGAGAGTTTACTCAACTACCAGACCATGGTGTGTGACATCACAGGCCTGGAC ATGGCCAATGCATCCCTGCTGGATGAGGGGACTGCAGCCGCAGAGGCACTGCAGCTGTGCTACAGACACAACAAGAGGAG GAAATTTCTCGTTGATCCCCGTTGCCACCCACAGACAATAGCTGTTGTCCAGACTCGAGCCAAATATACTGGAGTCCTCA CTGAGCTGAAGTTACCCTGTGAAATGGACTTCAGTGGAAAAGATGTCAGTGGAGTGTTGTTCCAGTACCCAGACACGGAG GGGAAGGTGGAAGACTTTACGGAACTCGTGGAGAGAGCTCATCAGAGTGGGAGCCTGGCCTGCTGTGCTACTGACCTTTT AGCTTTGTGCATCTTGAGGCCACCTGGAGAATTTGGGGTAGACATCGCCCTGGGCAGCTCCCAGAGATTTGGAGTGCCAC TGGGCTATGGGGGACCCCATGCAGCATTTTTTGCTGTCCGAGAAAGCTTGGTGAGAATGATGCCTGGAAGAATGGTGGGG GTAACAAGAGATGCCACTGGGAAAGAAGTGTATCGTCTTGCTCTTCAAACCAGGGAGCAACACATTCGGAGAGACAAGGC TACCAGCAACATCTGTACAGCTCAGGCCCTCTTGGCGAATATGGCTGCCATGTTTCGAATCTACCATGGTTCCCATGGGC TGGAGCATATTGCTAGGAGGGTACATAATGCCACTTTGATTTTGTCAGAAGGTCTCAAGCGAGCAGGGCATCAACTCCAG CATGACCTGTTCTTTGATACCTTGAAGATTCATTGTGGCTGCTCAGTGAAGGAGGTCTTGGGCAGGGCGGCTCAGCGGCA GATCAATTTTCGGCTTTTTGAGGATGGCACACTTGGTATTTCTCTTGATGAAACAGTCAATGAAAAAGATCTGGACGATT TGTTGTGGATCTTTGGTTGTGAGTCATCTGCAGAACTGGTTGCTGAAAGCATGGGAGAGGAGTGCAGAGGTATTCCAGGG TCTGTGTTCAAGAGGACCAGCCCGTTCCTCACCCATCAAGTGTTCAACAGCTACCACTCTGAAACAAACATTGTCCGGTA CATGAAGAAACTGGAAAATAAAGACATTTCCCTTGTTCACAGCATGATTCCACTGGGATCCTGCACCATGAAACTGAACA GTTCGTCTGAACTCGCACCTATCACATGGAAAGAATTTGCAAACATCCACCCCTTTGTGCCTCTGGATCAAGCTCAAGGA TATCAGCAGCTTTTCCGAGAGCTTGAGAAGGATTTGTGTGAACTCACAGGTTATGACCAGGTCTGTTTCCAGCCAAACAG CGGAGCCCAGGGAGAATATGCTGGACTGGCCACTATCCGAGCCTACTTAAACCAGAAAGGAGAGGGGCACAGAACGGTTT GCCTCATTCCGAAATCAGCACATGGGACCAACCCAGCAAGTGCCCACATGGCAGGCATGAAGATTCAGCCTGTGGAGGTG GATAAATATGGGAATATCGATGCAGTTCACCTCAAGGCCATGGTGGATAAGCACAAGGAGAACCTAGCAGCTATCATGAT	SEQ.ID NO.56 MQSCARAWGLRLGRGVGGGRRLAGGSGPCWA PRSRDSSSGGGDSAAAGASRLLERLLPRHDD FARRHIGPGDKDQREMLQTLGLASIDELIEK TVPANIRLKRPLKMEDPVCENEILATLHAIS SKNQIWRSYIGMGYYNCSVPQTILRNLLENS GWITQYTPYQPEVSQGRLESLLNYQTMVCDI TGLDMANASLLDEGTAAAEALQLCYRHNKRR KFLVDPRCHPQTIAVVQTRAKYTGVLTELKL PCEMDFSGKDVSGVLFQYPDTEGKVEDFTEL VERAHQSGSLACCATDLLALCILRPPGEFGV DIALGSSQRFGVPLGYGGPHAAFFAVRESLV RMMPGRMVGVTRDATGKEVYRLALQTREQHI RRDKATSNICTAQALLANMAAMFRIYHGSHG LEHIARRVHNATLILSEGLKRAGHQLQHDLF FDTLKIHCGCSVKEVLGRAAQRQINFRLFED GTLGISLDETVNEKDLDDLLWIFGCESSAEL VAESMGEECRGIPGSVFKRTSPFLTHQVFNS YHSETNIVRYMKKLENKDISLVHSMIPLGSC TMKLNSSSELAPITWKEFANIHPFVPLDQAQ GYQQLFRELEKDLCELTGYDQVCFQPNSGAQ GEYAGLATIRAYLNQKGEGHRTVCLIPKSAH GTNPASAHMAGMKIQPVEVDKYGNIDAVHLK AMVDKHKENLAAIMITYPSTNGVFEENISDV CDLIHQHGGQVYLDGANMNAQVGICRPGDFG SDVSHLNLHKTFCIPHGGGGPGMGPIGVKKH LAPFLPNHPVISLKRNEDACPVGTVSAAPWG SSSILPISWAYIKMMGGKGLKQATETAILNA NYMAKRLETHYRILFRGARGYVGHEFILDTR

TACATACCCATCCACCAATGGGGTGTTTGAAGAGAACATCAGTGACGTGTGTGACCTCATCCATCAACATGGAGGACAGG TCTACCTAGACGGGGCAAATATGAATGCTCAGGTGGGAATCTGTCGCCCTGGAGACTTCGGGTCTGATGTCTCGCACCTA AATCTTCACAAGACCTTCTGCATTCCCCACGGAGGAGGTGGTCCTGGCATGGGGCCCATCGGAGTGAAGAAACATCTCGC CCCGTTTTTGCCCAATCATCCCGTCATTTCACTAAAGCGGAATGAGGATGCCTGTCCTGTGGGAACCGTCAGTGCGGCCC CATGGGGCTCCAGTTCCATCTTGCCCATTTCCTGGGCTTATATCAAGATGATGGGAGGCAAGGGTCTTAAACAAGCCACG GAAACTGCGATATTAAATGCCAACTACATGGCCAAGCGATTAGAAACACACTACAGAATTCTTTTCAGGGGTGCAAGAGG TTATGTGGGTCATGAATTTATTTTGGACACGAGACCCTTCAAAAAGTCTGCAAATATTGAGGCTGTGGATGTGGCCAAGA GACTCCAGGATTATGGATTTCACGCCCCTACCATGTCCTGGCCTGTGGCAGGGACCCTCATGGTGGAGCCCACTGAGTCG GAGGACAAGGCAGAGCTGGACAGATTCTGTGATGCCATGATCAGCATTCGGCAGGAAATTGCTGACATTGAGGAGGGCCG CATCGACCCCAGGGTCAATCCGCTGAAGATGTCTCCACACTCCCTGACCTGCGTTACATCTTCCCACTGGGACCGGCCTT ATTCCAGAGAGGTGGCAGCATTCCCACTCCCCTTCATGAAACCAGAGAACAAATTCTGGCCAACGATTGCCCGGATTGAT GACATATATGGAGATCAGCACCTGGTTTGTACCTGCCCACCCATGGAAGTTTATGAGTCTCCATTTTCTGAACAAAAGAG GGCGTCTTCTTAGTCCTCTCTCCCTAAGTTTAAAGGACTGATTTGATGCCTCTCCCCAGAGCATTTGATAAGCAAGAAAG ATTTCATCTCCCACCCCAGCCTCAAGTAGGAGTTTTATATACTGTGTATATCTCTGTAATCTCTGTCAAGGTAAATGTAA ATACAGTAGCTGGAGGGAGTCGAAGCTGATGGTTGGAAGACGGATTTGCTTTGGTATTCTGCTTCCACATGTGCCAGTTG CCTGGATTGGGAGCCATTTTGTGTTTTGCGTAGAAAGTTTTAGGAACTTTAACTTTTAATGTGGCAAGTTTGCAGATGTC ATAGAGGCTATCCTGGAGACTTAATAGACATTTTTTTGTTCCAAAAGAGTCCATGTGGACTGTGCCATCTGTGGGAAATC CCAGGGCAAATGTTTACATTTTGTATACCCTGAAGAACTCTTTTTCCTCTAATATGCCTAATCTGTAATCACATTTCTGA GTGTTTTCCTCTTTTTCTGTGTGAGGTTTTTTTTTTTTTAATCTGCATTTATTAGTATTCTAATAAAAGCATTTTGATC GGAAAAAAAAAAAAAAAAAAAA	PFKKSANIEAVDVAKRLQDYGFHAPTMSWPV AGTLMVEPTESEDKAELDRFCDAMISIRQEI ADIEEGRIDPRVNPLKMSPHSLTCVTSSHWD RPYSREVAAFPLPFMKPENKFWPTIARIDDI YGDQHLVCTCPPMEVYESPFSEQKRASS
SEQ.ID NO.7 GGGTCGTCATGATCCGGACCCCATTGTCGGCCTCTGCCCATCGCCTGCTCCTCCCAGGCTCCCGCGGCCGACCCCCGCGC AACATGCAGCCCACGGGCCGCGAGGGTTCCCGCGCGCTCAGCCGGCGGTATCTGCGGCGTCTGCTGCTCCTGCTACTGCT GCTGCTGCTGCGGCAGCCCGTAACCCGCGCGGAGACCACGCCGGGCGCCCCCAGAGCCCTCTCCACGCTGGGCTCCCCCA GCCTCTTCACCACGCCGGGTGTCCCCAGCGCCCTCACTACCCCAGGCCTCACTACGCCAGGCACCCCCAAAACCCTGGAC CTTCGGGGTCGCGCGCAGGCCCTGATGCGGAGTTTCCCACTCGTGGACGGCCACAATGACCTGCCCCAGGTCCTGAGACA GCGTTACAAGAATGTGCTTCAGGATGTTAACCTGCGAAATTTCAGCCATGGTCAGACCAGCCTGGACAGGCTTAGAGACG GCCTCGTGGGTGCCCAGTTCTGGTCAGCCTCCGTCTCATGCCAGTCCCAGGACCAGACTGCCGTGCGCCTCGCCCTGGAG CAGATTGACCTCATTCACCGCATGTGTGCCTCCTACTCTGAACTCGAGCTTGTGACCTCAGCTGAAGGTCTGAACAGCTC TCAAAAGCTGGCCTGCCTCATTGGCGTGGAGGGTGGTCACTCACTGGACAGCAGCCTCTCTGTGCTGCGCAGTTTCTATG TGCTGGGGGTGCGCTACCTGACACTTACCTTCACCTGCAGTACACCATGGGCAGAGAGTTCCACCAAGTTCAGACACCAC ATGTACACCAACGTCAGCGGATTGACAAGCTTTGGTGAGAAAGTAGTAGAGGAGTTGAACCGCCTGGGCATGATGATAGA TTTGTCCTATGCATCGGACACCTTGATAAGAAGGGTCCTGGAAGTGTCTCAGGCTCCTGTGATCTTCTCCCACTCAGCTG CCAGAGCTGTGTGTGACAATTTGTTGAATGTTCCCGATGATATCCTGCAGCTTCTGAAGAAGAACGGTGGCATCGTGATG	SEQ.ID NO.57 MIRTPLSASAHRLLLPGSRGRPPRNMQPTGR EGSRALSRRYLRRLLLLLLLLLRQPVTRAE TTPGAPRALSTLGSPSLFTTPGVPSALTTPG LTTPGTPKTLDLRGRAQALMRSFPLVDGHND LPQVLRQRYKNVLQDVNLRNFSHGQTSLDRL RDGLVGAQFWSASVSCQSQDQTAVRLALEQI DLIHRMCASYSELELVTSAEGLNSSQKLACL IGVEGGHSLDSSLSVLRSFYVLGVRYLTLTF TCSTPWAESSTKFRHHMYTNVSGLTSFGEKV VEELNRLGMMIDLSYASDTLIRRVLEVSQAP VIFSHSAARAVCDNLLNVPDDILQLLKKNGG IVMVTLSMGVLQCNLLANVSTVADHFDHIRA VIGSEFIGIGGNYDGTGRFPQGLEDVSTYPV

GTGACACTGTCCATGGGGGTGCTGCAGTGCAACCTGCTTGCTAACGTGTCCACTGTGGCAGATCACTTTGACCACATCAG GGCAGTCATTGGATCTGAGTTCATCGGGATTGGTGGAAATTATGACGGGACTGGCCGGTTCCCTCAGGGGCTGGAGGATG TGTCCACATACCCAGTCCTGATAGAGGAGTTGCTGAGTCGTAGCTGGAGCGAGGAAGAGCTTCAAGGTGTCCTTCGTGGA AACCTGCTGCGGGTCTTCAGACAAGTGGAAAAGGTGAGAGAGGAGAGCAGGGCGCAGAGCCCCGTGGAGGCTGAGTTTCC ATATGGGCAACTGAGCACATCCTGCCACTCCCACCTCGTGCCTCAGAATGGACACCAGGCTACTCATCTGGAGGTGACCA AGCAGCCAACCAATCGGGTCCCCTGGAGGTCCTCAAATGCCTCCCCATACCTTGTTCCAGGCCTTGTGGCTGCTGCCACC ATCCCAACCTTCACCCAGTGGCTCTGCTGACACAGTCGGTCCCCGCAGAGGTCACTGTGGCAAAGCCTCACAAAGCCCCC TCTCCTAGTTCATTCACAAGCATATGCTGAGAATAAACATGTTACACATGGAAAAAAAAAAAAAAAAAAA	LIEELLSRSWSEEELQGVLRGNLLRVFRQVE KVREESRAQSPVEAEFPYGQLSTSCHSHLVP QNGHQATHLEVTKQPTNRVPWRSSNASPYLV PGLVAAATIPTFTQWLC
SEQ.ID NO.8 AGTCCTGCGTCCGGGCCCCGAGGCGCAGCAGGGCACCAGGTGGAGCACCAGCTACGCGTGGCGCAGCGCAGCGTCCCTAG CACCGAGCCTCCCGCAGCCGCCGAGATGCTGCGAACAGAGAGCTGCCGCCCCAGGTCGCCCGCCGGACAGGTGGCCGCGG CGTCCCCGCTCCTGCTGCTGCTGCTGCTGCTCGCCTGGTGCGCGGGCGCCTGCCGAGGTGCTCCAATATTACCTCAAGGA TTACAGCCTGAACAACAGCTACAGTTGTGGAATGAGATAGATGATACTTGTTCGTCTTTTCTGTCCATTGATTCTCAGCC TCAGGCATCCAACGCACTGGAGGAGCTTTGCTTTATGATTATGGGAATGCTACCAAAGCCTCAGGAACAAGATGAAAAAG ATAATACTAAAAGGTTCTTATTTCATTATTCGAAGACACAGAAGTTGGGCAAGTCAAATGTTGTGTCGTCAGTTGTGCAT CCGTTGCTGCAGCTCGTTCCTCACCTGCATGAGAGAAGAATGAAGAGATTCAGAGTGGACGAAGAATTCCAAAGTCCCTT TGCAAGTCAAAGTCGAGGATATTTTTTATTCAGGCCACGGAATGGAAGAAGGTCAGCAGGGTTCATTTAAAATGGATGCC AGCTAATTTTCCACAGAGCAATGCTATGGAATACAAAATGTACTGACATTTTGTTTTCTTCTGAAAAAAATCCTTGCTAA ATGTACTCTGTTGAAAATCCCTGTGTTGTCAATGTTCTCAGTTGTAACAATGTTGTAAATGTTCAATTTGTTGAAAATTA AAAAATCTAAAAATAAA	SEQ.ID NO.58 MLRTESCRPRSPAGQVAAASPLLLLLLLLAW CAGACRGAPILPQGLQPEQQLQLWNEIDDTC SSFLSIDSQPQASNALEELCFMIMGMLPKPQ EQDEKDNTKRFLFHYSKTQKLGKSNVVSSVV HPLLQLVPHLHERRMKRFRVDEEFQSPFASQ SRGYFLFRPRNGRRSAGFI
SEQ.ID NO.9 GGGCGCAGCGGGGCCCGTCTGCAGCAAGTGACCGACGGCCGGGACGGCCGCCTGCCCCCTCTGCCACCTGGGGCGGTGCG GGCCCGGAGCCCGGAGCCCGGGTAGCGCGTAGAGCCGGCGCGATGCACGTGCGCTCACTGCGAGCTGCGGCGCCGCACAG CTTCGTGGCGCTCTGGGCACCCCTGTTCCTGCTGCGCTCCGCCCTGGCCGACTTCAGCCTGGACAACGAGGTGCACTCGA GCTTCATCCACCGGCGCCTCCGCAGCCAGGAGCGGCGGGAGATGCAGCGCGAGATCCTCTCCATTTTGGGCTTGCCCCAC CGCCCGCGCCCGCACCTCCAGGGCAAGCACAACTCGGCACCCATGTTCATGCTGGACCTGTACAACGCCATGGCGGTGGA GGAGGGCGGCGGGCCCGGCGGCCAGGGCTTCTCCTACCCCTACAAGGCCGTCTTCAGTACCCAGGGCCCCCCTCTGGCCA GCCTGCAAGATAGCCATTTCCTCACCGACGCCGACATGGTCATGAGCTTCGTCAACCTCGTGGAACATGACAAGGAATTC TTCCACCCACGCTACCACCATCGAGAGTTCCGGTTTGATCTTTCCAAGATCCCAGAAGGGGAAGCTGTCACGGCAGCCGA ATTCCGGATCTACAAGGACTACATCCGGGAACGCTTCGACAATGAGACGTTCCGGATCAGCGTTTATCAGGTGCTCCAGG AGCACTTGGGCAGGGAATCGGATCTCTTCCTGCTCGACAGCCGTACCCTCTGGGCCTCGGAGGAGGGCTGGCTGGTGTTT GACATCACAGCCACCAGCAACCACTGGGTGGTCAATCCGCGGCACAACCTGGGCCTGCAGCTCTCGGTGGAGACGCTGGA TGGGCAGAGCATCAACCCCAAGTTGGCGGGCCTGATTGGGCGGCACGGGCCCCAGAACAAGCAGCCCTTCATGGTGGCTT	SEQ.ID NO.59 MHVRSLRAAAPHSFVALWAPLFLLRSALADF SLDNEVHSSFIHRRLRSQERREMQREILSIL GLPHRPRPHLQGKHNSAPMFMLDLYNAMAVE EGGGPGGQGFSYPYKAVFSTQGPPLASLQDS HFLTDADMVMSFVNLVEHDKEFFHPRYHHRE FRFDLSKIPEGEAVTAAEFRIYKDYIRERFD NETFRISVYQVLQEHLGRESDLFLLDSRTLW ASEEGWLVFDITATSNHWVVNPRHNLGLQLS VETLDGQSINPKLAGLIGRHGPQNKQPFMVA FFKATEVHFRSIRSTGSKQRSQNRSKTPKNQ EALRMANVAENSSSDQRQACKKHELYVSFRD LGWQDWIIAPEGYAAYYCEGECAFPLNSYMN

TCTTCAAGGCCACGGAGGTCCACTTCCGCAGCATCCGGTCCACGGGGAGCAAACAGCGCAGCCAGAACCGCTCCAAGACG CCCAAGAACCAGGAAGCCCTGCGGATGGCCAACGTGGCAGAGAACAGCAGCAGCGACCAGAGGCAGGCCTGTAAGAAGCA CGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTGAAGGCTACGCCGCCTACTACTGTG AGGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCACGCCATCGTGCAGACGCTGGTCCACTTCATC AACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACGCAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTC CAACGTCATCCTGAAGAAATACAGAAACATGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCTCCGAGAATTCAGACCCT TTGGGGCCAAGTTTTTCTGGATCCTCCATTGCTCGCCTTGGCCAGGAACCAGCAGACCAACTGCCTTTTGTGAGACCTTC CCCTCCCTATCCCCAACTTTAAAGGTGTGAGAGTATTAGGAAACATGAGCAGCATATGGCTTTTGATCAGTTTTTCAGTG GCAGCATCCAATGAACAAGATCCTACAAGCTGTGCAGGCAAAACCTAGCAGGAAAAAAAAACAACGCATAAAGAAAAATG GCCGGGCCAGGTCATTGGCTGGGAAGTCTCAGCCATGCACGGACTCGTTTCCAGAGGTAATTATGAGCGCCTACCAGCCA GGCCACCCAGCCGTGGGAGGAAGGGGGCGTGGCAAGGGGTGGGCACATTGGTGTCTGTGCGAAAGGAAAATTGACCCGGA AGTTCCTGTAATAAATGTCACAATAAAACGAATGAATG	ATNHAIVQTLVHFINPETVPKPCCAPTQLNA ISVLYFDDSSNVILKKY RNMVVRACGCH
SEQ.ID NO.10 CCGGTGAGTCGCCGGCGCTGCAGAGGGAGGCGGCACTGGTCTCGACGTGGGGCGGCCAGCGATGAAGCCGCCCAGTTCAA TACAAACAAGTGAGTTTGACTCATCAGATGAAGAGCCTATTGAAGATGAACAGACTCCAATTCATATATCATGGCTATCT TTGTCACGAGTGAATTGTTCTCAGTTTCTCGGTTTATGTGCTCTTCCAGGTTGTAAATTTAAAGATGTTAGAAGAAATGT CCAAAAAGATACAGAAGAACTAAAGAGCTGTGGTATACAAGACATATTTGTTTTCTGCACCAGAGGGGAACTGTCAAAAT ATAGAGTCCCAAACCTTCTGGATCTCTACCAGCAATGTGGAATTATCACCCATCATCATCCAATCGCAGATGGAGGGACT CCTGACATAGCCAGCTGCTGTGAAATAATGGAAGAGCTTACAACCTGCCTTAAAAATTACCGAAAAACCTTAATACACTG CTATGGAGGACTTGGGAGATCTTGTCTTGTAGCTGCTTGTCTCCTACTATACCTGTCTGACACAATATCACCAGAGCAAG CCATAGACAGCCTGCGAGACCTAAGAGGATCCGGGGCAATACAGACCATCAAGCAATACAATTATCTTCATGAGTTTCGG GACAAATTAGCTGCACATCTATCATCAAGAGATTCACAATCAAGATCTGTATCAAGATAAAGGAATTCAAATAGCATATA TATGACCATGTCTGAAATGTCAGTTCTCTAGCATAATTTGTATTGAAATGAAACCACCAGTGTTATCAACTTGAATGTAA ATGTACATGTGCAGATATTCCTAAAGTTTTATTGAC	SEQ.ID NO.60 MKPPSSIQTSEFDSSDEEPIEDEQTPIHISW LSLSRVNCSQFLGLCALPGCKFKDVRRNVQK DTEELKSCGIQDIFVFCTRGELSKYRVPNLL DLYQQCGIITHHHPIADGGTPDIASCCEIME ELTTCLKNYRKTLIHCYGGLGRSCLVAACLL LYLSDTISPEQAIDSLRDLRGSGAIQTIKQY NYLHEFRDKLAAHLSSRDSQSRSVSR
SEQ.ID NO.11 AGAGCGATCATGTCGCACAAACAAATTTACTATTCGGACAAATACGACGACGAGGAGTTTGAGTATCGACATGTCATGCT GCCCAAGGACATAGCCAAGCTGGTCCCTAAAACCCATCTGATGTCTGAATCTGAATGGAGGAATCTTGGCGTTCAGCAGA GTCAGGGATGGGTCCATTATATGATCCATGAACCAGAACCTCACATCTTGCTGTTCCGGCGCCCACTACCCAAGAAACCA AAGAAATGAAGCTGGCAAGCTACTTTTCAGCCTCAAGCTTTACACAGCTGTCCTTACTTCCTAACATCTTTCTGATAACA TTATTATGTTGCCTTCTTGTTTCTCACTTTGATATTTAAAAGATGTTCAATACACTGTTTGAATGTGCTGGTAACTGCTT TGCTTCTTGAGTAGAGCCACCACCACCATAGCCCAGCCAGATGAGTGCTCTGTGGACCCACAGCCTAAGCTGAGTGTGAC	SEQ.ID NO.61 MSHKQIYYSDKYDDEEFEYRHVMLPKDIAKL VPKTHLMSESEWRNLGVQQSQGWVHYMIHEP EPHILLFRRPLPKKPKK

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CCCAGAAGCCACGATGTGCTCTGTATCCAGAACACACTTGGCAGATGGAGGAAGCATCTGAGTTTGAGACCATGGCTGTT ACAGGGATCATGTAAACTTGCTGTTTTTGTTTTTTCTGCCGGGTGTTGTATGTGTGGTGACTTGCGGATTTATGTTTCAG TGTACTGGAAACTTTCCATTTTATTCAAGAAATCTGTTCATGTTAAAAGCCTTGATTAAAGAGGAAGTTTTTATAAT	
SEQ.ID NO.12 CGAGTTCCGGCGAGGCTTCAGGGTACAGCTCCCCCGCAGCCAGAAGCCGGGCCTGCAGCGCCTCAGCACCGCTCCGGGAC ACCCCACCCGCTTCCCAGGCGTGACCTGTCAACAGCAACTTCGCGGTGTGGTGAACTCTCTGAGGAAAAACCATTTTGAT TATTACTCTCAGACGTGCGTGGCAACAAGTGACTGAGACCTAGAAATCCAAGCGTTGGAGGTCCTGAGGCCAGCCTAAGT CGCTTCAAAATGGAACGAAGGCGTTTGTGGGGTTCCATTCAGAGCCGATACATCAGCATGAGTGTGTGGACAAGCCCACG GAGACTTGTGGAGCTGGCAGGGCAGAGCCTGCTGAAGGATGAGGCCCTGGCCATTGCCGCCCTGGAGTTGCTGCCCAGGG AGCTCTTCCCGCCACTCTTCATGGCAGCCTTTGACGGGAGACACAGCCAGACCCTGAAGGCAATGGTGCAGGCCTGGCCC TTCACCTGCCTCCCTCTGGGAGTGCTGATGAAGGGACAACATCTTCACCTGGAGACCTTCAAAGCTGTGCTTGATGGACT TGATGTGCTCCTTGCCCAGGAGGTTCGCCCCAGGAGGTGGAAACTTCAAGTGCTGGATTTACGGAAGAACTCTCATCAGG ACTTCTGGACTGTATGGTCTGGAAACAGGGCCAGTCTGTACTCATTTCCAGAGCCAGAAGCAGCTCAGCCCATGACAAAG AAGCGAAAAGTAGATGGTTTGAGCACAGAGGCAGAGCAGCCCTTCATTCCAGTAGAGGTGCTCGTAGACCTGTTCCTCAA GGAAGGTGCCTGTGATGAATTGTTCTCCTACCTCATTGAGAAAGTGAAGCGAAAGAAAAATGTACTACGCCTGTGCTGTA AGAAGCTGAAGATTTTTGCAATGCCCATGCAGGATATCAAGATGATCCTGAAAATGGTGCAGCTGGACTCTATTGAAGAT TTGGAAGTGACTTGTACCTGGAAGCTACCCACCTTGGCGAAATTTTCTCCTTACCTGGGCCAGATGATTAATCTGCGTAG ACTCCTCCTCTCCCACATCCATGCATCTTCCTACATTTCCCCGGAGAAGGAAGAGCAGTATATCGCCCAGTTCACCTCTC AGTTCCTCAGTCTGCAGTGCCTGCAGGCTCTCTATGTGGACTCTTTATTTTTCCTTAGAGGCCGCCTGGATCAGTTGCTC AGGCACGTGATGAACCCCTTGGAAACCCTCTCAATAACTAACTGCCGGCTTTCGGAAGGGGATGTGATGCATCTGTCCCA GAGTCCCAGCGTCAGTCAGCTAAGTGTCCTGAGTCTAAGTGGGGTCATGCTGACCGATGTAAGTCCCGAGCCCCTCCAAG CTCTGCTGGAGAGAGCCTCTGCCACCCTCCAGGACCTGGTCTTTGATGAGTGTGGGATCACGGATGATCAGCTCCTTGCC CTCCTGCCTTCCCTGAGCCACTGCTCCCAGCTTACAACCTTAAGCTTCTACGGGAATTCCATCTCCATATCTGCCTTGCA GAGTCTCCTGCAGCACCTCATCGGGCTGAGCAATCTGACCCACGTGCTGTATCCTGTCCCCCTGGAGAGTTATGAGGACA TCCATGGTACCCTCCACCTGGAGAGGCTTGCCTATCTGCATGCCAGGCTCAGGGAGTTGCTGTGTGAGTTGGGGCGGCCC AGCATGGTCTGGCTTAGTGCCAACCCCTGTCCTCACTGTGGGGACAGAACCTTCTATGACCCGGAGCCCATCCTGTGCCC CTGTTTCATGCCTAACTAGCTGGGTGCACATATCAAATGCTTCATTCTGCATACTTGGACACTAAAGCCAGGATGTGCAT GCATCTTGAAGCAACAAAGCAGCCACAGTTTCAGACAAATGTTCAGTGTGAGTGAGGAAAACATGTTCAGTGAGGAAAAA ACATTCAGACAAATGTTCAGTGAGGAAAAAAAGGGGAAGTTGGGGATAGGCAGATGTTGACTTGAGGAGTTAATGTGATC TTTGGGGAGATACATCTTATAGAGTTAGAAATAGAATCTGAATTTCTAAAGGGAGATTCTGGCTTGGGAAGTACATGTAG GAGTTAATCCCTGTGTAGACTGTTGTAAAGAAACTGTTGAAAATAAAGAGAAGCAATGTGAAGCAAAAAAAAAAAAAAAA AA	SEQ.ID NO.62 MERRRLWGSIQSRYISMSVWTSPRRLVELAG QSLLKDEALAIAALELLPRELFPPLFMAAFD GRHSQTLKAMVQAWPFTCLPLGVLMKGQHLH LETFKAVLDGLDVLLAQEVRPRRWKLQVLDL RKNSHQDFWTVWSGNRASLYSFPEPEAAQPM TKKRKVDGLSTEAEQPFIPVEVLVDLFLKEG ACDELFSYLIEKVKRKKNVLRLCCKKLKIFA MPMQDIKMILKMVQLDSIEDLEVTCTWKLPT LAKFSPYLGQMINLRRLLLSHIHASSYISPE KEEQYIAQFTSQFLSLQCLQALYVDSLFFLR GRLDQLLRHVMNPLETLSITNCRLSEGDVMH LSQSPSVSQLSVLSLSGVMLTDVSPEPLQAL LERASATLQDLVFDECGITDDQLLALLPSLS HCSQLTTLSFYGNSISISALQSLLQHLIGLS NLTHVLYPVPLESYEDIHGTLHLERLAYLHA RLRELLCELGRPSMVWLSANPCPHCGDRTFY DPEPILCPCFMPN
SEQ.ID NO.13	SEQ.ID NO.63

CGGCTGAGAGGCAGCGAACTCATCTTTGCCAGTACAGGAGCTTGTGCCGTGGCCCACAGCCCACAGCCCACAGCCATGGG CTGGGACCTGACGGTGAAGATGCTGGCGGGCAACGAATTCCAGGTGTCCCTGAGCAGCTCCATGTCGGTGTCAGAGCTGA AGGCGCAGATCACCCAGAAGATTGGCGTGCACGCCTTCCAGCAGCGTCTGGCTGTCCACCCGAGCGGTGTGGCGCTGCAG GACAGGGTCCCCCTTGCCAGCCAGGGCCTGGGCCCTGGCAGCACGGTCCTGCTGGTGGTGGACAAATGCGACGAACCTCT GAGCATCCTGGTGAGGAATAACAAGGGCCGCAGCAGCACCTACGAGGTCCGGCTGACGCAGACCGTGGCCCACCTGAAGC AGCAAGTGAGCGGGCTGGAGGGTGTGCAGGACGACCTGTTCTGGCTGACCTTCGAGGGGAAGCCCCTGGAGGACCAGCTC CCGCTGGGGGAGTACGGCCTCAAGCCCCTGAGCACCGTGTTCATGAATCTGCGCCTGCGGGGAGGCGGCACAGAGCCTGG CGGGCGGAGCTAAGGGCCTCCACCAGCATCCGAGCAGGATCAAGGGCCGGAAATAAAGGCTGTTGTAAGAGAAT	MGWDLTVKMLAGNEFQVSLSSSMSVSELKAQ ITQKIGVHAFQQRLAVHPSGVALQDRVPLAS QGLGPGSTVLLVVDKCDEPLSILVRNNKGRS STYEVRLTQTVAHLKQQVSGLEGVQDDLFWL TFEGKPLEDQLPLGEYGLKPLSTVFMNLRLR GGGTEPGGRS
SEQ.ID NO.14 **STAR clone:** TGCCCACTTGGCCCCTCCTTCCAAGGTGTACTTTACTTCCTTTCATTCCTGCTCTAATACTGTTTAGTACATTTTCACTC CTGCTCTAAAACTTGCCTCAGTCTCTCACTGTGCCTTATGCCCCTCAGCTGAATTCTTTCTTCTGAGCAGGCAGGAATTG AGGTTGCTGCAGACGTGTATGCATTTGCCACCAGTAACATACTTTGGTGCCACATGACTAGGATATGTTCTCTAGTGCTA ACATGTTCGTTTACAGTTCTTAGGACTCCCTGATA	
SEQ.ID NO.15 GGCCGCCTGCGCGCCGCCAACAGCCTAGCGCTGCGCCGCGTGGCCGCCGCCTTCTCGCTGGCCCCGCTGGCCGAGCGCTG CGGCCGCGTCCTGCGTCAGGCCTTCGCCGAGGTGGCGCGCCACGCCGACTTCCTGGAGCTGGCGCCTGACGAGGTGGTGG CGCTGCTGGCGGACCCCGCGCTGGGCGTGGCGCGCGAGGAGGCCGTGTTTGAAGCGGCCATGCGCTGGGTGCGCCACGAC GCGCCGGCCCGCCGCGGCCAGCTGCGACGCCTGCTGGAGCACGTGCGCCTGCCGCTACTGGCGCCCGCTTACTTCCTGGA GAAGGTGGAGGCGGACGAGCTGCTGCAGGCCTGCGGCGAGTGCCGCCCGCTGCTGCTCGAGGCTCGCGCCTGCTTCATCC TGGGCCGCGAGGCCGGTGCGCTGCGGACCCGGCCGCGGAGATTCATGGACCTAGCTGAAGTGATCGTGGTCATCGGCGGT TGCGACCGCAAAGGTCTCCTGAAGCTGCCCTTCGCCGATGCCTACCATCCAGAGAGCCAGCGGTGGACCCCACTGCCCAG CCTGCCCGGCTACACTCGCTCAGAATTCGCCGCCTGTGCTCTCCGCAATGACGTCTACGTCTCCGGAGGCCACATCAACA GTCATGATGTGTGGATGTTTAGCTCCCATCTGCACACCTGGATCAAGGTAGCCTCTCTGCACAAGGGCAGGTGGAGGCAC AAGATGGCAGTTGTGCAGGGGCAGCTGTTCGCGGTGGGTGGCTTCGACGGCCTGAGGCGCCTGCACAGCGTGGAGCGCTA CGACCCCTTCTCCAACACCTGGGCGGCCGCCGCGCCCCTCCCGGAGGCCGTGAGCTCGGCGGCGGTGGCGTCCTGCGCGG GCAAGCTCTTCGTGATTGGGGGCGCCAGGCAGGGCGGCGTCAACACGGACAAGGTGCAGTGCTTTGACCCCAAGGAGGAC CGGTGGAGCCTGCGGTCACCAGCACCCTTCTCACAGCGGTGTCTCGAGGCTGTCTCCCTTGAGGACACCATCTATGTCAT GGGGGGTCTCATGAGCAAAATCTTCACCTATGATCCAGGCACAGATGTGTGGGGGGAGGCAGCTGTCCTCCCCAGCCCTG TGGAAAGCTGTGGAGTCACTGTGTGTGACGGGAAGGTCCACATCCTTGGCGGGCGGGATGATCGCGGAGAAAGCACCGAT AAGGTCTTCACCTTTGACCCCAGCAGTGGGCAGGTGGAGGTCCAGCCATCCCTGCAGCGCTGCACCAGCTCCCACGGCTG TGTCACCATCATCCAGAGCTTGGGCAGGTGATTCAGATTTGGACAGCCTGAGCCAGGAGGCGGAGAGGCAGGCGGAGCTC AGATGCACACTCTGCTCCCTCATGGCACCTCCACGCAAACAGCCCTTAACTTAATGGTCCCTTTTCTTGTATAAATAAAA	SEQ.ID NO.64 MRWVRHDAPARRGQLRRLLEHVRLPLLAPAY FLEKVEADELLQACGECRPLLLEARACFILG REAGALRTRPRRFMDLAEVIVVIGGCDRKGL LKLPFADAYHPESQRWTPLPSLPGYTRSEFA ACALRNDVYVSGGHINSHDVWMFSSHLHTWI KVASLHKGRWRHKMAVVQGQLFAVGGFDGLR RLHSVERYDPFSNTWAAAAPLPEAVSSAAVA SCAGKLFVIGGARQGGVNTDKVQCFDPKEDR WSLRSPAPFSQRCLEAVSLEDTIYVMGGLMS KIFTYDPGTDVWGEAAVLPSPVESCGVTVCD GKVHILGGRDDRGESTDKVFTFDPSSGQVEV QPSLQRCTSSHGCVTIIQSLGR

TCTTGTTGGGTCTGTGTTCCAGCTGCAGTC TGCCCTGCCTGGAGATGGAATGTCTAAAAAAAAAAAAAAA	
SEQ.ID NO.16 **STAR clone:** TTTCTAGCAGCCTGGGCAATGGCGGGCGCCCCTCCCCCAGCCTCGCTGCTGCCTTGCAGTTTGATCTCAGACTGCTGTGC TAGCAATCAGCAAGACTCCGTGGGCGTAGGACCCTCCGAGCCAGGTTGCAAGAAAGCTCAAGTAGCCTATGGAGAGGATG CAAGGCTTCCAGCTGATGCCCTCAGCCAGGCTCAGTAGCAGCCAGAACTAGCCTACCAACGAACCTGCTGATCATGTGCA TAAGCCACCTTGAACGTCGATCCTCCTGCCTGGTGGAGCCATCCCAGCTGATGCCACATGAAGCAGACACAAGCTGTCCC TACTAAGCTCTGCTCAAGTTGGATATTCATGAGTGAAATAAATGACTGTTACTAA	
SEQ.ID NO.17 GAGTCACCAAGGAAGGCAGCGGCAGCTCCACTCAGCCAGTACCCAGATACGCTGGGAACCTTCCCCAGCCATGGCTTCCC TGGGGCAGATCCTCTTCTGGAGCATAATTAGCATCATCATTATTCTGGCTGGAGCAATTGCACTCATCATTGGCTTTGGT ATTTCAGGGAGACACTCCATCACAGTCACTACTGTCGCCTCAGCTGGGAACATTGGGGAGGATGGAATCCAGAGCTGCAC TTTTGAACCTGACATCAAACTTTCTGATATCGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTGGTCCATGAGTTCA AAGAAGGCAAAGATGAGCTGTCGGAGCAGGATGAAATGTTCAGAGGCCGGACAGCAGTGTTTGCTGATCAAGTGATAGTT GGCAATGCCTCTTTGCGGCTGAAAAACGTGCAACTCACAGATGCTGGCACCTACAAATGTTATATCATCACTTCTAAAGG CAAGGGGAATGCTAACCTTGAGTATAAAACTGGAGCCTTCAGCATGCCGGAAGTGAATGTGGACTATAATGCCAGCTCAG AGACCTTGCGGTGTGAGGCTCCCCGATGGTTCCCCCAGCCCACAGTGGTCTGGGCATCCCAAGTTGACCAGGGAGCCAAC TTCTCGGAAGTCTCCAATACCAGCTTTGAGCTGAACTCTGAGAATGTGACCATGAAGGTTGTGTCTGTGCTCTACAATGT TACGATCAACAACACATACTCCTGTATGATTGAAAATGACATTGCCAAAGCAACAGGGGATATCAAAGTGACAGAATCGG AGATCAAAAGGCGGAGTCACCTACAGCTGCTAAACTCAAAGGCTTCTCTGTGTGTCTCTTCTTTCTTTGCCATCAGCTGG GCACTTCTGCCTCTCAGCCCTTACCTGATGCTAAAATAATGTGCCTCGGCCACAAAAAAGCATGCAAAGTCATTGTTACA ACAGGGATCTACAGAACTATTTCACCACCAGATATGACCTAGTTTTATATTTCTGGGAGGAAATGAATTCATATCTAGAA GTCTGGAGTGAGCAAACAAGAGCAAGAAACAAAAAGAAGCCAAAAGCAGAAGGCTCCAATATGAACAAGATAAATCTATC TTCAAAGACATATTAGAAGTTGGGAAAATAATTCATGTGAACTAGAGTCAACTGTGTCAGGGCTAAGAAACCCTGGTTTT GAGTAGAAAAGGGCCTGGAAAGAGGGGAGCCAACAAATCTGTCTGCTTCCTCACATTAGTCATTGGCAAATAAGCATTCT GTCTCTTTGGCTGCTGCCTCAGCACAGAGAGCCAGAACTCTATCGGGCACCAGGATAACATCTCTCAGTGAACAGAGTTG ACAAGGCCTATGGGAAATGCCTGATGGGATTATCTTCAGCTTGTTGAGCTTCTAAGTTTCTTTCCCTTCATTCTACCCTG CAAGCCAAGTTCTGTAAGAGAAATGCCTGAGTTCTAGCTCAGGTTTTCTTACTCTGAATTTAGATCTCCAGACCCTGCCT GGCCACAATTCAAATTAAGGCAACAAACATATACCTTCCATGAAGCACACACAGACTTTTGAAAGCAAGGACAATGACTG CTTGAATTGAGGCCTTGAGGAATGAAGCTTTGAAGGAAAAGAATACTTTGTTTCCAGCCCCCTTCCCACACTCTTCATGT GTTAACCACTGCCTTCCTGGACCTTGGAGCCACGGTGACTGTATTACATGTTGTTATAGAAAACTGATTTTAGAGTTCTG ATCGTTCAAGAGAATGATTAAATATACATTTCCTAAAAAAAAAAAAAAAAA	SEQ.ID NO.65 MASLGQILFWSIISIIIILAGAIALIIGFGI SGRHSITVTTVASAGNIGEDGIQSCTFEPDI KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQ DEMFRGRTAVFADQVIVGNASLRLKNVQLTD AGTYKCYIITSKGKGNANLEYKTGAFSMPEV NVDYNASSETLRCEAPRWFPQPTVVWASQVD QGANFSEVSNTSFELNSENVTMKVVSVLYNV TINNTYSCMIENDIAKATGDIKVTESEIKRR SHLQLLNSKASLCVSSFFAISWALLPLSPYL MLK

SEQ.ID NO.18	SEQ.ID NO.66
TCTTCGGACCTAGGCTGCCCTGCCGTCATGTCGCAAGGGATCCTTTCTCCGCCAGCGGGCTTGCTGTCCGATGACGATGT CGTAGTTTCTCCCATGTTTGAGTCCACAGCTGCAGATTTGGGGTCTGTGGTACGCAAGAACCTGCTATCAGACTGCTCTG TCGTCTCTACCTCCCTAGAGGACAAGCAGCAGGTTCCATCTGAGGACAGTATGGAGAAGGTGAAAGTATACTTGAGGGTT AGGCCCTTGTTACCTTCAGAGTTGGAACGACAGGAAGATCAGGGTTGTGTCCGTATTGAGAATGTGGAGACCCTTGTTCT ACAAGCACCCAAGGACTCGTTTGCCCTGAAGAGCAATGAACGGGGAATTGGCCAAGCCACACACAGGTTCACCTTTTCCC AGATCTTTGGGCCAGAAGTGGGACAGGCATCCTTCTTCAACCTAACTGTGAAGGAGATGGTAAAGGATGTACTCAAAGGG CAGAACTGGCTCATCTATACATATGGAGTCACTAACTCAGGGAAAACCCACACGATTCAAGGTACCATCAAGGATGGAGG GATTCTCCCCCGGTCCCTGGCGCTGATCTTCAATAGCCTCCAAGGCCAACTTCATCCAACACCTGATCTGAAGCCCTTGC TCTCCAATGAGGTAATCTGGCTAGACAGCAAGCAGATCCGACAGGAGGAAATGAAGAAGCTGTCCCTGCTAAATGGAGGC CTCCAAGAGGAGGAGCTGTCCACTTCCTTGAAGAGGAGTGTCTACATCGAAAGTCGGATAGGTACCAGCACCAGCTTCGA CAGTGGCATTGCTGGGCTCTCTTCTATCAGTCAGTGTACCAGCAGTAGCCAGCTGGATGAAACAAGTCATCGATGGGCAC AGCCAGACACTGCCCCACTACCTGTCCCGGCAAACATTCGCTTCTCCATCTGGATCTCATTCTTTGAGATCTACAACGAA CTGCTTTATGACCTATTAGAACCGCCTAGCCAACAGCGCAAGAGGCAGACTTTGCGGCTATGCGAGGATCAAAATGGCAA TCCCTATGTGAAAGATCTCAACTGGATTCATGTGCAAGATGCTGAGGAGGCCTGGAAGCTCCTAAAAGTGGGTCGTAAGA ACCAGAGCTTTGCCAGCACCCACCTCAACCAGAACTCCAGCCGCAGTCACAGCATCTTCTCAATCAGGATCCTACACCTT CAGGGGGAAGGAGATATAGTCCCCAAGATCAGCGAGCTGTCACTCTGTGATCTGGCTGGCTCAGAGCGCTGCAAAGATCA GAAGAGTGGTGAACGGTTGAAGGAAGCAGGAAACATTAACACCTCTCTACACACCCTGGGCCGCTGTATTGCTGCCCTTC GTCAAAACCAGCAGAACCGGTCAAAGCAGAACCTGGTTCCCTTCCGTGACAGCAAGTTGACTCGAGTGTTCCAAGGTTTC TTCACAGGCCGAGGCCGTTCCTGCATGATTGTCAATGTGAATCCCTGTGCATCTACCTATGATGAAACTCTTCATGTGGC CAAGTTCTCAGCCATTGCTAGCCAGCTTGTGCATGCCCCACCTATGCAACTGGGATTCCCATCCCTGCACTCGTTCATCA AGGAACATAGTCTTCAGGTATCCCCCAGCTTAGAGAAAGGGGCTAAGGCAGACACAGGCCTTGATGATGATATTGAAAAT GAAGCTGACATCTCCATGTATGGCAAAGAGGAGCTCCTACAAGTTGTGGAAGCCATGAAGACACTGCTTTTGAAGGAACG ACAGGAAAAGCTACAGCTGGAGATGCATCTCCGAGATGAAATTTGCAATGAGATGGTAGAACAGATGCAACAGCGGGAAC AGTGGTGCAGTGAACATTTGGACACCCAAAAGGAACTATTGGAGGAAATGTATGAAGAAAAACTAAATATCCTCAAGGAG TCACTGACAAGTTTTTACCAAGAAGAGATTCAGGAGCGGGATGAAAAGATTGAAGAGCTAGAAGCTCTCTTGCAGGAAGC CAGACAACAGTCAGTGGCCCATCAGCAATCAGGGTCTGAATTGGCCCTACGGCGGTCACAAAGGTTGGCAGCTTCTGCCT CCACCCAGCAGCTTCAGGAGGTTAAAGCTAAATTACAGCAGTGCAAAGCAGAGCTAAACTCTACCACTGAAGAGTTGCAT AAGTATCAGAAAATGTTAGAACCACCACCCTCAGCCAAGCCCTTCACCATTGATGTGGACAAGAAGTTAGAAGAGGGCCA GAAGAATATAAGGCTGTTGCGGACAGAGCTTCAGAAACTTGGTGAGTCTCTCCAATCAGCAGAGAGAGCTTGTTGCCACA GCACTGGGGCAGGAAAACTTCGTCAAGCCTTGACCACTTGTGATGACATCTTAATCAAACAGGACCAGACTCTGGCTGAA CTGCAGAACAACATGGTGCTAGTGAAACTGGACCTTCGGAAGAAGGCAGCATGTATTGCTGAGCAGTATCATACTGTGTT GAAACTCCAAGGCCAGGTTTCTGCCAAAAAGCGCCTTGGTACCAACCAGGAAAATCAGCAACCAAACCAACAACCACCAG GGAAGAAACCATTCCTTCGAAATTTACTTCCCCGAACACCAACCTGCCAAAGCTCAACAGACTGCAGCCCTTATGCCCGG ATCCTACGCTCACGGCGTTCCCCTTTACTCAAATCTGGGCCTTTTGGCAAAAAGTACTAAGGCTGTGGGGAAAGAGAAGA GCAGTCATGGCCCTGAGGTGGGTCAGCTACTCTCCTGAAGAAATAGGTCTCTTTTATGCTTTACCATATATCAGGAATTA	MSQGILSPPAGLLSDDDVVVSPMFESTAADL GSVVRKNLLSDCSVVSTSLEDKQQVPSEDSM EKVKVYLRVRPLLPSELERQEDQGCVRIENV ETLVLQAPKDSFALKSNERGIGQATHRFTFS QIFGPEVGQASFFNLTVKEMVKDVLKGQNWL IYTYGVTNSGKTHTIQGTIKDGGILPRSLAL IFNSLQGQLHPTPDLKPLLSNEVIWLDSKQI RQEEMKKLSLLNGGLQEEELSTSLKRSVYIE SRIGTSTSFDSGIAGLSSISQCTSSSQLDET SHRWAQPDTAPLPVPANIRFSIWISFFEIYN ELLYDLLEPPSQQRKRQTLRLCEDQNGNPYV KDLNWIHVQDAEEAWKLLKVGRKNQSFASTH LNQNSSRSHSIFSIRILHLQGEGDIVPKISE LSLCDLAGSERCKDQKSGERLKEAGNINTSL HTLGRCIAALRQNQQNRSKQNLVPFRDSKLT RVFQGFFTGRGRSCMIVNVNPCASTYDETLH VAKFSAIASQLVHAPPMQLGFPSLHSFIKEH SLQVSPSLEKGAKADTGLDDDIENEADISMY GKEELLQVVEAMKTLLLKERQEKLQLEMHLR DEICNEMVEQMQQREQWCSEHLDTQKELLEE MYEEKLNILKESLTSFYQEEIQERDEKIEEL EALLQEARQQSVAHQQSGSELALRRSQRLAA SASTQQLQEVKAKLQQCKAELNSTTEELHKY QKMLEPPPSAKPFTIDVDKKLEEGQKNIRLL RTELQKLGESLQSAERACCHSTGAGKLRQAL TTCDDILIKQDQTLAELQNNMVLVKLDLRKK AACIAEQYHTVLKLQGQVSAKKRLGTNQENQ QPNQQPPGKKPFLRNLLPRTPTCQSSTDCSP YARILRSRRSPLLKSGPFGKKY

TATCCAGGATGCAATACTCAGACACTAGCTTTTTTCTCACTTTTGTATTATAACCACCTATGTAATCTCATGTTGTTGTT TTTTTTTATTTACTTATATGATTTCTATGCACACAAAAACAGTTATATTAAAGATATTAT TGTTCACATTTTTTATTGAAAAAAAAAAAAAA	
STAR clone (SEQ.ID NO.19): TCCTTGTTACGATGAAGAAACTAAATCTCAGGAAGAAAAAACTAAGTGAAGACNAAAGAAGGATTTGAACTGAGGTTTGT CAGACTCTCGGGACCATGCTGTTGAAACCACTAAACCACGCTGCCTCTGGGTCACTTGGTAAACAGCATTTAACCATTAA GAAAGTCATTAATAAAATTCCTTGTGCTCTCCTTGAGATTACAAGCCATTGATTTGCCAA **NM_005832:** GCTGGGCACCGTTCTGTTTTCTTTCTTTTCTTAATCCTATCCAAGTATGCAGTACGCTCTTGGGTCGTCTCATGAGACCC AGGGGCATGTTGGAAAGAACTGAGAGAAAGAGCAACAAAGCGGCGAGTGGTGTGAGAGGGCAGCACGCGCTGTGGGGCCC TTCCAGAGAAATGTACTGAAAAAGTCTACGCAATGTCTGGGATTTGCTAAACAATACCTGGAAAGCAGACAGGTCTTTTT GCCATTCCTCCAGGACATCCACCATAAGGAAAGGAGACCCTGGACCAACATTCTCTAAGATGTTTATATGGACCAGTGGC CGGACCTCTTCATCTTATAGACATGATGAAAAAAGAAATATTTACCAGAAAATCAGGGACCATGACCTCCTGGACAAAAG GAAAACAGTCACAGCACTGAAGGCAGGAGAGGACCGAGCTATTCTCCTGGGACTGGCTATGATGGTGTGCTCCATCATGA TGTATTTTCTGCTGGGAATCACACTCCTGCGCTCATACATGCAGAGCGTGTGGACCGAAGAGTCTCAATGCACCTTGCTG AATGCGTCCATCACGGAAACATTTAATTGCTCCTTCAGCTGTGGTCCAGACTGCTGGAAACTTTCTCAGTACCCCTGCCT CCAGGTGTACGTTAACCTGACTTCTTCCGGGGAAAAGCTCCTCCTCTACCACACAGAAGAGACAATAAAAATCAATCAGA AGTGCTCCTATATACCTAAATGTGGAAAAAATTTTGAAGAATCCATGTCCCTGGTGAATGTTGTCATGGAAAACTTCAGG AAGTATCAACACTTCTCCTGCTATTCTGACCCAGAAGGAAACCAGAAGAGTGTTATCCTAACAAAACTCTACAGTTCCAA CGTGCTGTTCCATTCACTCTTCTGGCCAACCTGTATGATGGCTGGGGGTGTGGCAATTGTTGCCATGGTGAAACTTACAC AGTACCTCTCCCTACTATGTGAGAGGATCCAACGGATCAATAGATAAATGCAAAAATGGATAAAATAATTTTTGTTAAAG CTCAAATACTGTTTTCTTTCATTCTTCACCAAAGAACCTTAAGTTTGTAACGTGCAGTCTGTTATGAGTTCCCTAATATA TTCTTATATGTAGAGCAATAATGCAAAAGCTGTTCTATATGCAAACATGATGTCTTTATTATTCAGGAGAATAAATAACT GTTTTGTGTTGGTTGGTGGTTTTCATAATCTTATTTCTGTACTGGAACTAGTACTTTCTTCTCTCATTCCGCCAAAACAG GGCTCAGTTATTCATTTGCCAAGCTTCGTGGAGGAATGTAGGTGACATCAATGTGATAAAGTCTGTGTTCTGAGTTGTCA GATCTCTTGAAGACAATATTTTTCATCACTTATTGTTTACTAAAGCTACAGCCAAAAATATTTTTTTTTCTTATTCTAAA CTGAGCCCTATAGCAAGTGAAGGGACCAGATTTCCTAATTAAAGGAAGTTAGGTACTTTTCTTGTATTTTTTACCATATC ACTGTAAAGAAGAGGGGAAACCCAGCCAGCTACTTTTTTTCATCACTTTTTATTCATAACTTCAGATTTGTAAAACTAAT TTCCAAAATATAAGCTGTTTTCATTAGCCAGTTCTATAATATCTTCCTGTGATTTATGTAGAAAATGAACACACCCCTTT TCCATTTAAGACCCTGCTACTGTGTGAAGAGATGATACTTACAAGGAGTGTCATTACCTGTGAGCTGACTGAATGTTGGT AGGTGCTCCATTACAATCCAGGAAAGTCTGTGTTACTGATATTTGTGTGGAAATCTTTATTTCACTTCAATTTAACCATT AGATGGTAAAATTAAGATGCTACTTGTTGGTAAAAATTGGTGGACTGGTTTCAATGGGTAAATGTGTTGTGGCAAATTAA TGTGTTGGAATATTGCTCTTTGTGAATTTGTGCTTAAGTCAATGAATGTGTAGTATCTCCTTCTGACAAGCATTCCCTAT	SEQ.ID NO.67 MFIWTSGRTSSSYRHDEKRNIYQKIRDHDLL DKRKTVTALKAGEDRAILLGLAMMVCSIMMY FLLGITLLRSYMQSVWTEESQCTLLNASITE TFNCSFSCGPDCWKLSQYPCLQVYVNLTSSG EKLLLYHTEETIKINQ KCSYIPKCGKNFEESMSLVNVVMENFRKYQH FSCYSDPEGNQKSVILTKLYSSNVLFHSLFW PTCMMAGGVAIVAMVKLTQYLSLLCERIQRI NR

TGGGATTTTAAAGCTATGTGCACAGAATATTAGTCTCTTCTACATGTTTTATTTTTCTATTTATAATTCCCTTTTTTGTT GTTATATTTTATACACAGAATAGATCTTTTTTCTAACACATATTTGAACTGAATAACAGACTTAAAGAAAGCCTTTGTTC ACATTGCTATTTACTTTTGTGTTTGGGGGAAAATACGAGGGATTGATTTTAAATAAAAAACATTCCATCTTTCATTTAAT ATCAATATCAAAAGAAGAAGACAAACATCTATCTTTCTCATCTATATTTAAGTACCTTTTTGTAATGTAGTATCAAAGTT TTTTAGGTAATGCAAAATTTTACAAATCATTTGTGGAATGAATGGTAAAACTAATCTGATGAAATGGAAAATTATTCTGC AATATTGTAATTCATAGTTTGACTTTTCATAAGCAAATAAATCCCTAGGA TGTAATCAGGACTTCAAATGTGTAATTAAATTTTTTTAAAAAAAATCTA	
SEQ.ID NO.20 **STAR clone:** GAACACAGCTAAGCAGATGGCTTGGGTCATCAGGACGTCCATTACATCCAAAGGAAGACAGCCTGTGACGTTTCAAAAGC AAAAGTCCCCTACCAGCCAGTGAAGCTACCTGATTTCTCAGTATCTTACGCCCAGTGACACGATCTACCCTCAAAACTTA	
SEQ.ID NO.21 GAGACATTCCTCAATTGCTTAGACATATTCTGAGCCTACAGCAGAGGAACCTCCAGTCTCAGCACCATGAATCAAACTGC GATTCTGATTTGCTGCCTTATCTTTCTGACTCTAAGTGGCATTCAAGGAGTACCTCTCTCTAGAACCGTACGCTGTACCT GCATCAGCATTAGTAATCAACCTGTTAATCCAAGGTCTTTAGAAAAACTTGAAATTATTCCTGCAAGCCAATTTTGTCCA CGTGTTGAGATCATTGCTACAATGAAAAAGAAGGGTGAGAAGAGATGTCTGAATCCAGAATCGAAGGCCATCAAGAATTT ACTGAAAGCAGTTAGCAAGGAAATGTCTAAAAGATCTCCTTAAAACCAGAGGGGAGCAAAATCGATGCAGTGCTTCCAAG GATGGACCACACAGAGGCTGCCTCTCCCATCACTTCCCTACATGGAGTATATGTCAAGCCATAATTGTTCTTAGTTTGCA GTTACACTAAAAGGTGACCAATGATGGTCACCAAATCAGCTGCTACTACTCCTGTAGGAAGGTTAATGTTCATCATCCTA AGCTATTCAGTAATAACTCTACCCTGGCACTATAATGTAAGCTCTACTGAGGTGCTATGTTCTTAGTGGATGTTCTGACC CTGCTTCAAATATTTCCCTCACCTTTCCCATCTTCCAAGGGTACTAAGGAATCTTTCTGCTTTGGGGTTTATCAGAATTC TCAGAATCTCAAATAACTAAAAGGTATGCAATCAAATCTGCTTTTTAAAGAATGCTCTTTACTTCATGGACTTCCACTGC CATCCTCCCAAGGGGCCCAAATTCTTTCAGTGGCTACCTACATACAATTCCAAACACATACAGGAAGGTAGAAATATCTG AAAATGTATGTGTAAGTATTCTTATTTAATGAAAGACTGTACAAAGTATAAGTCTTAGATGTATATATTTCCTATATTGT TTTCAGTGTACATGGAATAACATGTAATTAAGTACTATGTATCAATGAGTAACAGGAAAATTTTAAAAATACAGATAGAT ATATGCTCTGCATGTTACATAAGATAAATGTGCTGAATGGTTTTCAAATAAAAATGAGGTACTCTCCTGGAAATATTAAG AAAGACTATCTAAATGTTGAAAGATCAAAAGGTTAATAAAGTAATTATAACT	MNQTAILICCLIFLTLSGIQGVPLSRTVRCT CISISNQPVNPRSLEKLEIIPASQFCPRVEI IATMKKKGEKRCLNPESKAIKNLLKAVSKEM SKRSP
SEQ.ID NO.22 **STAR clone:** TTTGCAGGTTTGATCTCAGACTGCTGTGCTAGTAATCAGCGAGATTCCGTGGGCGTAGGAGCCTCCAAGCCAGGTCCTGA	

AGAAAATGAAGTTGATGTTTCAGTGAGACACCTGTATGCCAGAGAGTAAAAGGGATTATTGTGGATTCCTGAGAATTTTC TACATATGAAATCATGTCATCTATGAACAGAGATGGGACTGTCTCGTTGGAGGAAAACAAGCTCAGGGCTCCCACTGATT CCACATTATGTTGCAAGCTCCTACGAAGCTCCCACTCA	
SEQ.ID NO.23 TTTCTCCGCATGCGCGGGATCCCGGATGTGGATCAAGTTGGTGGGAAGCGTGCGGTGCCGCAGCAATGGCGGCGCTCACA ATTGCCACGGGTACTGGCAATTGGTTTTCGGCTTTGGCGCTCGGGGTGACTCTTCTCAAATGCCTTCTCATCCCCACATA CCATTCCACAGATTTTGAAGTACACCGAAACTGGCTTGCTATCACTCACAGTTTGCCAATATCACAGTGGTATTATGAGG CAACTTCAGAGTGGACGTTGGATTACCCCCCTTTCTTTGCATGGTTTGAGTATATCCTGTCACATGTTGCCAAATATTTT GATCAAGAAATGCTGAATGTCCATAATTTGAATTACTCCAGCTCAAGGACCTTACTTTTCCAGAGATTTTCCGTCATCTT TATGGATGTACTCTTTGTGTATGCTGTCCGTGAGTGCTGTAAATGCATTGATGGAAAAAAAGTGGGTAAAGAACTTACAG AAAAGCCAAAATTTATTCTGTCGGTATTACTTCTGTGGAACTTCGGGTTATTAATTGTGGACCATATTCATTTTCAGTAC AATGGCTTTTTATTTGGATTAATGCTACTCTCCATTGCACGATTATTTCAGAAAAGGCATATGGAAGGAGCATTTCTCTT TGCTGTTCTCCTACATTTCAAGCATATCTACCTCTATGTAGCACCAGCTTATGGTGTATATCTGCTGCGATCCTACTGTT TCACTGCAAATAAACCAGATGGGTCTATTCGATGGAAGAGTTTCAGCTTTGTTCGTGTTATTTCCCTGGGACTGGTTGTT TTCTTAGTTTCTGCTCTTTCATTGGGTCCTTTCCTGGCCTTGAATCAGCTGCCTCAAGTCTTTTCCCGACTCTTTCCTTT CAAGAGGGGCCTCTGTCATGCATATTGGGCTCCAAACTTCTGGGCTTTGTACAATGCTTTGGACAAAGTGCTGTCTGTCA TCGGTTTGAAATTGAAATTTCTTGATCCCAACAATATTCCCAAGGCCTCAATGACAAGTGGTTTGGTTCAGCAGTTCCAA CACACAGTCCTTCCCTCAGTGACTCCCTTGGCAACCCTCATCTGCACACTGATTGCCATATTGCCCTCTATTTTCTGTCT TTGGTTTAAACCCCAAGGGCCCAGAGGCTTTCTCCGATGTCTAACTCTTTGTGCCTTGAGCTCCTTTATGTTTGGGTGGC ATGTTCATGAAAAAGCCATACTTCTAGCAATTCTCCCAATGAGCCTTTTGTCTGTGGGAAAAGCAGGAGACGCTTCGATT TTTCTGATTCTGACCACAACAGGACATTATTCCCTCTTTCCTCTGCTCTTCACTGCACCAGAACTTCCCATTAAAATCTT ACTCATGTTACTATTCACCATATATAGTATTTCGTCACTGAAGACTTTATTCAGACGGAGTTTCACCCTTGTTGCCCAGG CTGGAGTGCAATGGCACGATCTCAGCTAACTGAAACCTCCGCCTCCCAGAAAAGAAAAACCTCTTTTTAATTGGATGGAA ACTTTCTACCTGCTTGGCCTGGGGCCTCTGGAAGTCTGCTGTGAATTTGTATTCCCTTTCACCTCCTGGAAGGTGAAGTA CCCCTTCATCCCTTTGTTACTAACCTCAGTGTATTGTGCAGTAGGCATCACATATGCTTGGTTCAAACTGTATGTTTCAG TATTGATTGACTCTGCTATTGGCAAGACAAAGAAACAATGAATAAAGGAACTGCTTAGATATG	SEQ.ID NO.69 MAALTIATGTGNWFSALALGVTLLKCLLIPT YHSTDFEVHRNWLAITHSLPISQWYYEATSE WTLDYPPFFAWFEYILSHVAKYFDQEMLNVH NLNYSSSRTLLFQRFSVIFMDVLFVYAVREC CKCIDGKKVGKELTEKPKFILSVLLLWNFGL LIVDHIHFQYNGFLFGLMLLSIARLFQKRHM EGAFLFAVLLHFKHIYLYVAPAYGVYLLRSY CFTANKPDGSIRWKSFSFVRVISLGLVVFLV SALSLGPFLALNQLPQVFSRLFPFKRGLCHA YWAPNFWALYNALDKVLSVIGLKLKFLDPNN IPKASMTSGLVQQFQHTVLPSVTPLATLICT LIAILPSIFCLWFKPQGPRGFLRCLTLCALS SFMFGWHVHEKAILLAILPMSLLSVGKAGDA SIFLILTTTGHYSLFPLLFTAPELPIKILLM LLFTIYSISSLKTLFRRSFTLVAQAGVQWHD LS
SEQ.ID NO.24 CATTATGCTAACAGCATAAACATGCAGGGGGTGGGAGCAGGGTCACAAAAGTGAGTGTTGTCAATTCTACTTGGAATGAA AGGTTGAAATAATTTAAACAGTACGGGAAATGCAGAGCAATTTTCTCCTCTGGTGACAATATAGTGTCCAACACTTGGAA GTGATTTTTAAGAATGTTTATTTAAATTAAAAGGATGGATTTCCAAGGAAAAAAAATAAGGAAAAGGAAAGAAAAAACTG AACAGAAAACGCAAAAGTATCAGTTTGGTCACTAACCTTTGCAAGGATACCTTTTTATTTTCTTTAAGATTCCTGTTGTT TATACACAGATTTTAAGTTTACTCCTACTGCTGACCCAAGTGAAATTCCTTCTCCAGTCACAGTGTCAACCTCTACCCCC CAACTGCAACGAGAGTTTTGAGGGGCATCAATCACACCGAGAAGTCACAGCCCCTCAACCACTGAGGTGTGGGGGGGTAG	SEQ.ID NO.70 MDDDAAPRVEGVPVAVHKHALHDGLRQVAGP GAAAAHLPRWPPPQLAASRREAPPLSQRPHR TQGAGSPPETNEKLTNPQVKEK

GGATCTGCATTTCTTCATATCAACCCCACACTATAGGGCACCTAAATGGGTGGGCGGTGGGGGAGACCGACTCACTTGAG TTTCTTGAAGGCTTCCTGGCCTCCAGCCACGTAATTGCCCCCGCTCTGGATCTGGTCTAGCTTCCGGATTCGGTGGCCAG TCCGCGGGGTGTAGATGTTCCTGACGGCCCCAAAGGGTGCCTGAACGCCGCCGGTCACCTCCTTCAGGAAGACTTCGAAG CTGGACACCTTCTTCTCATGGATGACGACGCGGCGCCCCGCGTAGAAGGGGTCCCCGTTGCGGTACACAAGCACGCTCTT CACGACGGGCTGAGACAGGTGGCTGGACCTGGCGCTGCTGCCGCTCATCTTCCCCGCTGGCCGCCGCCTCAGCTCGCTGC TTCGCGTCGGGAGGCACCTCCGCTGTCCCAGCGGCCTCACCGCACCCAGGGCGCGGGATCGCCTCCTGAAACGAACGAGA AACTGACGAATCCACAGGTGAAAGAGAAGTAACGGCCGTGCGCCTAGGCGTCCACCCAGAGGAGACACTAGGAGCTTGCA GGACTCGGAGTAGACGCTCAAGTTTTTCACCGTGGCGTGCACAGCCAATCAGGACCCGCAGTGCGCGCACCACACCAGGT TCACCTGCTACGGGCAGAATCAAGGTGGACAGCTTCTGAGCAGGAGCCGGAAACGCGCGGGGCCTTCAAACAGGCACGCC TAGTGAGGGCAGGAGAGAGGAGGACGCACACACACACACACACACACAAATATGGTGAAACCCAATTTCTTACATCATATCT GTGCTACCCTTTCCAAACAGCCTAATTTTTCTTTTCTCTCTTCTTGCACCTTTACCCCTCAATCTCCTGCTTCCTCCCAA ATTAAAGCAATTAAGTTCCTGG	
SEQ.ID NO.25 CTCCTCCGAGCACTCGCTCACGGCGTCCCCTTGCCTGGAAAGATACCGCGGTCCCTCCAGAGGATTTGAGGGACAGGGTC GGAGGGGGCTCTTCCGCCAGCACCGGAGGAAGAAAGAGGAGGGGCTGGCTGGTCACCAGAGGGTGGGGCGGACCGCGTGC GCTCGGCGGCTGCGGAGAGGGGGAGAGCAGGCAGCGGGCGGCGGGGAGCAGCATGGAGCCGGCGGCGGGGAGCAGCATGG AGCCTTCGGCTGACTGGCTGGCCACGGCCGCGGCCCGGGGTCGGGTAGAGGAGGTGCGGGCGCTGCTGGAGGCGGGGGCG CTGCCCAACGCACCGAATAGTTACGGTCGGAGGCCGATCCAGGTCATGATGATGGGCAGCGCCCGAGTGGCGGAGCTGCT GCTGCTCCACGGCGCGGAGCCCAACTGCGCCGACCCCGCCACTCTCACCCGACCCGTGCACGACGCTGCCCGGGAGGGCT TCCTGGACACGCTGGTGGTGCTGCACCGGGCCGGGGCGCGGCTGGACGTGCGCGATGCCTGGGGCCGTCTGCCCGTGGAC CTGGCTGAGGAGCTGGGCCATCGCGATGTCGCACGGTACCTGCGCGCGGCTGCGGGGGGCACCAGAGGCAGTAACCATGC CCGCATAGATGCCGCGGAAGGTCCCTCAGACATCCCCGATTGAAAGAACCAGAGAGGCTCTGAGAAACCTCGGGAAACTT AGATCATCAGTCACCGAAGGTCCTACAGGGCCACAACTGCCCCCGCCACAACCCACCCCGCTTTCGTAGTTTTCATTTAG AAAATAGAGCTTTTAAAAATGTCCTGCCTTTTAACGTAGATATATGCCTTCCCCCACTACCGTAAATGTCCATTTATATC ATTTTTTATATATTCTTATAAAAATGTAAAAAAGAAAAACACCGCTTCTGCCTTTTCACTGTGTTGGAGTTTTCTGGAGT GAGCACTCACGCCCTAAGCGCACATTCATGTGGGCATTTCTTGCGAGCCTCGCAGCCTCCGGAAGCTGTCGACTTCATGA CAAGCATTTTGTGAACTAGGGAAGCTCAGGGGGGTTACTGGCTTCTCTTGAGTCACACTGCTAGCAAATGGCAGAACCAA AGCTCAAATAAAAATAAAATAATTTTCATTCATTCACTCAAAA	SEQ.ID NO.71 MEPAAGSSMEPSADWLATAAARGRVEEVRAL LEAGALPNAPNSYGRRPIQVMMMGSARVAEL LLLHGAEPNCADPATLTRPVHDAAREGFLDT LVVLHRAGARLDVRDAWGRLPVDLAEELGHR DVARYLRAAAGGTRGS NHARIDAAEGPSDIPD
SEQ.ID NO.26 AGTGGACTCACGCAGGCGCAGGAGACTACACTTCCCAGGAACTCCGGGCCGCGTTGTTCGCTGGTACCTCCTTCTGACTT CCGGTATTGCTGCGGTCTGTAGGGCCAATCGGGAGCCTGGAATTGCTTTCCCGGCGCTCTGATTGGTGCATTCGACTAGG CTGCCTGGGTTCAAAATTTCAACGATACTGAATGAGTCCCGCGGCGGGTTGGCTCGCGCTTCGTTGTCAGATCTGAGGCG AGGCTAGGTGAGCCGTGGGAAGAAAAGAGGGAGCAGCTAGGGCGCGGGTCTCCCTCCTCCCGGAGTTTGGAACGGCTGAA	SEQ.ID NO.72 MSQVKSSYSYDAPSDFINFSSLDDEGDTQNI DSWFEEKANLENKLLGKNGTGGLFQGKTPLR KANLQQAIVTPLKPVDNTYYKEAEKENLVEQ SIPSNACSSLEVEAAISRKTPAQPQRRSLRL

GTTCACCTTCCAGCCCCTAGCGCCGTTCGCGCCGCTAGGCCTGGCTTCTGAGGCGGTTGCGGTGCTCGGTCGCCGCCTAG	SAQKDLEQKEKHHVKMKAKRCATPVIIDEIL
GCGGGGCAGGGTGCGAGCAGGGGCTTCGGGCCACGCTTCTCTTGGCGACAGGATTTTGCTGTGAAGTCCGTCCGGGAAAC	PSKKMKVSNNKKKPEEEGSAHQDTAEKNASS
GGAGGAAAAAAAGAGTTGCGGGAGGCTGTCGGCTAATAACGGTTCTTGATACATATTTGCCAGACTTCAAGATTTCAGAA	PEKAKGRHTVPCMPPAKQKFLKSTEEQELEK
AAGGGGTGAAAGAGAAGATTGCAACTTTGAGTCAGACCTGTAGGCCTGATAGACTGATTAAACCACAGAAGGTGACCTGC	SMKMQQEVVEMRKKNEEFKKLALAGIGQPVK
TGAGAAAAGTGGTACAAATACTGGGAAAAACCTGCTCTTCTGCGTTAAGTGGGAGACAATGTCACAAGTTAAAAGCTCTT	KSVSQVTKSVDFHFRTDERIKQHPKNQEEYK
ATTCCTATGATGCCCCCTCGGATTTCATCAATTTTTCATCCTTGGATGATGAAGGAGATACTCAAAACATAGATTCATGG	EVNFTSELRKHPSSPARVTKGCTIVKPFNLS
TTTGAGGAGAAGGCCAATTTGGAGAATAAGTTACTGGGGAAGAATGGAACTGGAGGGCTTTTTCAGGGCAAAACTCCTTT	QGKKRTFDETVSTYVPLAQQVEDFHKRTPNR
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TGCCCCTTACGACTCTCACCCTCTCCCCACTTTTTTTAAAAATTTTAACCAGAAAATAAAGATAGTTAAATCCTAAGATA GAGATTAAGTCATGGTTTAAATGAGGAACAATCAGTAAATCAGATTCTGTCCTCTTCTCTGCATACCGTGAATTTATAGT TAAGGATCCCTTTGCTGTGAGGGTAGAAAACCTCACCAACTGCACCAGTGAGGAAGAAGACTGCGTGGATTCATGGGGAG CCTCACAGCAGCCACGCAGCAGGCTCTGGGTGGGGCTGCCGTTAAGGCACGTTCTTTCCTTACTGGTGCTGATAACAACA GGGAACCGTGCAGTGTGCATTTTAAGACCTGGCCTGGAATAAATACGTTTTGTCTTTCCCTCAAAAAAAAAAAAAAAAAA AAAAA	
SEQ.ID NO.27 AAACGCGGGCGGGCGGGCCCGCAGTCCTGCAGTTGCAGTCGTGTTCTCCGAGTTCCTGTCTCTCTGCCAACGCCGCCCGG ATGGCTTCCCAAAACCGCGACCCAGCCGCCACTAGCGTCGCCGCCGCCCGTAAAGGAGCTGAGCCGAGCGGGGGCGCCGC CCGGGGTCCGGTGGGCAAAAGGCTACAGCAGGAGCTGATGACCCTCATGATGTCTGGCGATAAAGGGATTTCTGCCTTCC CTGAATCAGACAACCTTTTCAAATGGGTAGGGACCATCCATGGAGCAGCTGGAACAGTATATGAAGACCTGAGGTATAAG CTCTCGCTAGAGTTCCCCAGTGGCTACCCTTACAATGCGCCCACAGTGAAGTTCCTCACGCCCTGCTATCACCCCAACGT GGACACCCAGGGTAACATATGCCTGGACATCCTGAAGGAAAAGTGGTCTGCCCTGTATGATGTCAGGACCATTCTGCTCT CCATCCAGAGCCTTCTAGGAGAACCCAACATTGATAGTCCCTTGAACACACATGCTGCCGAGCTCTGGAAAAACCCCACA GCTTTTAAGAAGTACCTGCAAGAAACCTACTCAAAGCAGGTCACCAGCCAGGAGCCCTGACCCAGGCTGCCCAGCCTGTC CTTGTGTCGTCTTTTTAATTTTTCCTTAGATGGTCTGTCCTTTTTGTGATTTCTGTATAGGACTCTTTATCTTGAGCTGT GGTATTTTTGTTTTGTTTTTGTCTTTTAAATTAAGCCTCGGTTGAGCCCTTGTATATTAAATAAATGCATTTTTGTCCTT TTTTAGACAAAAAAAAAAAAAAA	SEQ.ID NO.73 MASQNRDPAATSVAAARKGAEPSGGAARGPV GKRLQQELMTLMMSGDKGISAFPESDNLFKW VGTIHGAAGTVYEDLRYKLSLEFPSGYPYNA PTVKFLTPCYHPNVDTQGNICLDILKEKWSA LYDVRTILLSIQSLLGEPNIDSPLNTHAAEL WKNPTAFKKYLQETYSKQVTSQEP
SEQ.ID NO.28 CAGCTAAATTTTAAAGGTGTTTTTGTAGAGATGAGGTTTCACTATATTGCCCAGGCTGGTCTCGAACTCCTGGACTTAAG TGATCCTTCCTCTTTGGCCTCCCAAAGTGCTGGGATTACAGGCATGAGCCACTGCCCCAGCCAAGACTGTCTTTTCTCCA TTGTATTGCGTTTGCTTCCTTGTCAAAGATCAGTTGACTATATTTGTGTGGGGCTATTTCTGGGCTCCCTATTTGTTTCC AGTGATTATGTCTATTTTTTCACCATTACCACCCTATCTTAATTACTGTAGCTTTATAGTGAGTCTTAAAGTTGGGTAAT ATCAGTCTTCTGACCTTTTTTCTCTTTCAATATTGTGCCAGCTATTCTGGGTCTTTTGCCTTTCCATGTAAACTTTAGAAC CAGTTTGTCAGGATCCACAAAATACTTTGCTGGGTTTTGATTGGGATTGCATTGAATCCACAGGTCAAGTTGGCAAAAAC TGACATACAGCAATGCCAGTTTATTGTTTTGTGATAGCCTTAATCCAGCTAGTTTCTTCACAGGATGATGTTGAAAATAT GGGATGCTCATAATCCCTGAATATTTTTTATGTGGATAATTAAACTTGTTCTGGGTGGATGGTTGGATAGCCAGAATAGT AATAACCTCTCTTCCAGCCACTCAAAGAAAATGATATAAACGTAGGGTTGGTTTAATTGTTGAGAGGTCACGTTTTTTCC ATTCTTGCTCTCAGGTAAGGAAAGAGCACTGTTGGTTCACGCATTCCTTTTTCCCTCATACACTTTGTTGGGCACTGATA TGGTTTGGCTCTGTGTTCCCACCCAAATCTCATGTTGAATTGTGATCCTGAGTGTTGGAGGTGGGGCCTCGCGGGAGACG ACTGGATCATGGGGGCGGATTTTCCCCTTGCTGTTCTCATGATAGTGAGTTCTCATGAGATCTGGTTGTTTAAAAGTGTA TAGCACTTCCTGCTTCACTCTCTCCCACTCCACCATGTGAAGAAGGTGCCTTTGCCCTTCCGCCACGACTGTGTTTCCTG AGGCCTCCCCAGCCATGCCTCCTGTACAGCCTGCGGAACTGTCAGTTAAACCTCTTTTCTTCATTAATTACCCACTCTCA	

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SEQ.ID NO.29 AGCTTTGGGGTTGTCCCTGGACTTGTCTTGGTTCCAGAACCTGACGACCCGGCGACGGCGACGTCTCTTTTGACTAAAAG ACAGTGTCCAGTGCTCCAGCCTAGGAGTCTACGGGGACCGCCTCCCGCGCCGCCACCATGCCCAACTTCTCTGGCAACTG GAAAATCATCCGATCGGAAAACTTCGAGGAATTGCTCAAAGTGCTGGGGGTGAATGTGATGCTGAGGAAGATTGCTGTGG CTGCAGCGTCCAAGCCAGCAGTGGAGATCAAACAGGAGGGAGACACTTTCTACATCAAAACCTCCACCACCGTGCGCACC ACAGAGATTAACTTCAAGGTTGGGGAGGAGTTTGAGGAGCAGACTGTGGATGGGAGGCCCTGTAAGAGCCTGGTGAAATG GGAGAGTGAGAATAAAATGGTCTGTGAGCAGAAGCTCCTGAAGGGAGAGGGCCCCAAGACCTCGTGGACCAGAGAACTGA CCAACGATGGGGAACTGATCCTGACCATGACGGCGGATGACGTTGTGTGCACCAGGGTCTACGTCCGAGAGTGAGTGGCC ACAGGTAGAACCGCGGCCGAAGCCCACCACTGGCCATGCTCACCGCCCTGCTTCACTGCCCCCTCCGTCCCACCCCCTCC TTCTAGGATAGCGCTCCCCTTACCCCAGTCACTTCTGGGGGTCACTGGGATGCCTCTTGCAGGGTCTTGCTTTCTTTGAC	SEQ.ID NO.74 MPNFSGNWKIIRSENFEELLKVLGVNVMLRK IAVAAASKPAVEIKQEGDTFYIKTSTTVRTT EINFKVGEEFEEQTVDGRPCKSLVKWESENK MVCEQKLLKGEGPKTSWTRELTNDGELILTM TADDVVCTRVYVRE

CTCTTCTCTCCTCCCCTACACCAACAAAGAGGAATGGCTGCAAGAGCCCAGATCACCCATTCCGGGTTCACTCCCCGCCT CCCCAAGTCAGCAGTCCTAGCCCCAAACCAGCCCAGAGCAGGGTCTCTCTAAAGGGGACTTGAGGGCCTGAGCAGGAAAG ACTGGCCCTCTAGCTTCTACCCTTTGTCCCTGTAGCCTATACAGTTTAGAATATTTATTTGTTAATTTTATTAAAATGCT TTAAAAAAA	
SEQ.ID NO.30 CTCGCTTTTCGGTTGCCGTTGTCTTTTTTCCTTGACTCGGAAATGTCCGGTCGTGGTAAGCAGGGTGGCAAGGCGCGCGC CAAGGCTAAGTCGCGCTCGTCGCGCGCGGGGCTGCAGTTCCCCGTGGGCCGCGTGCACCGGTTGCTCCGCAAGGGCAACT ATTCGGAGCGCGTGGGCGCCGGCGCCCCGGTCTATCTGGCCGCGGTGCTCGAGTACTTGACTGCCGAGATCCTGGAGCTT GCCGGCAACGCGGCGCGCGACAACAAGAAGACGCGCATCATCCCGCGCCACCTGCAGCTGGCCATCCGCAACGACGAGGA GCTCAACAAGCTGCTGGGCCGCGTGACCATCGCGCAGGGTGGCGTCCTGCCCAACATCCAGGCCGTACTGCTGCCCAAGA AGACGGAGAGCCACCACAAGGCCAAGGGCAAGTGAGGCCGCCCGCCGCCCCCGGGGCCCCTTTGATGGACATAAAGGCTC TTTTCAGAGC CACCTA	SEQ.ID NO.75 MSGRGKQGGKARAKAKSRSSRAGLQFPVGRV HRLLRKGNYSERVGAGAPVYLAAVLEYLTAE ILELAGNAARDNKKTRIIPRHLQLAIRNDEE LNKLLGRVTIAQGGVLPNIQAVLLPKKTESH HKAKGK
SEQ.ID NO.31 ATGTCTGGCCGTGGTAAAGGTGGAAAAGGTTTGGGTAAGGGAGGAGCTAAGCGTCATCGCAAGGTTTTGCGCGATAACAT CCAGGGCATCACTAAGCCAGCTATCCGGCGCCTTGCTCGTCGCGGCGGTGTCAAGCGAATTTCTGGCCTTATCTATGAGG AGACTCGTGGTGTTCTGAAGGTGTTCCTGGAGAACGTGATTCGTGACGCTGTCACTTACACAGAGCACGCCAAACGCAAG ACCGTGACAGCAATGGATGTGGTCTACGCGCTGAAGCGACAGGGACGCACTCTTTACGGCTTCGGTGGCTAAGGCTCCTG CTTGCTGCACTCTTATTTTCATTTTCAACCAAAGGCCCTTTTCAGGGCCGCCCA	SEQ.ID NO.76 MSGRGKGGKGLGKGGAKRHRKVLRDNIQGIT KPAIRRLARRGGVKRISGLIYEETRGVLKVF LENVIRDAVTYTEHAKRKTVTAMDVVYALKR QGRTLYGFGG
SEQ.ID NO.32 GCCTCCACAGATATCAAAAGAAACCTGAAGAGCCTACAAAAAAAAAAAGAGATAAAGACAAAATTCAAGAAAACACACACA TACATAATTGTGGTCACCTGGAGCCTGGGGGCCGGCCCAGCTCTCTCAGGATTCAGCAGACATTGGAGGTGGCAGTGAAG GATACAGTGGTAGTCAATGTTATTTGAGCAGGGTCAGCAGGCCCTGGAGCTTCCTGAGTGCACAATGCAGAAGGCTGCTT ACTATGAAAACCCAGGACTGTTTGGAGGCTATGGCTACAGCAAAACTACGGACACTTACGGCTACAGCACCCCCCACCAG CCCTACCCACCCCCTGCTGCTGCCAGCTCCCTGGACACTGACTATCCAGGTTCTGCCTGCTCCATCCAGAGCTCTGCCCC TCTGAGAGCCCCAGCCCACAAAGGAGCTGAACTCAATGGCAGCTGCATGCGGCCGGGCACTGGGAACAGCCAGGGTGGGG GTGGTGGCAGCCAGCCTCCTGGTCTGAACTCAGAGCAGCAGCCACCACAACCCCCTCCTCCACCACCGACCCTGCCCCCA	SEQ.ID NO.77 MLFEQGQQALELPECTMQKAAYYENPGLFGG YGYSKTTDTYGYSTPHQPYPPPAAASSLDTD YPGSACSIQSSAPLRAPAHKGAELNGSCMRP GTGNSQGGGGGSQPPGLNSEQQPPQPPPPPP TLPPSSPTNPGGGVPAKKPKGGPNASSSSAT ISKQIFPWMKESRQNSKQKNSCATAGESCED KSPPGPASKRVRTAYTSAQLVELEKEFHFNR

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TCTTCACCCACCAATCCTGGAGGTGGAGTGCCTGCCAAGAAGCCCAAAGGTGGGCCCAATGCTTCTAGCTCCTCAGCCAC CATCAGCAAGCAGATCTTCCCCTGGATGAAAGAGTCTCGACAGAACTCCAAGCAGAAGAACAGCTGTGCCACTGCAGGAG AGAGCTGCGAGGACAAGAGCCCGCCAGGCCCAGCATCCAAGCGGGTACGCACGGCATACACGAGCGCGCAGCTGGTGGAA TTGGAAAAGGAATTCCACTTCAACCGCTACTTGTGCCGGCCGCGCCGCGTGGAGATGGCCAACCTGCTGAATCTCACGGA ACGCCAGATCAAGATCTGGTTCCAGAACCGGCGCATGAAGTACAAGAAGGACCAGAAGGCCAAGGGCATCCTGCACTCGC CGGCTAGCCAGTCCCCTGAGCGCAGCCCACCGCTCGGCGGCGCCGCTGGCCACGTGGCCTACTCCGGCCAGCTGCCGCCA GTGCCCGGCCTGGCCTACGACGCGCCCTCGCCGCCTGCTTTCGCCAAATCACAGCCCAATATGTACGGCCTGGCCGCCTA CACGGCGCCACTCAGCAGCTGCCTGCCACAACAGAAGCGCTACGCAGCGCCGGAGTTCGAGCCCCATCCCATGGCGAGCA ACGGCGGCGGCTTCGCCAGCGCCAACTTGCAGGGCAGCCCGGTGTACGTGGGCGGCAACTTCGTCGAGTCCATGGCGCCC GCGTCCGGGCCTGTCTTCAACCTGGGCCACCTCTCGCACCCGTCGTCGGCCAGCGTGGACTACAGTTGCGCCGCGCAGAT TCCAGGCAACCACCACCATGGACCTTGCGACCCTCATCCCACCTACACAGATCTCTCGGCCCACCACTCGTCTCAGGGAC GACTGCCGGAGGCTCCCAAACTGACGCATCTGTAGCGGCCGCCGCCAGCCCGAACTCGCGGCAAAATTACCTCTCTTGCT GTAGTGGTGGGGTAGAGGGTGGGGCCCGCGGGGCAGTTCGGGAACCCCCTTCCCCGCTCTTGCCCTGCCGCCGCCTCCCG GGTCTCAGGCCTCCAGCGGCGGAGGCGCAGGCGACCGGGCCTCCCCTCCATGGGCGTCCTTTGGGTGACTCGCCATAAAT CAGCCGCAAGGATCCTTCCCTGTAAATTTGACAGTGCCACATACTGCGGACCAAGGGACTCCAATCTGGTAATGGTGTCC CAAAGGTAAGTCTGAGACCCATCAGCGGCGCGCCCTGCAGAGGGACCAGAGCTTGGAGAGTCTTGGGCCTGGCCCGCGTC TAGCTTAGTTTCAGAGACCTTAATTTATATTCTCCTTCCTGTGCCGTAAGGATTGCATCGGACTAAACTATCTGTATTTA TTATTTGAAGCGAGTCATTTCGTTCCCTGATTATTTATCCTTGTCTGAATGTATTTATGTGTATATTTGTAGATTTATCC AGCCGAGCTTAGGAATTCGCTTCCAGGCCGTGGGGGCCACATTTCACCTCCTTAGTCCCCCTGGTCTGAACTAGTTGAGA GAGTAGTTTTGAACAGTCGTAACCGTGGCTGGTGTTTGTAGTTGACATAAAGGATTAAGACCGCAAATTGTCCTTCATGG GTAGAGTCAGGAAGCCCGGTGGCGTGGCACAACACACTTTGGTCATTTCTCAAAAACCACAGTCCTCACCACAGTTTATT GATTTCAAATTGTCTGGTACTATTGGAACAAATATTTAGAATAAAAAAAATTTCCCAGTCAAAAAAAAAAAAAAAAAAAA	YLCRPRRVEMANLLNLTERQIKIWFQNRRMK YKKDQKAKGILHSPASQSPERSPPLGGAAGH VAYSGQLPPVPGLAYDAPSPPAFAKSQPNMY GLAAYTAPLSSCLPQQKRYAAPEFEPHPMAS NGGGFASANLQGSPVYVGGNFVESMAPASGP VFNLGHLSHPSSASVDYSCAAQIPGNHHHGP CDPHPTYTDLSAHHSSQGRLPEAPKLTHL
SEQ.ID NO.33 CCAGCCCTGAGATTCCCAGGTGTTTCCATTCGGTGATCAGCACTGAACACAGAACTCACCATGGAGTTTGGACTGAGCTG GGTTTTCCTTGTTGCTATTTTAAAAGGTGTCCAGTGTGAAGTGCAGCTGGTGGAGTCTGGGGGAGTCGTGGTACAGCCTG GGGGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTGATGACTATGCCATGCACTGGGTCCGTCAAGCTCCG GGGAAGGGTCTGGAGTGGGTCTCCCTTATTAGTTGGGATGGTGGTAGCACCTACTATGCAGACTCTGTGAAGGGTCGATT CACCATCTCCAGAGACAATAGTAAAAATTCCTTGTATCTGCAAATGAACAGTCTGAGAGCTGAGGACACCGCCTTGTATT ACTGTGCAACCCGGGGGGGTTATTCCACCGCCGGCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCAGCC TCCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCT GGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGCGGCGTGCACACCTTCCCGG CTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTAC ATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGAAAGTTGAGCCCAAATCTTGTGACAAAACTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCA TGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTAC	SEQ.ID NO. 78 MEFGLSWVFLVAILKGVQCEVQLVESGGVVV QPGGSLRLSCAASGFTFDDYAMHWVRQAPGK GLEWVSLISWDGGSTYYADSVKGRFTISRDN SKNSLYLQMNSLRAEDTALYYCATRGGYSTA GFDYWGQGTLVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT QTYICNVNHKPSNTKVDKKVEPKSCDKTHTC PPCPAPELLGGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYT

GTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGT CCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCA TCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGG GCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCG TGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAG AAGAGCCTCTCCCTGTCTCCGGGTAAATGAGTGCGACGGCCGGCAAGCCCCCGCTCCCCGGGCTCTCGCGGTCGCACGAG GATGCTTGGCACGTACCCCGTGTACATACTTCCCGGGCGCCCAGCATGGAAATAAAGCACCCAGCGCTGCCCTGGGCCCC TGCGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAA	LPPSRDELTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTV DKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK
SEQ.ID NO.34 GAGGGAACCATGGAAACCCCAGCGCAGCTTCTCTTCCTCCTGCTACTCTGGCTCCCAGATATCACCGGAGAAATTGTGTT GACGCAGTCTCCAGGCACCCTGTCTTTGTCTCCAGGAGAAAGAGCCGCCCTCTCATGCAGGGCCAGTCAGAGTGTTAACA GCAAGTACTTAGCCTGGTACCAGCAGAAGCCTGGCCAGGCTCCCAGGCTCCTCATGTATGCTGCATCCATCAGGGCCACT GGCATCCCAGACAGGTTCAGTGGCAGTGGGTCTGGGACAGACTTCACTCTCACCATCAGCAGACTGGAATCTGAGGACTT TGCACTGTATTTCTGTCAGCAATATGGTACTTCACCTCTCACTTTCGGCGGAGGGACCAAGGTGGAGATCAAACGAACTG TGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTG AATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGT CACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACA AAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGTTAGAGG GAGAAGTGCCCCCACCTGCTCCTCAGTTCCAGCCTGACCCCCTCCCATCCTTTGGCCTCTGACCCTTTTTCCACAGGGGA CCTACCCCTATTGCGGTCCTCCAGCTCATCTTTCACCTCACCCCCCTCCTCCTCCTTGGCTTTAATTATGCTAATGTTGG AGGAGAATGAATAAATAAAGTGAATCTTTGCACCTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAA	SEQ.ID NO.79 METPAQLLFLLLLWLPDITGEIVLTQSPGTL SLSPGERAALSCRASQSVNSKYLAWYQQKPG QAPRLLMYAASIRATGIPDRFSGSGSGTDFT LTISRLESEDFALYFCQQYGTSPLTFGGGTK VEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEV THQGLSSPVTKSFNRGEC
SEQ.ID NO.35 ACGCGGGGGGCCCGCTCTCGGCGAGCCCGAGCCGCCGCCGGCCCCGCGGCGGAGATGAGCAGGTCCGCGACGCTGCTGCT GTGCCTGCTGGGCTGCCACGTCTGGAAGGCGGTGACCAAGACGCTGCGGGAGCCCGGCGCCGGAGCCCAAGAGGTGACGT TAAAGGTGCACATCAGCGACGCCAGCACCCACCAGCCCGTAGCAGATGCGCTCATCGAGATCTTCACCAACCAGGCCTCC ATAGCCTCTGGCACCTCGGGGACTGATGGCGTCGCCTTTATCAAGTTCCAGTATAAGCTGGGCAGTCAGTTGATTGTCAC CGCCTCGAAGCATGCCTACGTGCCAAACTCTGCCCCATGGAAGCCAATCCGGTTACCTGTATTTTCCTCTCTGAGCCTTG GCCTGCTTCCAGAACGCTCTGCCACTCTAATGGTATATGAAGATGTCGTCCAAATAGTATCAGGATTCCAAGGTGCCCGG CCACAGCCTCGCGTTCATTTCCAGAGAAGGGCTCTGAGGTTGCCTGAGAACACCAGCTACAGTGACCTGACCGCGTTTCT CACGGCCGCCAGCTCCCCTTCGGAGGTGGACAGTTTTCCTTATTTGCGAGGATTAGACGGAAATGGAACAGGAAACAGCA	SEQ.ID NO.80 MSRSATLLLCLLGCHVWKAVTKTLREPGAGA QEVTLKVHISDASTHQPVADALIEIFTNQAS IASGTSGTDGVAFIKFQYKLGSQLIVTASKH AYVPNSAPWKPIRLPVFSSLSLGLLPERSAT LMVYEDVVQIVSGFQGARPQPRVHFQRRALR LPENTSYSDLTAFLTAASSPSEVDSFPYLRG LDGNGTGNSTRHDLTPVTAVSVHLLSSNGTP VLVDGPIYVTVPLATQSSLRHNAYVAAWRFD

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CCCATCTATGTCACTGTGCCCCTGGCCACGCAGAGCAGCCTGAGGCACAATGCCTATGTCGCGGCGTGGCGGTTTGACCA	YWVAAMSPPIPGPVVTQDITTYHTVFLLAIL
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SEQ.ID NO.38 GTTGGGAAAGAGCAGCCTGGGCGGCAGGGGCGGTGGCTGGAGCTCGGTAAAGCTCGTGGGACCCCATTGGGGGAATTTGA TCCAAGGAAGCGGTGATTGCCGGGGGAGGAGAAGCTCCCAGATCCTTGTGTCCACTTGCAGCGGGGGAGGCGGAGACGGC GGAGCGGGCCTTTTGGCGTCCACTGCGCGGCTGCACCCTGCCCCATCCTGCCGGGATCATGGTCTGCGGCAGCCCGGGAG GGATGCTGCTGCTGCGGGCCGGGCTGCTTGCCCTGGCTGCTCTCTGCCTGCTCCGGGTGCCCGGGGCTCGGGCTGCAGCC TGTGAGCCCGTCCGCATCCCCCTGTGCAAGTCCCTGCCCTGGAACATGACTAAGATGCCCAACCACCTGCACCACAGCAC TCAGGCCAACGCCATCCTGGCCATCGAGCAGTTCGAAGGTCTGCTGGGCACCCACTGCAGCCCCGATCTGCTCTTCTTCC TCTGTGCCATGTACGCGCCCATCTGCACCATTGACTTCCAGCACGAGCCCATCAAGCCCTGTAAGTCTGTGTGCGAGCGG GCCCGGCAGGGCTGTGAGCCCATACTCATCAAGTACCGCCACTCGTGGCCGGAGAACCTGGCCTGCGAGGAGCTGCCAGT GTACGACAGGGGCGTGTGCATCTCTCCCGAGGCCATCGTTACTGCGGACGGAGCTGATTTTCCTATGGATTCTAGTAACG GAAACTGTAGAGGGGCAAGCAGTGAACGCTGTAAATGTAAGCCTATTAGAGCTACACAGAAGACCTATTTCCGGAACAAT TACAACTATGTCATTCGGGCTAAAGTTAAAGAGATAAAGACTAAGTGCCATGATGTGACTGCAGTAGTGGAGGTGAAGGA GATTCTAAAGTCCTCTCTGGTAAACATTCCACGGGACACTGTCAACCTCTATACCAGCTCTGGCTGCCTCTGCCCTCCAC TTAATGTTAATGAGGAATATATCATCATGGGCTATGAAGATGAGGAACGTTCCAGATTACTCTTGGTGGAAGGCTCTATA GCTGAGAAGTGGAAGGATCGACTCGGTAAAAAAGTTAAGCGCTGGGATATGAAGCTTCGTCATCTTGGACTCAGTAAAAG TGATTCTAGCAATAGTGATTCCACTCAGAGTCAGAAGTCTGGCAGGAACTCGAACCCCCGGCAAGCACGCAACTAAATCC CGAAATACAAAAAGTAACACAGTGGACTTCCTATTAAGACTTACTTGCATTGCTGGACTAGCAAAGGAAAATTGCACTAT TGCACATCATATTCTATTGTTTACTATAAAAATCATGTGATAACTGATTATTACTTCTGTTTCTCTTTTGGTTTCTGCTT CTCTCTTCTCTCAACCCCTTTGTAATGGTTTGGGGGCAGACTCTTAAGTATATTGTGAGTTTTCTATTTCACTAATCATG AGAAAAACTGTTCTTTTGCAATAATAATAAATTAAACATGCTGTTACCAGAGCCTCTTTGCTGGAGTCTCCAGATGTTAA TTTACTTTCTGCACCCCAATTGGGAATGCAATATTGGATGAAAAGAGAGGTTTCTGGTATTCACAGAAAGCTAGATATGC CTTAAAACATACTCTGCCGATCTAATTACAGCCTTATTTTTGTATGCCTTTTGGGCATTCTCCTCATGCTTAGAAAGTTC CAAATGTTTATAAAGGTAAAATGGCAGTTTGAAGTCAAATGTCACATAGGCAAAGCAATCAAGCACCAGGAAGTGTTTAT GAGGAAACAACACCCAAGATGAATTATTTTTGAGACTGTCAGGAAGTAAAATAAATAGGAGCTTAAGAAAGAACATTTTG CCTGATTGAGAAGCACAACTGAAACCAGTAGCCGCTGGGGTGTTAATGGTAGCATTCTTCTTTTGGCAATACATTTGATT TGTTCATGAATATATTAATCAGCATTAGAGAAATGAATTATAACTAGACATCTGCTGTTATCACCATAGTTTTGTTTAAT TTGCTTCCTTTTAAATAAACCCATTGGTGAAAGTCCCAAAAAAAAAAAAAAAAAAAA	SEQ.ID NO.82 MVCGSPGGMLLLRAGLLALAALCLLRVPGAR AAACEPVRIPLCKSLPWNMTKMPNHLHHSTQ ANAILAIEQFEGLLGTHCSPDLLFFLCAMYA PICTIDFQHEPIKPCKSVCERARQGCEPILI KYRHSWPENLACEELPVYDRGVCISPEAIVT ADGADFPMDSSNGNCRGASSERCKCKPIRAT QKTYFRNNYNYVIRAKVKEIKTKCHDVTAVV EVKEILKSSLVNIPRDTVNLYTSSGCLCPPL NVNEEYIIMGYEDEERSRLLLVEGSIAEKWK DRLGKKVKRWDMKLRHLGLSKSDSSNSDSTQ SQKSGRNSNPRQARN
SEQ.ID NO.39 ACTGAAAGCTCCGGTGCCAGACCCCACCCCCGGCCCCGGCCCGGGACCCCCTCCCCTCCCGGGATCCCCCGGGGTTCCCA CCCCGCCCGCACCGCCGGGGACCCGGCCGGTCCGGCGCGAGCCCCCGTCCGGGGCCCTGGCTCGGCCCCCAGGTTGGAGG AGCCCGGAGCCCGCCTTCGGAGCTACGGCCTAACGGCGGCGGCGACTGCAGTCTGGAGGGTCCACACTTGTGATTCTCAA	SEQ,ID NO.83 MKTSPRRPLILKRRRLPLPVQNAPSETSEEE PKRSPAQQESNQAEASKEVAESNSCKFPAGI KIINHPTMPNTQVVAIPNNANIHSIITALTA

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SEQ.ID NO.41 **STAR clone:** AAAAAATAAGTATATCTGTCNAGAATCNTATTTATGTGAGATGTGTCAATACTGGTCTTGCGTTATTTCGGCTACTTGAA AATAAGTTAAAAAAGATAGTGTTTGGTTCCAAAAAGGAAAAGTCAGCCTCTCCTGCNTGAGTGGGAGCTGCAACCTTTTA GAATTGATAATCACAAACCCCTCAGACCCAAAGTGGAATAAAGAAAAATATGTAACATTAGGCATTGATGGAAAAGGACT AGATCCTAGTGTAAGCATCCTAATAAAAGGAGAGGTTCACAA	
SEQ.ID NO.42	SEQ.ID NO.85

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SEQ.ID NO.43 GCGAAGTGAAGGGTGGCCCAGGTGGGGCCAGGCTGACTGAATGTATCTCCTAGCTATGGACTAAATAATACATGGGGGGA AATAAACAAGTATTCATGAGGGTGAAAATGTGACCCAGCAGGAAAATTACAACTATTTTCAATTGACGTTGAATAGGATG AGTCATGGAATTTAAGTGATTTACTGAAGATTATACTACTGGTAGATAGAAGAGCTAAAGAAAGATGGATACTATGATGC TGAATGTGCGGAATCTGTTTGAGCAGCTTGTGCGCCGGGTGGAGATTCTCAGTGAAGGAAATGAAGTCCAATTTATCCAG TTGGCGAAGGACTTTGAGGATTTCCGTAAAAAGTGGCAGAGGACTGACCATGAGCTGGGGAAATACAAGGATCTTTTGAT GAAAGCAGAGACTGAGCGAAGTGCTCTGGATGTTAAGCTGAAGCATGCACGTAATCAGGTGGATGTAGAGATCAAACGGA GACAGAGAGCTGAGGCTGACTGCGAAAAGCTGGAACGACAGATTCAGCTGATTCGAGAGATGCTCATGTGTGACACATCT GGCAGCATTCAACTAAGCGAGGAGCAAAAATCAGCTCTGGCTTTTCTCAACAGAGGCCAACCATCCAGCAGCAATGCTGG GAACAAAAGACTATCAACCATTGATGAATCTGGTTCCATTTTATCAGATATCAGCTTTGACAAGACTGATGAATCACTGG ATTGGGACTCTTCTTTGGTGAAGACTTTCAAACTGAAGAAGAGAGAAAAGAGGCGCTCTACTAGCCGACAGTTTGTTGAT GGTCCCCCTGGACCTGTAAAGAAAACTCGTTCCATTGGCTCTGCAGTAGACCAGGGGAATGAATCCATAGTTGCAAAAAC TACAGTGACTGTTCCCAATGATGGCGGGCCCATCGAAGCTGTGTCCACTATTGAGACTGTGCCATATTGGACCAGGAGCC GAAGGAAAACAGGTACTTTACAACCTTGGAACAGTGACTCCACCCTGAACAGCAGGCAGCTGGAGCCAAGAACTGAGACA GACAGTGTGGGCACGCCACAGAGTAATGGAGGGATGCGCCTGCATGACTTTGTTTCTAAGACGGTTATTAAACCTGAATC CTGTGTTCCATGTGGAAAGCGGATAAAATTTGGCAAATTATCTCTGAAGTGTCGAGACTGTCGTGTGGTCTCTCATCCAG AATGTCGGGACCGCTGTCCCCTTCCCTGCATTCCTACCCTGATAGGAACACCTGTCAAGATTGGAGAGGGAATGCTGGCA GACTTTGTGTCCCAGACTTCTCCAATGATCCCCTCCATTGTTGTGCATTGTGTAAATGAGATTGAGCAAAGAGGTCTGAC	SEQ.ID NO.86 MDTMMLNVRNLFEQLVRRVEILSEGNEVQFI QLAKDFEDFRKKWQRTDHELGKYKDLLMKAE TERSALDVKLKHARNQVDVEIKRRQRAEADC EKLERQIQLIREMLMCDTSGSIQLSEEQKSA LAFLNRGQPSSSNAGNKRLSTIDESGSILSD ISFDKTDESLDWDSSLVKTFKLKKREKRRST SRQFVDGPPGPVKKTRSIGSAVDQGNESIVA KTTVTVPNDGGPIEAVSTIETVPYWTRSRRK TGTLQPWNSDSTLNSRQLEPRTETDSVGTPQ SNGGMRLHDFVSKTVIKPESCVPCGKRIKFG KLSLKCRDCRVVSHPECRDRCPLPCIPTLIG TPVKIGEGMLADFVSQTSPMIPSIVVHCVNE IEQRGLTETGLYRISGCDRTVKELKEKFLRV KTVPLLSKVDDIHAICSLLKDFLRNLKEPLL TFRLNRAFMEAAEITDEDNSIAAMYQAVGEL PQANRDTLAFLMIHLQRVAQSPHTKMDVANL AKVFGPTIVAHAVPNPDPVTMLQDIKRQPKV

TGAGACAGGCCTGTATAGGATCTCTGGCTGTGACCGCACAGTAAAAGAGCTGAAAGAGAAATTCCTCAGAGTGAAAACTG TACCCCTCCTCAGCAAAGTGGATGATATCCATGCTATCTGTAGCCTTCTAAAAGACTTTCTTCGAAACCTCAAAGAACCT CTTCTGACCTTTCGCCTTAACAGAGCCTTTATGGAAGCAGCAGAAATCACAGATGAAGACAACAGCATAGCTGCCATGTA CCAAGCTGTTGGTGAACTGCCCCAGGCCAACAGGGACACATTAGCTTTCCTCATGATTCACTTGCAGAGAGTGGCTCAGA GTCCACATACTAAAATGGATGTTGCCAATCTGGCTAAAGTCTTTGGCCCTACAATAGTGGCCCATGCTGTGCCCAATCCA GACCCAGTGACAATGTTACAGGACATCAAGCGTCAACCCAAGGTGGTTGAGCGCCTGCTTTCCTTGCCTCTGGAGTATTG GAGTCAGTTCATGATGGTGGAGCAAGAGAACATTGACCCCCTACATGTCATTGAAAACTCAAATGCCTTTTCAACACCAC AGACACCAGATATTAAAGTGAGTTTACTGGGACCTGTGACCACTCCTGAACATCAGCTTCTCAAGACTCCTTCATCTAGT TCCCTGTCACAGAGAGTCCGTTCCACCCTCACCAAGAACACTCCTAGATTTGGGAGCAAAAGCAAGTCTGCCACTAACCT AGGACGACAAGGCAACTTTTTTGCTTCTCCAATGCTCAAGTGAAGTCACATCTGCCTGTTACTTCCCAGCATTGACTGAC TATAAGAAAGGACACATCTGTACTCTGCTCTGCAGCCTCCTGTACTCATTACTACTTTTAGCATTCTCCAGGCTTTTACT CAAGTTTAATTGTGCATGAGGGTTTTATTAAAACTATATATATCTCCCCTTCCTTCTCCTCAAGTCACATAATATCAGCA CTTTGTGCTGGTCATTGTTGGGAGCTTTTAGATGAGACATCTTTCCAGGGGTAGAAGGGTTAGTATGGAATTGGTTGTGA TTCTTTTTGGGGAAGGGGGTTATTGTTCCTTTGGCTTAAAGCCAAATGCTGCTCATAGAATGATCTTTCTCTAGTTTCAT TTAGAACTGATTTCCGTGAGACAATGACAGAAACCCTACCTATCTGATAAGATTAGCTTGTCTCAGGGTGGGAAGTGGGA GGGCAGGGCAAAGAAAGGATTAGACCAGAGGATTTAGGATGCCTCCTTCTAAGAACCAGAAGTTCTCATTCCCCATTATG AACTGAGCTATAATATGGAGCTTTCATAAAAATGGGATGCATTGAGGACAGAACTAGTGATGGGAGTATGCGTAGCTTTG ATTTGGATGATTAGGTCTTTAATAGTGTTGAGTGGCACAACCTTGTAAATGTGAAAGTACAACTCGTATTTATCTCTGAT GTGCCGCTGGCTGAACTTTGGGTTCATTTGGGGTCAAAGCCAGTTTTTCTTTTAAAATTGAATTCATTCTGATGCTTGGC CCCCATACCCCCAACCTTGTCCAGTGGAGCCCAACTTCTAAAGGTCAATATATCATCCTTTGGCATCCCAACTAACAATA AAGAGTAGGCTATAAGGGAAGATTGTCAATATTTTGTGGTAAGAAAAGCTACAGTCATTTTTTCTTTGCACTTTGGATGC TGAAATTTTTCCCATGGAACATAGCCACATCTAGATAGATGTGAGCTTTTTCTTCTGTTAAAATTATTCTTAATGTCTGT AAAAACGATTTTCTTCTGTAGAATGTTTGACTTCGTATTGACCCTTATCTGTAAAACACCTATTTGGGATAATATTTGGA AAAAAAGTAAATAGCTTTTTCAAAATGAAAAAAAAAA	VERLLSLPLEYWSQFMMVEQENIDPLHVIEN SNAFSTPQTPDIKVSLLGPVTTPEHQLLKTP SSSSLSQRVRSTLTKNTPRFGSKSKSATNLG RQGNFFASPMLK
SEQ.ID NO.44 AGGCGCTAGAGGCGGGGGCGCCGGGAGGCGCGGGCTTTGCTCCTGGGGTCTCGGCCTTGGCCGGCTGGACCTGACCCTAG GGCGGCTTGCGCAGCTGTCGGGACGTGACTGCGTTCAGCCGCGTCGGGCGTGCTTCCCAGACTTGCCCAAGTTCGGGTGC CCTAGCTGCCCCTTTGCAGCCGCTGGCCTACCCGGCCCGCGGGTGAGAAGGTTGCGACGGGAGGTGGGTGGAACTCGCCA GCGCCGGGACCGCGGATTGGCTGCCTCGGCTTTCTCTTTTCCCCGTGGGCTCCGGCGTGAGGCGCTGAAGCGGCCGGCAG CCGGCGACCGGCCCTCACCGTCCGCCGGGTTGCGCTCTGCTTTTGCGGTGAGGCGTTGACCACGCCCATATGAATTGGAG CTCTCCGCCAGTAGGAGTTTCCGGAAGGAGTTTGAATTTTTGTGATTTTTATGCTTGTTTGGTCGGTGGAATATGTTGGG ATTTATGTTTGCCTCTGAACAAGTGTCTTGCTCACATCGTAAATGACTTTCTCTCCGAAACGCTAAATATTCTTTCCCGC AGGAGCTCATATCCTTATTTTCCATGACAGATCTTAACGACAATATATGCAAAAGATATATAAAGATGATAACTAATATA GTTATACTGAGCCTGATCATTTGCATTTCGTTAGCTTTCTGGATTATATCAATGACTGCAAGCACCTATTATGGTAACTT ACGACCTATTTCTCCGTGGCGTTGGCTGTTTTCTGTTGTTGTTCCTGTTCTGATCGTCTCTAATGGCCTTAAAAAGAAAA	SEQ.ID NO.87 MTDLNDNICKRYIKMITNIVILSLIICISLA FWIISMTASTYYGNLRPISPWRWLFSVVVPV LIVSNGLKKKSLDHSGALGGLVVGFILTIAN FSFFTSLLMFFLSSSKLTKWKGEVKKRLDSE YKEGGQRNWVQVFCNGAVPTELALLYMIENG PGEIPVDFSKQYSASWMCLSLLAALACSAGD TWASEVGPVLSKSSPRLITTWEKVPVGTNGG VTVVGLVSSLLGGTFVGIAYFLTQLIFVNDL DISAPQWPIIAFGGLAGLLGSIVDSYLGATM QYTGLDESTGMVVNSPTNKARHIAGKPILDN

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GGGAGACTCCATCTAGACTCCATCTCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGAATATTCTAAGCAC TAGAACTACATAAGAATGTCCTAAAGCACTGTATCTAAGCACTTGAAAAGAATGGGACTTTTCGGTTTTAGGGAGATAAC TATTAGCAACCACACAATATGTTATCTTTATGGATGAATAACTTCTGGTAATGACACAGTGTCTTACAGCTACATCATTT ATAAAATCATGTGTCAGTTTTCACACAGCCTGCACATCGTTCTGACATGCCCTTTTTTTCCCTGGAGATTTATCCTCATG ACATACAAGGGGACAAAAATATTTATTGGGACTGTCTTTGAATTTAGTAGAATCACTGTATCATTAACAGTTTGGGGAAG TACTGCTTTGCAGTCCTTTATTTGAAAACTTAGGTCTAGCTGTGTTTTGCATCAAAATTTTTGAGCTATTCAAAAACTAA TAGGATCTGTGTAAAATATTTCACTCAAAACTACTAAAAAAAAGTCTGGGATGGCAGCTCATTATCAAATATACTCCTAT TTTTGTGGTGATTTATGAACATCCCCACTAAGTATAACTAAAGATCATAAAGAGCCTCAGATCAAGTTTGGTCAGGTTTT GTCACCAAGCTTTGTAAATAAACTGGTTTTCATAGCTTTTTGGAGATGAGAATTGAGGATAAGAAATTGTGTCTCTGTCC TTTTTTTTTTTTTTTGTTAAGTCTTACATGTATTTTACTGTAACATCTTTTGAATTGGATATTTAACTAATTCAACATAT TTTTCCTCTTTGCAGAATGGGCAGTTCATGTTAAAATCACTTTTCATGGAAAGAGCTCTATGTAACAGCATAATAAAACT GCCTACCTAGCAGCATAAA	
SEQ.ID NO.45 **STAR clone:** CNGGACACATCAAACTGCTTATCCAGGNACCACTAGAAGTGAATCTCTTCTTGAGTATTCCATACTGCTGCCCCTGCTAT TCACTTGGGGTCCCAGTCAGTTGTTACTATATATTTGTCATCTATTGTGAGAGTCGTGATATCACCTTCCACATCAGTGA TACTGAGAAGGAACAAATCTGCCAAAGATGCTTCACAGTTAGTTGTTACCTTTTTAAGAAGACTGTGCTTGAAAATTATG GTAAAACACATTTAGAAGAAGGATGTGCATTTTCACATCAGTCTATGAAGTATAACTTGACATTTAAATTAAAATGCTGT TCTTCAAAATCGA	
SEQ.ID NO.46 **STAR clone:** GTTCCCGACTAGCTGCCCNTGCACATTATCTTCATTTTCCTGGAATTTGATACAGAGAGCAATTTATAGCCNATTGATAG CTTATGCTGTTTCAATGTAAATTCGTGGTAAATAACTTAGGAACTGCCTCTTCTTTTTCTTTGAAAACCTACTTATAACT GTTGCTAATAAGAATGTGTATTGTTCAGGACAACTTGTCTCCATACAGTTGGGTTGTAACCCTCATGCTTGGCCCAAATA AACTCTCTACTTATATCAGTA	
SEQ.ID NO.47 **STAR clone:** CTAGGGGTCCTGACGGTTCTCTGGCTCCAAGTCTGGCCCCTCAACCTCCCTGGTCATCAGTGGGCTCCAGGCTGAGGATG AGGCTGATTACTACTGTGCAGCATGGGATGACAGCCTGAAAGGTCCTGCGTTCGGAGGAGGCACCCACCTGACCGTCCTC GGTCAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTCCCACCCTCCTCTGAGGAGCTTCAAGCCAACAAGGCCACACTGGT	

GTGTCTCGTAAGTGACTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGGCAGATGGCAGCCCCGTCAAGGTGGGAGTGG AGACCACCAAACCCTCCAAACAAAGCAACAACAAGTATGCGGCCAGCAGCTACCTGAGCCTGACGCCCGAGCAGTGGAAG TCCCACAGAAGCTACAGCTGCCGGGTCACGCATGAAGGGAGCACCGTGGAGAAGACAGTGGCCCCTGCAGAATGCTCTTA GGCCCCCGACCCTCACCCCACCCACAGGGGCCTGGAGCTGCAGGTTCCCAGGGGAGGGGTCTCTGCCCCCATCCCAAGTC ATCCAGCCCTTCTCAATAAATATCCTCATCGTCAACGA	
SEQ.ID NO.48 GGTAGTTGGTTGTGGGCACTGGGTTAGAGGTATCACGTGGGGGCACTTTCGTCTTAGCTTTTGGACAAGACGCAGGCGCA ACCCACGGCTGCTGCGGGGATCCTTGTGGCCCTTCCGGTCGGTGGAACCAATCCGTGCACAGAGAAGCGGGGCGAACTGA GGCGAGTGAAGTGGACTCTGAGGGCTACCGCTACCGCCACTGCTGCGGCAGGGGCGTGGAGGGCAGAGGGCCGCGGAGGC CGCAGTTGCAAACATGGCTCAGAGCAGAGACGGCGGAAACCCGTTCGCCGAGCCCAGCGAGCTTGACAACCCCTTTCAGG ACCCAGCTGTGATCCAGCACCGACCCAGCCGGCAGTATGCCACGCTTGACGTCTACAACCCTTTTGAGACCCGGGAGCCA CCACCAGCCTATGAGCCTCCAGCCCCTGCCCCATTGCCTCCACCCTCAGCTCCCTCCTTGCAGCCCTCGAGAAAGCTCAG CCCCACAGAACCTAAGAACTATGGCTCATACAGCACTCAGGCCTCAGCTGCAGCAGCCACAGCTGAGCTGCTGAAGAAAC AGGAGGAGCTCAACCGGAAGGCAGAGGAGTTGGACCGAAGGGAGCGAGAGCTGCAGCATGCTGCCCTGGGGGGCACAGCT ACTCGACAGAACAATTGGCCCCCTCTACCTTCTTTTTGTCCAGTTCAGCCCTGCTTTTTCCAGGACATCTCCATGGAGAT CCCCCAAGAATTTCAGAAGACTGTATCCACCATGTACTACCTCTGGATGTGCAGCACGCTGGCTCTTCTCCTGAACTTCC TCGCCTGCCTGGCCAGCTTCTGTGTGGAAACCAACAATGGCGCAGGCTTTGGGCTTTCTATCCTCTGGGTCCTCCTTTTC ACTCCCTGCTCCTTTGTCTGCTGGTACCGCCCCATGTATAAGGCTTTCCGGAGTGACAGTTCATTCAATTTCTTCGTTTT CTTCTTCATTTTCTTCGTCCAGGATGTGCTCTTTGTCCTCCAGGCCATTGGTATCCCAGGTTGGGGATTCAGTGGCTGGA TCTCTGCTCTGGTGGTGCCGAAGGGCAACACAGCAGTATCCGTGCTCATGCTGCTGGTCGCCCTGCTCTTCACTGGCATT GCTGTGCTAGGAATTGTCATGCTGAAACGGATCCACTCCTTATACCGCCGCACAGGTGCCAGCTTTCAGAAGGCCCAGCA AGAATTTGCTGCTGGTGTCTTCTCCAACCCTGCGGTGCGAACCGCAGCTGCCAATGCAGCCGCTGGGGCTGCTGAAAATG CCTTCCGGGCCCCGTGACCCCTGACTGGGATGCCCTGGCCCTGCTACTTGAGGGAGCTGACTTAGCTCCCGTCCCTAAGG TCTCTGGGACTTGGAGAGACATCACTAACTGATGGCTCCTCCGTAGTGCTCCCAATCCTATGGCCATGACTGCTGAACCT GACAGGCGTGTGGGGAGTTCACTGTGACCTAGTCCCCCCATCAGGCCACACTGCTGCCACCTCTCACACGCCCCAACCCA GCTTCCCTCTGCTGTGCCACGGCTGTTGCTTCGGTTATTTAAATAAAAAGAAAGTGGAACTGGAACTGACAAAAAAAAAA AAAAAAAAAAAAAA	SEQ.ID NO.88 MAQSRDGGNPFAEPSELDNPFQDPAVIQHRP SRQYATLDVYNPFETREPPPAYEPPAPAPLP PPSAPSLQPSRKLSPTEPKNYGSYSTQASAA AATAELLKKQEELNRKAEELDRRERELQHAA LGGTATRQNNWPPLPSFCPVQPCFFQDISME IPQEFQKTVSTMYYLWMCSTLALLLNFLACL ASFCVETNNGAGFGLSILWVLLFTPCSFVCW YRPMYKAFRSDSSFNFFVFFFIFFVQDVLFV LQAIGIPGWGFSGWISALVVPKGNTAVSVLM LLVALLFTGIAVLGIVMLKRIHSLYRRTGAS FQKAQQEFAAGVFSNPAVRTAAANAAAGAAE NAFRAP
SEQ.ID NO.49 **STAR clone:** CTGCAAGAACTANTCATTCNAGGTCACCAGANAGGAGCCCTGACCCNTCGCTGCCCAGCCTGTCCTTGTGTCGTCTTTTT ACGGGAGACGACTGGATCATGGGGGCGGATTTTCCCCTTGCTGTTCTCATGATAGTGAGTTCTCATGAGATCTGGTTGTT TAAAAGTGTATAGCACTTCCTGCTTCACTCTCTCCCACTCCACCATGTGAAGAAGGTGCCTTTGCCCTTCCGCCACGACT GTGTTTCCTGAGGCCTCCCCAGCCATGCTTCCTGTACAGCCTGCAGAACTGTGAGTTAATTAAACCTCTTTTCTTCATAA	

AGAACA	
SEQ.ID NO.50 TCAAGATTAAACGACAAGGACAGACATGGCTCAGCGGATGACAACACAGCTGCTGCTCCTTCTAGTGTGGGTGGCTGTAG TAGGGGAGGCTCAGACAAGGATTGCATGGGCCAGGACTGAGCTTCTCAATGTCTGCATGAACGCCAAGCACCACAAGGAA AAGCCAGGCCCCGAGGACAAGTTGCATGAGCAGTGTCGACCCTGGAGGAAGAATGCCTGCTGTTCTACCAACACCAGCCA GGAAGCCCATAAGGATGTTTCCTACCTATATAGATTCAACTGGAACCACTGTGGAGAGATGGCACCTGCCTGCAAACGGC ATTTCATCCAGGACACCTGCCTCTACGAGTGCTCCCCCAACTTGGGGCCCTGGATCCAGCAGGTGGATCAGAGCTGGCGC AAAGAGCGGGTACTGAACGTGCCCCTGTGCAAAGAGGACTGTGAGCAATGGTGGGAAGATTGTCGCACCTCCTACACCTG CAAGAGCAACTGGCACAAGGGCTGGAACTGGACTTCAGGGTTTAACAAGTGCGCAGTGGGAGCTGCCTGCCAACCTTTCC ATTTCTACTTCCCCACACCCACTGTTCTGTGCAATGAAATCTGGACTCACTCCTACAAGGTCAGCAACTACAGCCGAGGG AGTGGCCGCTGCATCCAGATGTGGTTCGACCCAGCCCAGGGCAACCCCAATGAGGAGGTGGCGAGGTTCTATGCTGCAGC CATGAGTGGGGCTGGGCCCTGGGCAGCCTGGCCTTTCCTGCTTAGCCTGGCCCTAATGCTGCTGTGGCTGCTCAGCTGAC CTCCTTTTACCTTCTGATACCTGGAAATCCCTGCCCTGTTCAGCCCCACAGCTCCCAACTATTTGGTTCCTGCTCCATGG TCGGGCCTCTGACAGCCACTTTGAATAAACCAGACACCGCACATGTGTCTTGAGAATTATTTGG	SEQ.ID NO.89 MAQRMTTQLLLLLVWVAVVGEAQTRIAWART ELLNVCMNAKHHKEKPGPEDKLHEQCRPWRK NACCSTNTSQEAHKDVSYLYRFNWNHCGEMA PACKRHFIQDTCLYECSPNLGPWIQQVDQSW RKERVLNVPLCKEDCEQWWEDCRTSYTCKSN WHKGWNWTSGFNKCAVGAACQPFHFYFPTPT VLCNEIWTHSYKVSNYSRGSGRCIQMWFDPA QGNPNEEVARFYAAAMSGAGPWAAWPFLLSL ALMLLWLLS
SEQ.ID NO.90 biotin-actgtactAACCCTGCGGCCGCTTTTTTTTTTTTTTTTTTTTV	
SEQ.ID NO.91 GGAATTCTAATACGACTCACTATAGGGAGACGAAGACAGTAGACAGG	
SEQ.ID NO.92 CGCGCCTGTCTACTGTCTTCGTCTCCCTATAGTGAGTCGTATTAGAATTC	
SEQ.ID NO.93 GGAATTCTAATACGACTCACTATAGGGAGAGCCTGCACCAACAGTTAACAGG	
SEQ.ID NO.94 CGCGCCTGTTAACTGTTGGTGCAGGCTCTCCCTATAGTGAGTCGTATTAGAATTC	

SEQ.ID NO.95 GGGAGACGAAGACAGTAGA	
SEQ.ID NO.96 GCCTGCACCAACAGTTAACA	
SEQ.ID NO.97 GGAATTCTAATACGACTCACTATAGGGA	
SEQ.ID NO.98 CGCGTCCCTATAGTGAGTCGTATTAGAATTC	
SEQ.ID NO.99 TTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTCTAATACGACTCACTATAGGGAGATGGAGAAAAAAATCA CTGGACGCGTGGCGCGCCATTAATTAATGCGGCCGCTAGCTCGAGTGATAATAAGCGGATGAATGGCTGCAGGCATGCAA GCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTATCCGCTCACAATTCCACACAACATACGAGCCGGA AGCATAAAGTGTAAAGCCTGGGGTGCCTAATGAGTGAGCTAACTCACATTAATTGCGTTGCGCTCACTGCCCGCTTTCCA GTCGGGAAACCTGTCGTGCCAGCTGCATTAATGAATCGGCCAACGCGCGGGGAGAGGCGGTTTGCGTATTGGGCGCTCTT CCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGAGCGGTATCAGCTCACTCAAAGGCGGTAATA CGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAA GGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGC GAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCG CTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTC GGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACT ATCGTCTTGAGTCCAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGG TATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGC TCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTT TTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGAC GCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAA TTAAAAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGG CACCTATCTCAGCGATCTGTCTATTTCGTTCATCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAG GGCTTACCATCTGGCCCCAGTGCTGCAATGATACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCA GCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTCCTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAG	

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ggcttattattcaactgtggatcaagttaaggacctctacagtggattaattggccccctgattgtttgtcgaagacctt	
acttgaaagtattcaatcccagaaggaaactggaatttgcccttctgtttctagttttgatgagaatgaatcttggtac	

ttagatgacaacatcaaaacatactctgatcaccccgagaaagtaaacaaagatgatgaggaattcatagaaagcaataa aatgcatgctattaatggaagaatgtttggaaacctacaaggcctcacaatgcacgtgggagatgaagtcaactggtatc tgatgggaatgggcaatgaaatagacttacacactgtacattttcacggccatagcttccaatacaagcacaggggagtt tatagttctgatgtctttgacattttccctggaacataccaaaccctagaaatgtttccaagaacacctggaatttggtt actccactgccatgtgaccgaccacattcatgctggaatggaaaccacttacaccgttctacaaaatgaagacaccaaat ctggctgaatgaaataaattggtgataagtggaaaaaagagaaaaaccaatgattcataacaatgtatgtgaaagtgtaa aatagaatgttactttggaatgactataaacattaaaagaagactggaagcatacaactttgtacatttgtgggggaaaa ctattaatttttttgcaaatggaaagatcaacagactatataatgatacatgactgacacttgtacactaggtaataaaac tgattcatacagtctaatgatatcaccgctgttagggttttataaaactgcatttaaaaaaagatctatgaccagatatt ctcctgggtgctcctcaaaggaacactattaaggttcattgaaatgttttcaatcattgccttcccattgatccttctaa catgctgttgacatcacacctaatattcagagggaatgggcaaggtatgagggaaggaaataaaaaataaaataaataaa atagaatgacacaaatttgagttttgtgaacccctgaacagatggtcttaaggacgttatctggaactggagaaaagcag agttgagagacaattctatagattaaatcctggtaaggacaaacattgccattagaagaaaagcttcaaaatagacctgt ggcagatgtcacatgagtagaatttctgcccagccttaactgcattcagaggataatatcaatgaactaaacttgaacta aaaatttttaaacaaaaagttataaatgaagacacatggttgtgaatacaatgatgtatttctttatttcacatacac tctagctaaaagagcaagagtacacatcaacaaaaatggaaacaaggctttggctgaaaaaaacatgcatttgacaaatc atgttaatagctagacaagaagaaagttagctttgtaaacttctacttcatttgattcagagaaacagagcatgagtttt cttaaaagtaacaagaaaa	
SEQ.ID NO.171 GCTTAAAAGAGTCCTCCTGTGGC	
SEQ.ID NO.172 TGGACATTGTTCTTAAAGTGTGG	
SEQ.ID NO.173 AGGTTTTATGGCCACCGTCAG	
SEQ.ID NO.174 ATCCTATACCGCTCGGTTATGC	
SEQ.ID NO.175 GGGCGGCGGCTCTTTCCTCCTC	
SEQ.ID NO.176	

GCTAGCGGCCCCATACTCG	
SEQ.ID NO.177 ACACTGGATGCCCTGAATGACACA	
SEQ.ID NO.178 GCTTTGGCCCTTTTTGCTAA	
SEQ.ID NO.179 CCCACTTCTGTCTTACTGCATC	
SEQ.ID NO.180 CATAGTACTCCAGGGCTTATTC	
SEQ.ID NO.181 AACGATTGCCCGGATTGATGACA	
SEQ.ID NO.182 TACTTGAGGCTGGGGTGGGAGATG	
SEQ.ID NO.183 CACTACGCCAGGCACCCCCAAA	
SEQ.ID NO.184 CGAGGCGCACGGCAGTCT	
SEQ.ID NO.185 ATCCGTTGCTGCAGCTCGTTCCTC	
SEQ.ID NO.186 ACCCTGCTGACCTTCTTCCATTCC	
SEQ.ID NO.187 TCGGAGGAGGGCTGGCTGGTGTTT	
SEQ.ID NO.188	

CTTGGGCGTCTTGGAGCGGTTCTG	
SEQ.ID NO.189 AGAGCCTATTGAAGATGAACAG	
SEQ.ID NO.190 TGATTGCCCCGGATCCTCTTAGG	
SEQ.ID NO.191 GGACAAATACGACGACGAGG	
SEQ.ID NO.192 GGTTTCTTGGGTAGTGGGC	
SEQ.ID NO.193 CCCCGGAGAAGGAAGAGCAGTA	
SEQ.ID NO.194 CGAAAGCCGGCAGTTAGTTATTGA	
SEQ.ID NO.195 GGCGGGCAACGAATTCCAGGTGTC	
SEQ.ID NO.196 TCAGAGGTTCGTCGCATTTGTCCA	
SEQ.ID NO.197 CAACAGTCATGATGTGTGGATG	
SEQ.ID NO.198 ACTGCACCTTGTCCGTGTTGAC	
SEQ.ID NO.199 CCGGCTGGCTGCTTTGTTTA	
SEQ.ID NO.200	

ATGATCAGCAGGTTCGTTGGTAGG	
SEQ.ID NO.201 ATGCCGGAAGTGAATGTGG	
SEQ.ID NO.202 GGTGACTCCGCCTTTTGAT	
SEQ.ID NO.203 ACATTCGCTTCTCCATCTGG	
SEQ.ID NO.204 TGTCACGGAAGGGAACCAGG	
SEQ.ID NO.205 ACGCTGCCTCTGGGTCACTT	
SEQ.ID NO.206 TTGGCAAATCAATGGCTTGTAAT	
SEQ.ID NO.207 ATGGCTTGGGTCATCAGGAC	
SEQ.ID NO.208 GTGTCACTGGGCGTAAGATACTG	
SEQ.ID NO.209 CACCAAATCAGCTGCTACTACTCC	
SEQ.ID NO.210 GATAAACCCCAAAGCAGAAAGATT	
SEQ.ID NO.211 CGAGATTCCGTGGGCGTAGG	
SEQ.ID NO.212	

TGAGTGGGAGCTTCGTAGG	
SEQ.ID NO.213 TCAGAGTGGACGTTGGATTAC	
SEQ.ID NO.214 TGCTTGAAATGTAGGAGAACA	
SEQ.ID NO.215 GAGGGGCATCAATCACACCGAGAA	
SEQ.ID NO.216 CCCCACCGCCCACCCATTTAGG	
SEQ.ID NO.217 GGGGGCACCAGAGGCAGTAA	
SEQ.ID NO.218 GGTTGTGGCGGGGGCAGTTGTG	
SEQ.ID NO.219 ACAGACTCCTGTACTGCAAACC	
SEQ.ID NO.220 TACCGGTTCGTCCTCTTCCTC	
SEQ.ID NO.221 GAAGTTCCTCACGCCCTGCTATC	
SEQ.ID NO.222 CTGGCTGGTGACCTGCTTTGAGTA	
SEQ.ID NO.223 TAGGCGCGCCTGACATACAGCAATGCCAGTT	
SEQ.ID NO.224	

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SEQ.ID NO.225 TGGGGAGGAGTTTGAGGAGCAGAC	
SEQ.ID NO.226 GTGGGACGGAGGGGGCAGTGAAG	
SEQ.ID NO.227 GCAACTATTCGGAGCGCGTG	
SEQ.ID NO.228 CCAGCAGCTTGTTGAGCTCC	
SEQ.ID NO.229 GGAGGAGCTAAGCGTCATCGC	
SEQ.ID NO.230 TCGCTTCAGCGCGTAGACC	
SEQ.ID NO.231 TATTAGTTGGGATGGTGGTAGCAC	
SEQ.ID NO.232 GAGAATTCGAGTCGACGATGAC	
SEQ.ID NO.233 GAAATTGTGTTGACGCAGTCTCC	
SEQ.ID NO.234 AGGCACACAACAGAGGCAGTTC	
SEQ.ID NO.235 GTACATCAACCTCCTGCTGTCC	
SEQ.ID NO.236	

GACATCTCCAAGTCCCAGCATG	
SEQ.ID NO.237 AGTCTCTCACTGTGCCTTATGCC	
SEQ.ID NO.238 AGTCCTAAGAACTGTAAACG	
SEQ.ID NO.239 CATCTATACGTGGATTGAGGA	
SEQ.ID NO.240 ATAGGTACCAGGTATGAGCTG	
SEQ.ID NO.241 TGTCCACATCATCATCGTCATCC	
SEQ.ID NO.242 TGTCACTGGTCGGTCGCTGAGG	
SEQ.ID NO.243 CATGGGGCTTAAGATGTC	
SEQ.ID NO.244 GTCGATTTCTCCATCATCTG	
SEQ.ID NO.245 AAGAGGCGCTCTACTAGCCG	
SEQ.ID NO.246 CTTTCCACATGGAACACAGG	
SEQ.ID NO.247 CATTTTCCTGGAATTTGATACAG	
SEQ.ID NO.248	

GTAGAGAGTTTATTTGGGCCAAG	
SEQ.ID NO.249 CATCTATGGTAACTACAATCG	
SEQ.ID NO.250 GTAGAAGTCACTGATCAGACAC	
SEQ.ID NO.251 CTGCCTGCCAACCTTTCCATTTCT	
SEQ.ID NO.252 TGAGCAGCCACAGCAGCATTAGG	
SEQ.ID NO.253 CACCTGATCAGGTGGATAAGG	
SEQ.ID NO.254 TCCCAGGTAGAAGGTGGAATCC	

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CLAIMS:

1. An antibody or an antigen binding fragment thereof, which specifically binds to the polypeptide set forth in SEQ ID NO.:70 for use in the detection, diagnosis, prognosis or identification of ovarian cancer.

2. The antibody or antigen binding fragment thereof for the use as defined in claim 1, wherein the antibody or antigen binding fragment thereof has sub-nanomolar affinity for the polypeptide.

3. A pharmaceutical composition comprising the antibody or antigen binding fragment of any one of claims 1 or 2 and a pharmaceutically acceptable carrier.

4. Use of an antibody, or an antigen binding fragment thereof, which specifically binds to the polypeptide set forth in SEQ ID NO.:70 for the detection, diagnosis, prognosis or identification of ovarian cancer.

5. The use as defined in claim 4, wherein the ovarian cancer is of epithelial origin.

6. The use as defined in claim 5, wherein the ovarian cancer is malignant.

7. The use as defined in claim 5, wherein the ovarian cancer is classified as serous, clear cell or endometroid.

8. The use as defined in claim 7, wherein the ovarian cancer is malignant.

9. The use as defined in any one of claims 4 to 8, wherein the ovarian cancer is characterized as a late-stage.

10. A method for detecting or identifying an ovarian cancer cell, the method comprising contacting a test cell, a test cell sample, a test body fluid or a test tissue with a reagent which specifically binds to at least one polynucleotide sequence selected from the group consisting of:

a) a polynucleotide comprising SEQ ID NO.:24, and;

d) a polynucleotide having at least 80% sequence identity with SEQ ID NO.:24 over the entire length of SEQ ID NO.:24,

and detecting a complex formed by the reagent and polynucleotide whereby the presence of a complex is indicative of an ovarian cancer cell.

11. The method as defined in claim 10, wherein the presence of a complex is indicative of ovarian cancer.

12. The method of any one of claims 10 or 11, further comprising a step of **a)** qualitatively or quantitatively comparing the level of at least one complex present in the test cell, the test sample, the test fluid or the test tissue with the level of complex in a normal cell, a normal cell sample, a normal body fluid, a normal tissue or a reference value or **b)** qualitatively or quantitatively comparing the level of at least one complex present in the test cell, the test sample, the test fluid or the test tissue with the level of complex in a cell, a cell sample, a body fluid or a tissue of a low malignant potential ovarian cancer or with a reference value attributed to a low malignant potential ovarian cancer.

13. The method of claim 12a), wherein the normal cell, cell sample or tissue is a normal ovarian cell, a normal ovarian cell sample or a normal ovarian tissue and wherein a normal body fluid is from an individual which does not have a cancerous condition.

14. The method of claim 10, wherein said cell, cell sample, body fluid or tissue originates from an individual which has or is suspected of having an ovarian cancer.

15. The method of claim 14, wherein said ovarian cancer is a low malignant potential ovarian cancer or is a malignant ovarian cancer.

16. An isolated polypeptide for use in the identification or detection of an ovarian cancer cell, said polypeptide being selected from the group consisting of :

a) a polypeptide comprising SEQ ID NO.:70,

b) a polypeptide encoded by the polynucleotide set forth in SEQ ID NO.:24,

c) a derivative of any one of a) or b) wherein said derivative has at least 80% sequence identity to the polypeptide, over the entire length of said polypeptide of a) or b) and;

d) an analog of any one of a) or b) wherein said analogue has at least 80% sequence identity to the polypeptide over the entire length of said polypeptide of a) or b).

17. A pharmaceutical composition comprising the polypeptide of claim 16 and a pharmaceutically acceptable carrier for use in the identification or detection of an ovarian cancer cell.

18. A polypeptide as defined in claim 16, for use in the prognosis or diagnosis of ovarian cancer.

19. A polypeptide for a use as claimed in claim 18, wherein said ovarian cancer is a malignant ovarian cancer, or a low malignant potential ovarian cancer.

20. A polypeptide for a use as claimed in claim 19, wherein detection of said polypeptide in a cell, tissue, sample or body fluid from an individual is **a)** preferentially indicative of a malignant ovarian cancer diagnosis over a low malignant potential ovarian cancer diagnosis or **b)** preferentially indicative of a malignant ovarian cancer than a low malignant potential ovarian cancer or **c)** is preferentially indicative of a late-stage malignant ovarian cancer.

21. A method for the diagnosis or prognosis of ovarian cancer, the method comprising measuring the presence or absence of SEQ ID NO.:70 in a sample obtained from an ovary or an ovarian tissue, whereby the presence of the polypeptide is indicative of the presence of an ovarian cancer cell.

22. A method for the diagnosis or prognosis of ovarian cancer, the method comprising measuring the level of expression of SEQ ID NO.:70 in a sample obtained from an ovary or an ovarian tissue.

23. The method of claim 22, further comprising comparing the level obtained with at least one reference level or value.

24. A method of identifying a compound that inhibits the activity or function of a polypeptide comprising SEQ ID NO.:70, or a polypeptide comprising a polypeptide sequence encoded by SEQ ID NO.:24, the method comprising contacting a cell expressing the polypeptide with a putative compound and isolating or identifying a compound which is able to specifically bind the polypeptide and determining the effect of the putative compound on ovarian cancer cells, wherein the method is performed *in vitro*.

25. A method of identifying a compound that inhibits the expression of a polynucleotide comprising SEQ ID NO.:24, the method comprising contacting a cell able to express said polynucleotide with a putative compound and quantifying the level of expression of the polynucleotide in the presence of said putative compound, wherein said cell is an ovarian cancer cell expressing said polynucleotide and wherein the method is performed *in vitro*.

26. An isolated polynucleotide for use in reducing, lowering or inhibiting the growth of an ovarian cancer cell, said polynucleotide being a polynucleotide comprising a sequence that is at least 80% complementary to SEQ ID NO.:24.

27. An antibody or an antigen binding fragment thereof, which specifically binds to the polypeptide set forth in SEQ ID NO.:70 for use in the treatment of ovarian cancer comprising tumor cells expressing the polypeptide set forth in SEQ ID NO.:70.

28. The antibody or antigen binding fragment thereof for the use of claim 27, wherein the antibody or antigen binding fragment thereof inhibits migration, growth, colony formation, or survival of ovarian cancer cells.

29. The antibody or antigen binding fragment thereof for the use of claim 27, wherein the antibody or antigen binding fragment thereof inhibits migration, growth, colony formation, or survival of ovarian cancer cells in an *in vitro* assay.

30. The antibody or antigen binding fragment thereof for the use of any one of claims 27 to 29, wherein the antibody or antigen binding fragment thereof is a polyclonal antibody, a monoclonal antibody, a human antibody or an antigen binding fragment thereof.

31. The antibody or antigen binding fragment thereof for the use of any one of claims 27 to 30, wherein the antibody or antigen binding fragment thereof has sub-nanomolar affinity for the polypeptide.

32. An antibody or antigen binding fragment which specifically binds to the polypeptide set forth in SEQ ID NO.:70 and impairs an activity of the polypeptide in ovarian tumor cells expressing the polypeptide set forth in SEQ ID NO.:70.

33. The antibody or antigen binding fragment thereof of claim 32, wherein the antibody inhibits migration, growth, colony formation, or survival of ovarian cancer cells.

34. The antibody or antigen binding fragment thereof of claim 32, wherein the antibody inhibits migration, growth, colony formation, or survival of ovarian cancer cells in an *in vitro* assay.

35. The antibody or antigen binding fragment of any one of claims 32 to 34, wherein the antibody is a polyclonal antibody.

36. The antibody or antigen binding fragment of any one of claims 32 to 34, wherein the antibody is a monoclonal antibody.

37. The antibody or antigen binding fragment of any one of claims 32 to 34, wherein the antibody comprises the complementarity determining regions of a monoclonal antibody or of a human antibody.

38. The antibody or antigen binding fragment of any one of claims 32 to 34, wherein the antibody is a human antibody.

39. The antibody or antigen binding fragment of any one of claims 32 to 38, wherein said antibody has sub-nanomolar affinity for the polypeptide.

40. A pharmaceutical composition comprising the antibody or antigen binding fragment of any one of claims 27 to 39 and a pharmaceutically acceptable carrier.

41. Use of an antibody, or an antigen binding fragment thereof, which specifically binds to the polypeptide set forth in SEQ ID NO.:70 for the treatment of ovarian cancer comprising tumor cells expressing the polypeptide set forth in SEQ ID NO.:70.

42. The use as defined in claim 41, wherein the antibody, or antigen binding fragment thereof, impairs ovarian cancer tumorigenesis.

43. The use as defined in claim 41, wherein the ovarian cancer is of epithelial origin.

44. The use as defined in claim 43, wherein the ovarian cancer is malignant.

45. The use as defined in claim 43, wherein the ovarian cancer is classified as serous, clear cell or endometroid.

46. The use as defined in claim 45, wherein the ovarian cancer is malignant.

47. The use as defined in any one of claims 41 to 46, wherein the ovarian cancer is characterized as a late-stage.

48. The use as defined in any one of claims 41 to 47, wherein the antibody or antigen binding fragment is as defined in any one of claims 32 to 39.

49. The use as defined in any one of claims 41 to 47, wherein the antibody or antigen binding fragment thereof is a polyclonal antibody, a monoclonal antibody, a human antibody or an antigen binding fragment thereof.

50. Use of an antibody, or an antigen binding fragment thereof, which specifically binds to the polypeptide set forth in SEQ ID NO.:70 for inhibiting ovarian cancer

formation, for inhibiting ovarian cancer development, for reducing malignancy of ovarian cancer or tumor invasion by ovarian cancer cells.

51. The use as defined in claim 50, wherein the antibody or antigen binding fragment thereof is as defined in any one of claims 32 to 39.

52. The use as defined in claim 51, wherein the antibody or antigen binding fragment thereof is a polyclonal antibody, a monoclonal antibody, a human antibody or an antigen binding fragment thereof.

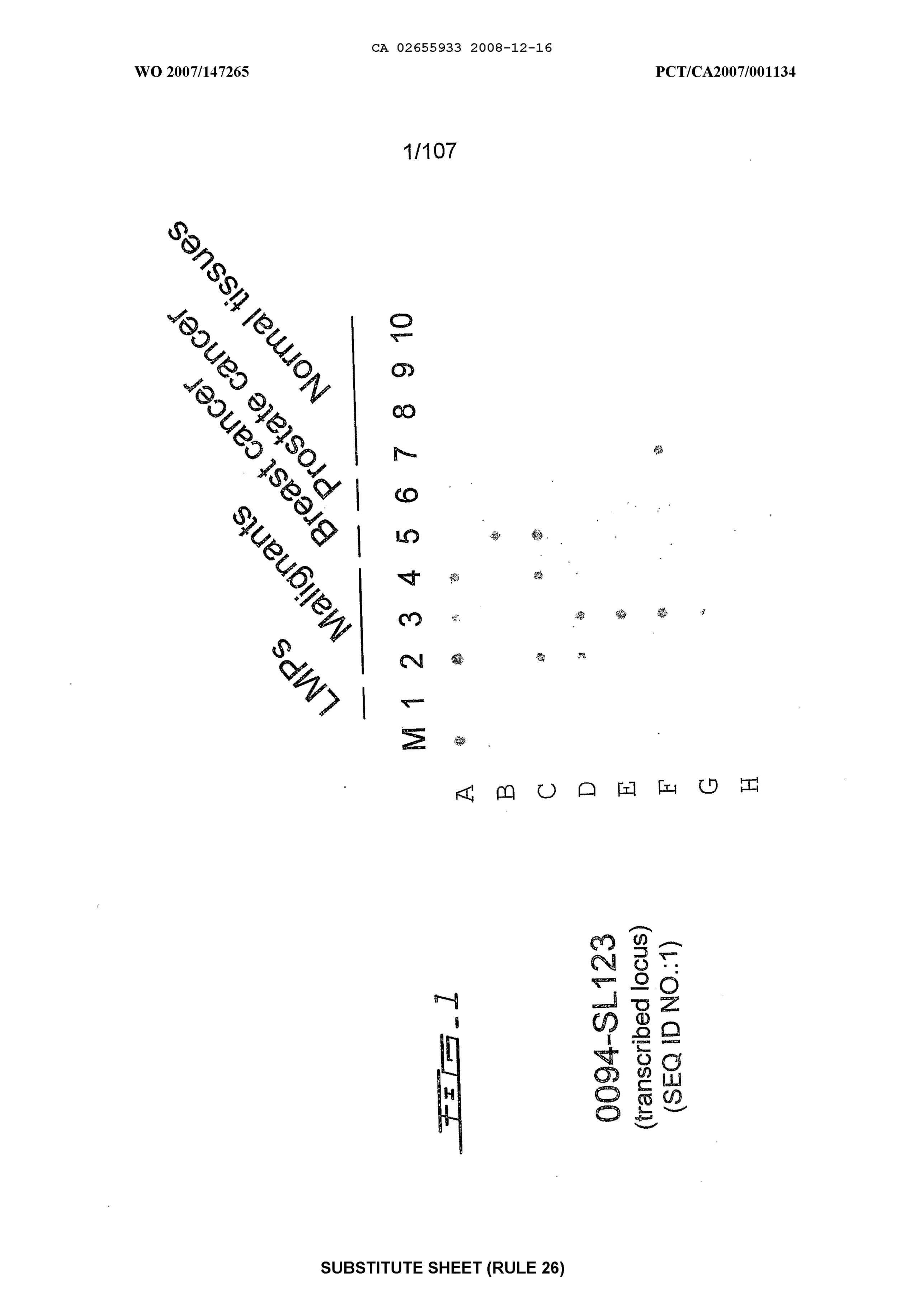

Normal tissues
Prostate cancer
Breast cancer
Malignants
LMPS
M 1 2 3 4 5 6 7 8 9 10
A B C D E E G H
0094-SL123
(transcribed locus)
(SEQ ID NO:1)

FIG. 1

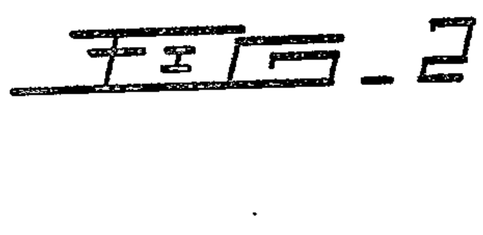
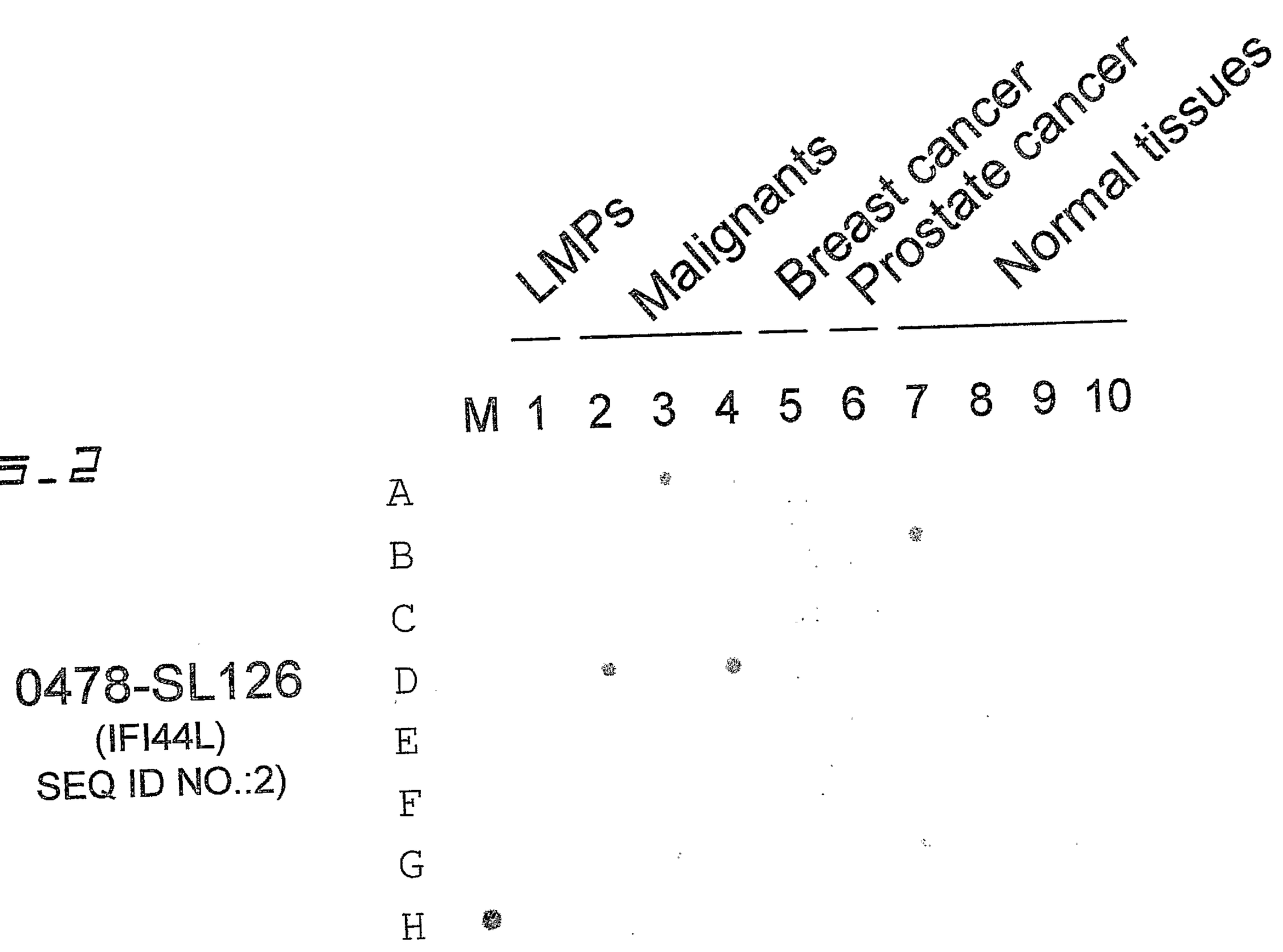
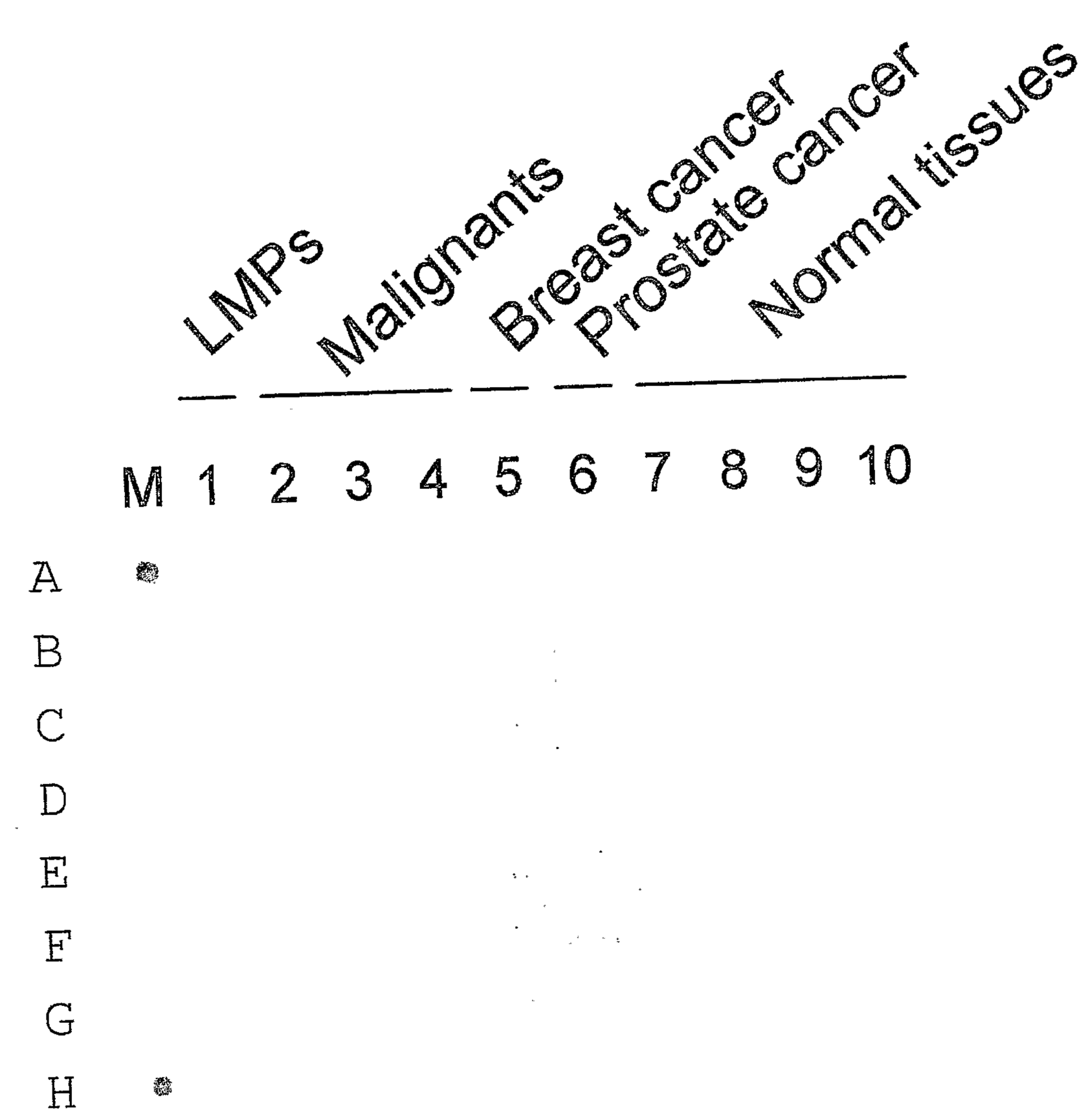


FIG-2



0478-SL126
(IFI44L)
SEQ ID NO.:2)

Fig-3



0671-SL126
(HOXD1)
(SEQ ID NO.:3)

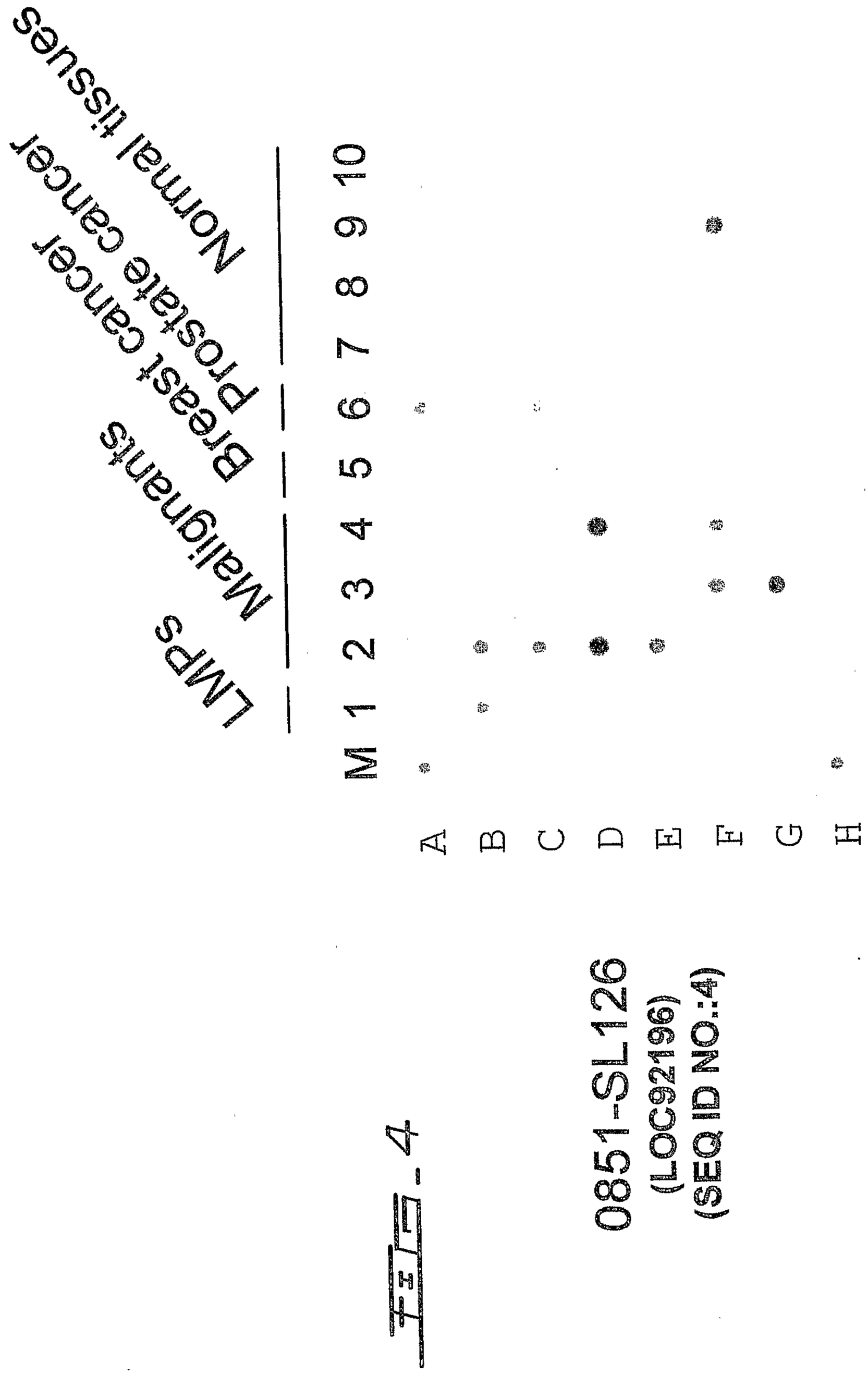

0851-SL126
(LOC216196)
(SEQ ID NO:4)
A
B
C
D
E
F
G
H
M 1 2 3 4 5 6 7 8 9 10
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues

Fig. 4

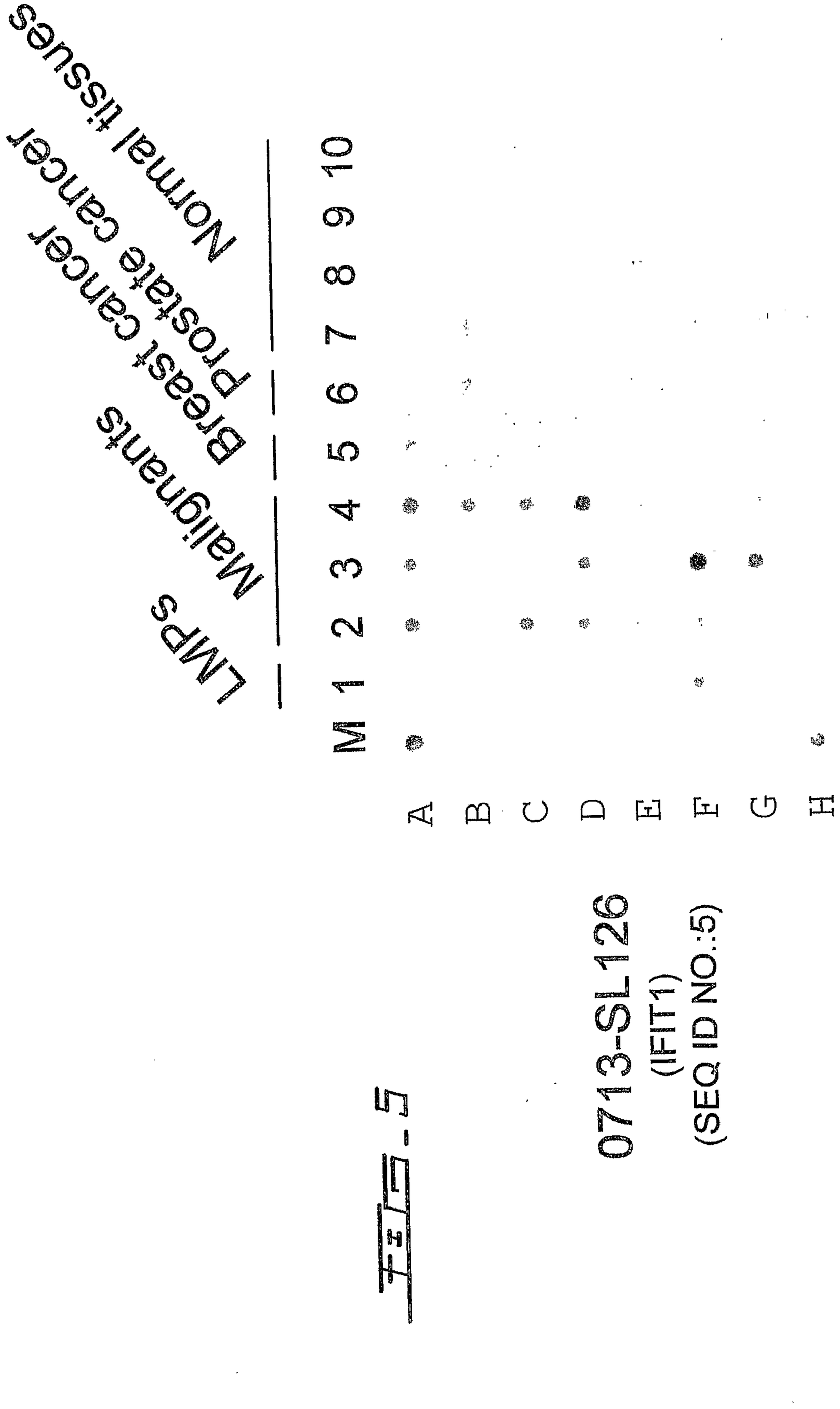

Sensitive tissues
Normal tissue
Prostate cancer
Breast cancer
Malignants
LMPs
1 2 3 4 5 6 7 8 9 10
A
B
C
D
E
F
G
H
M
07 13-S L126
(IFIT1)
(SEQ ID NO:5)

FIG-5

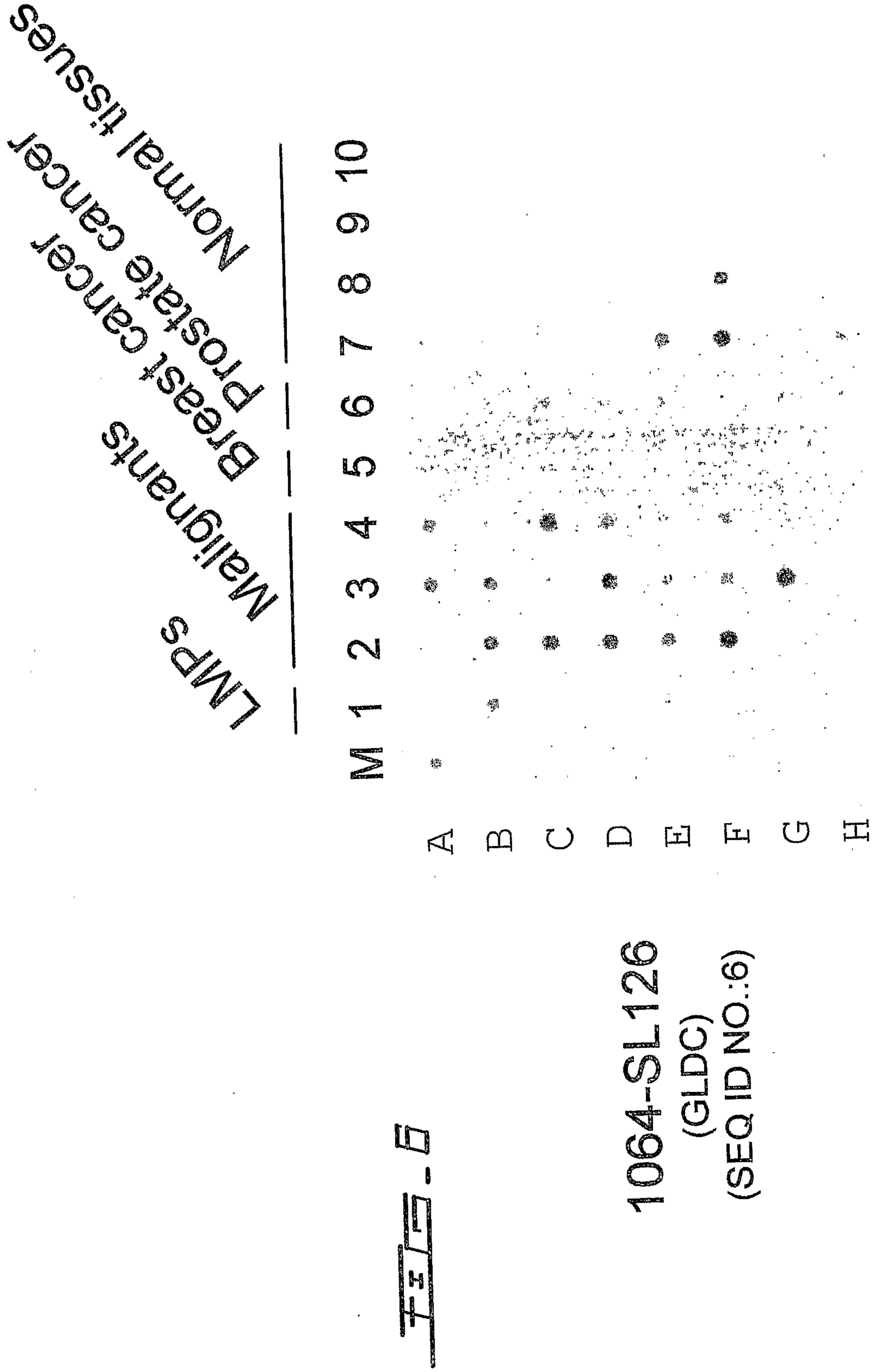
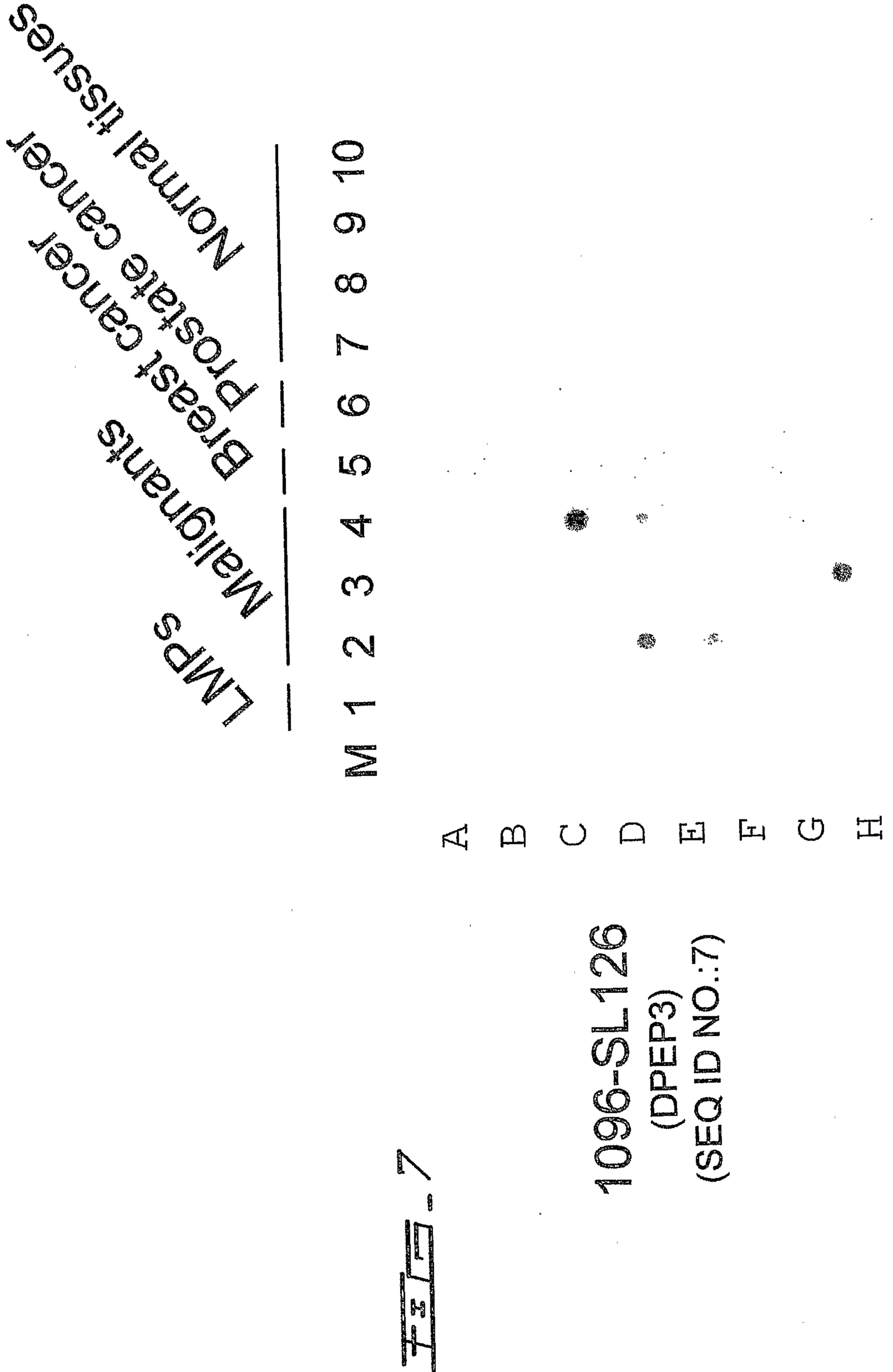
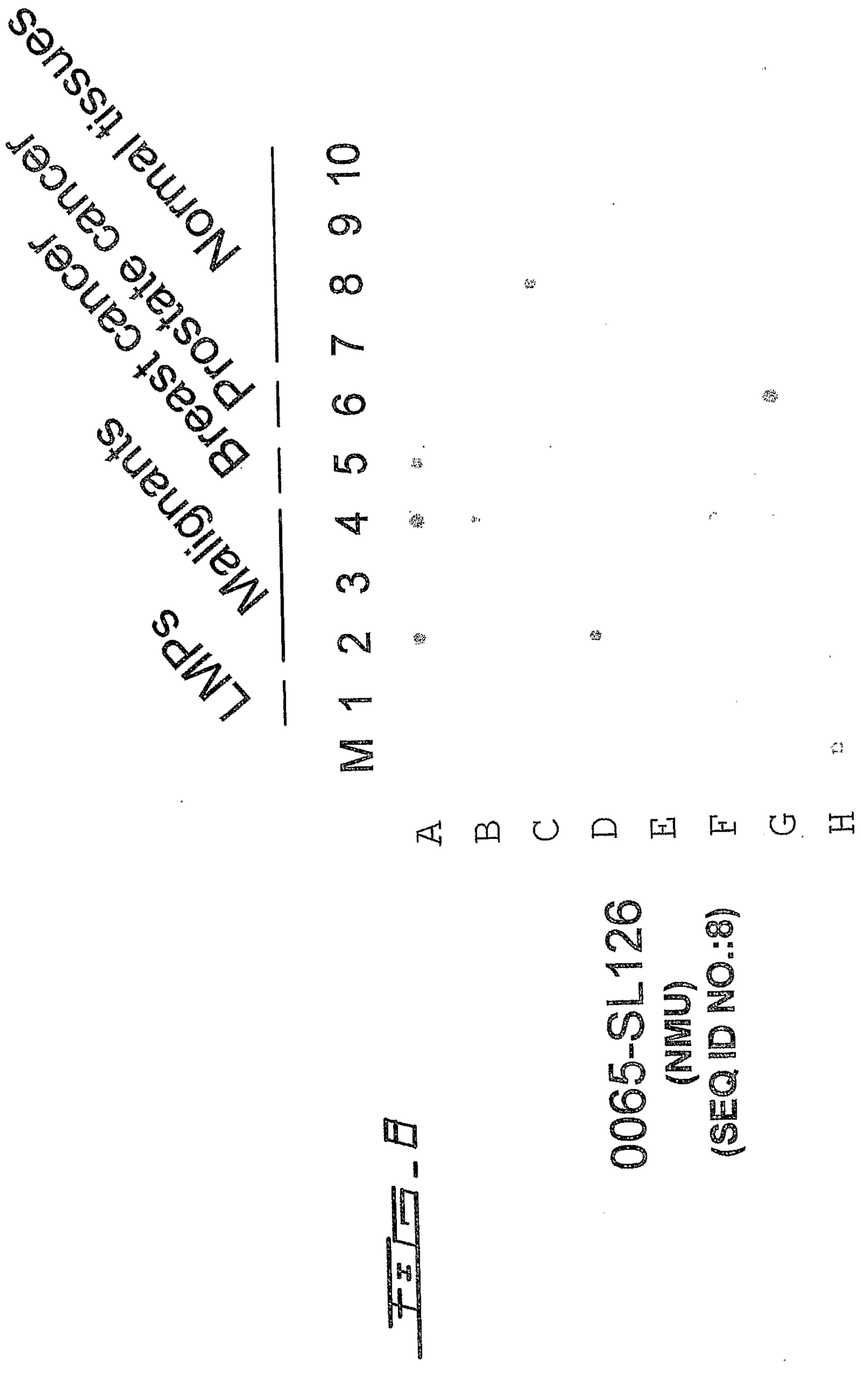


FIG-6

1064-SL126
(GLDC)
(SEQ ID NO:6)


sensitivity
Normal tissues
Prostate cancer
Breast cancer
Malignants
LMPs
M 1 2 3 4 5 6 7 8 9 10
A B C D E F G H
1096-SL126
(DPEP3)
(SEQ ID NO.:7)
7


FIG. 8
0065-SL126
(MMU)
(SEQ ID NO:8)
A B C D E E G H
M 1 2 3 4 5 6 7 8 9 10
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues

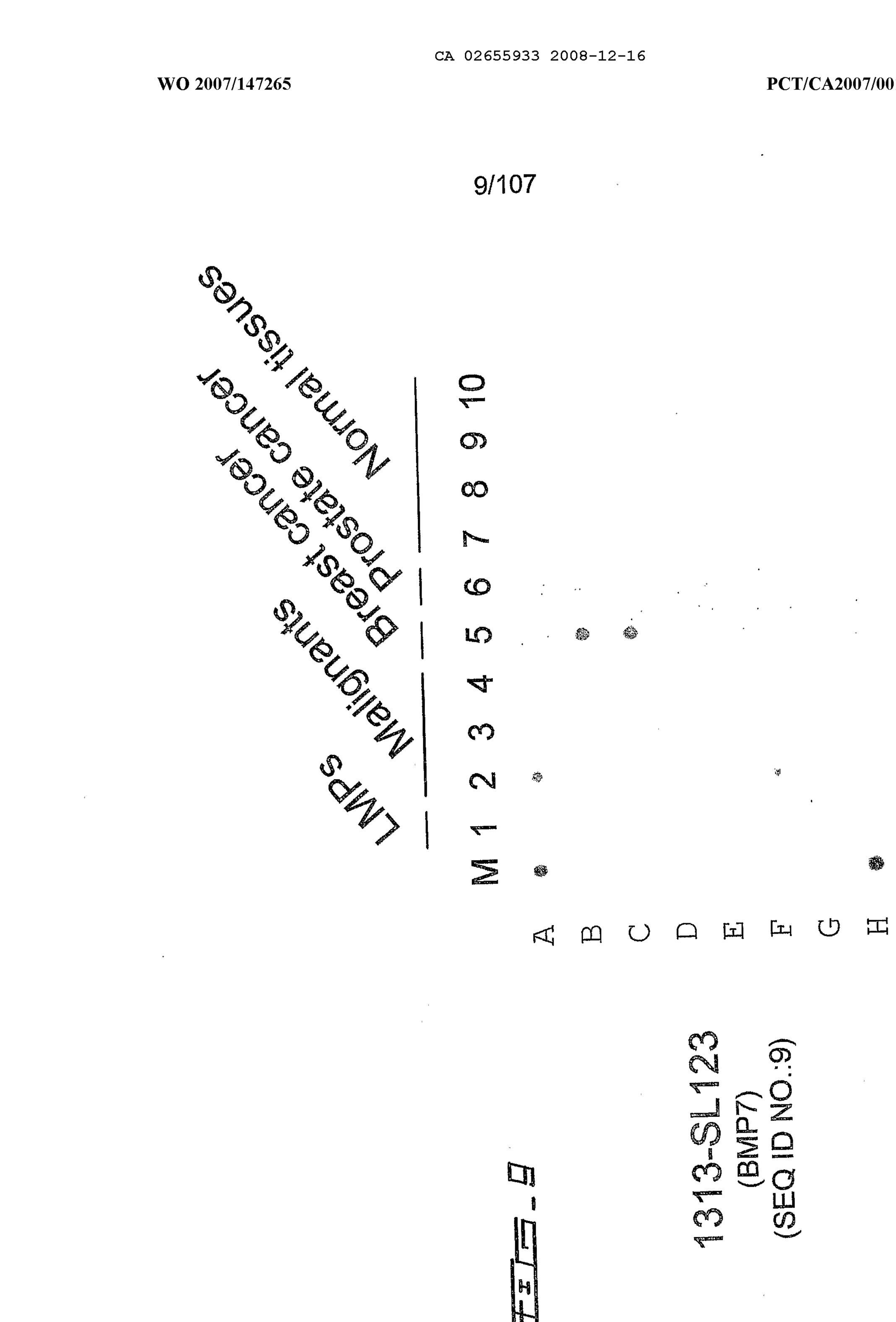


FIG - 9

13-SL123
(BMP7)
(SEQ ID NO:9)

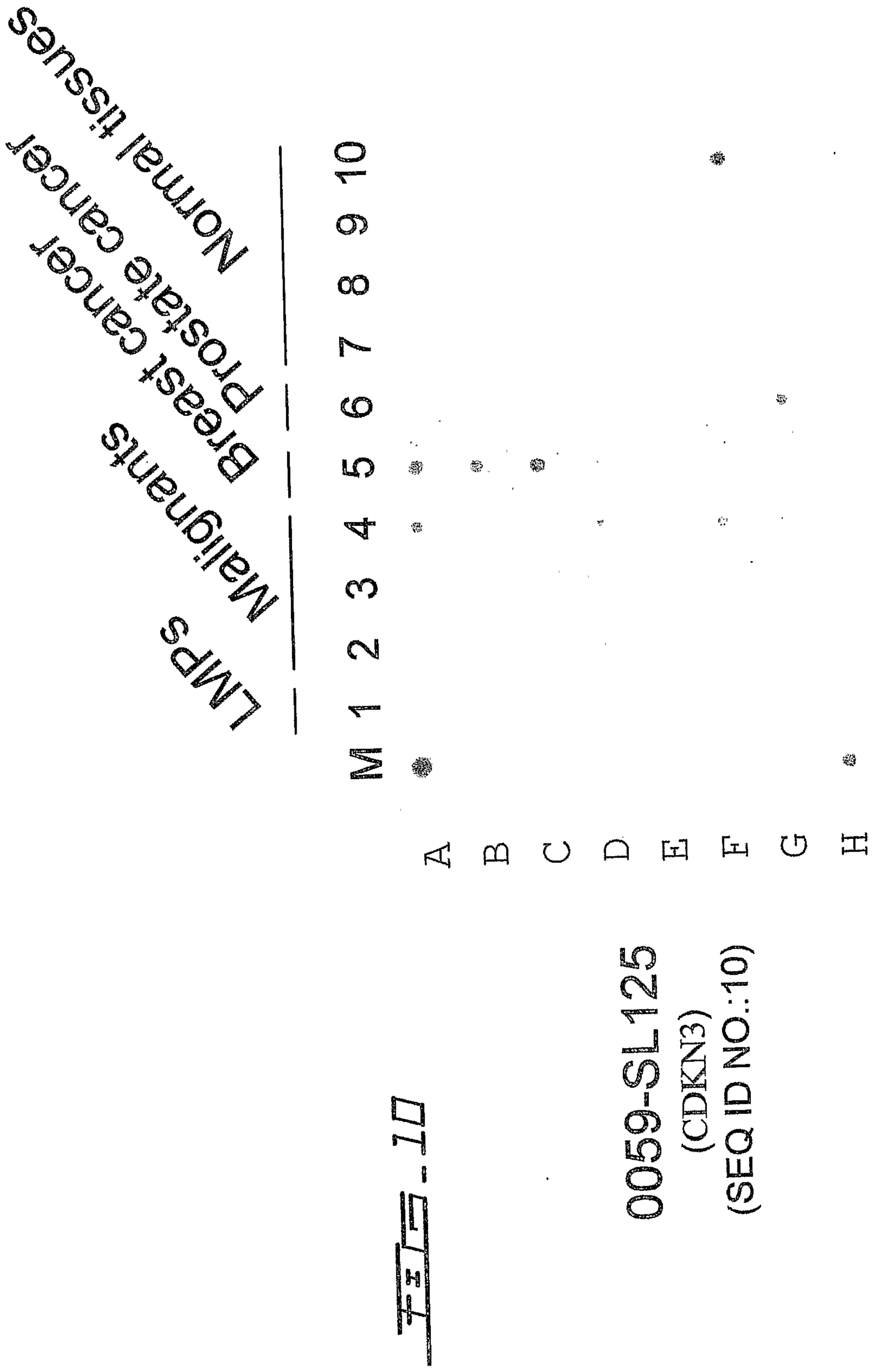
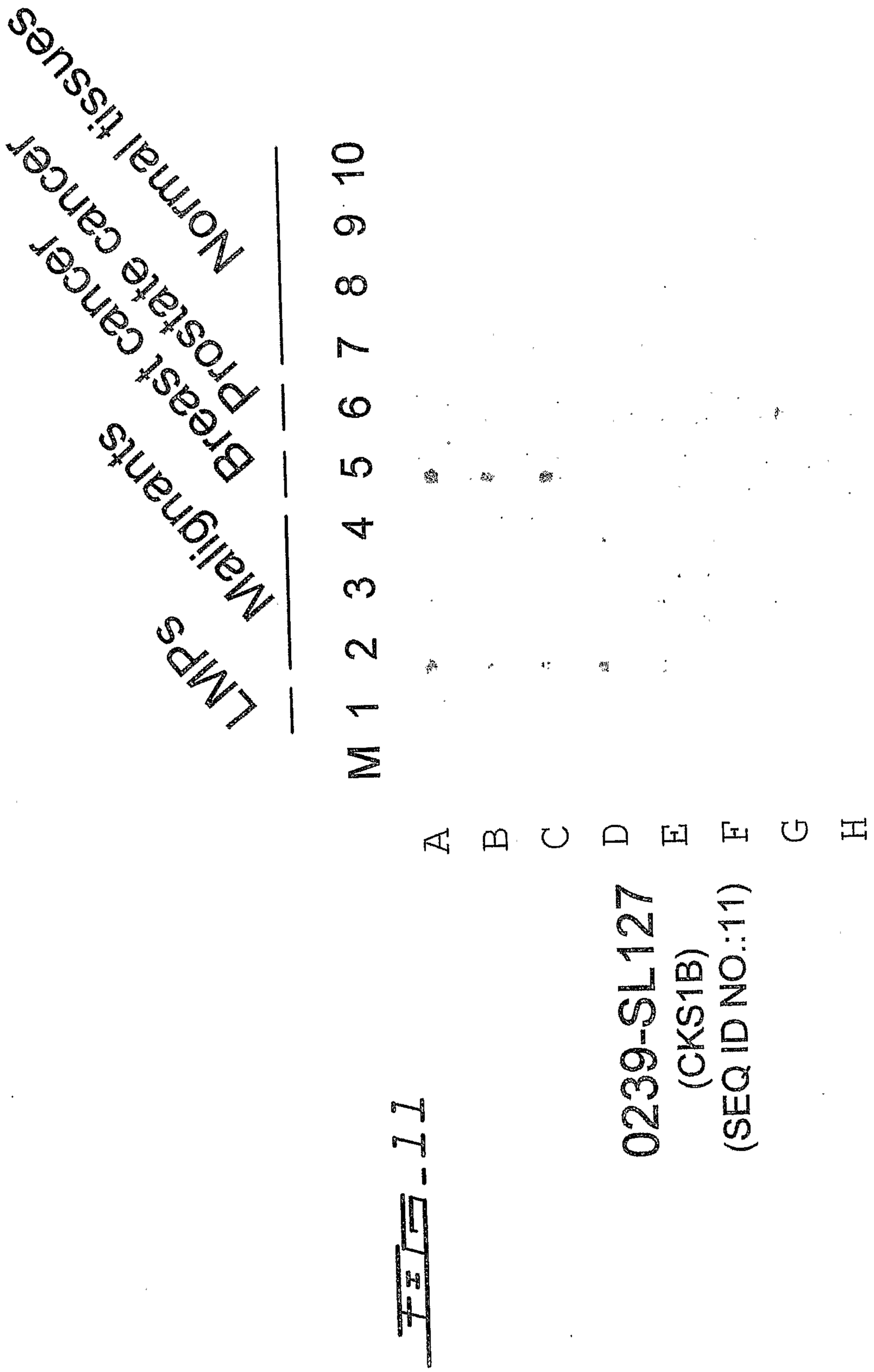
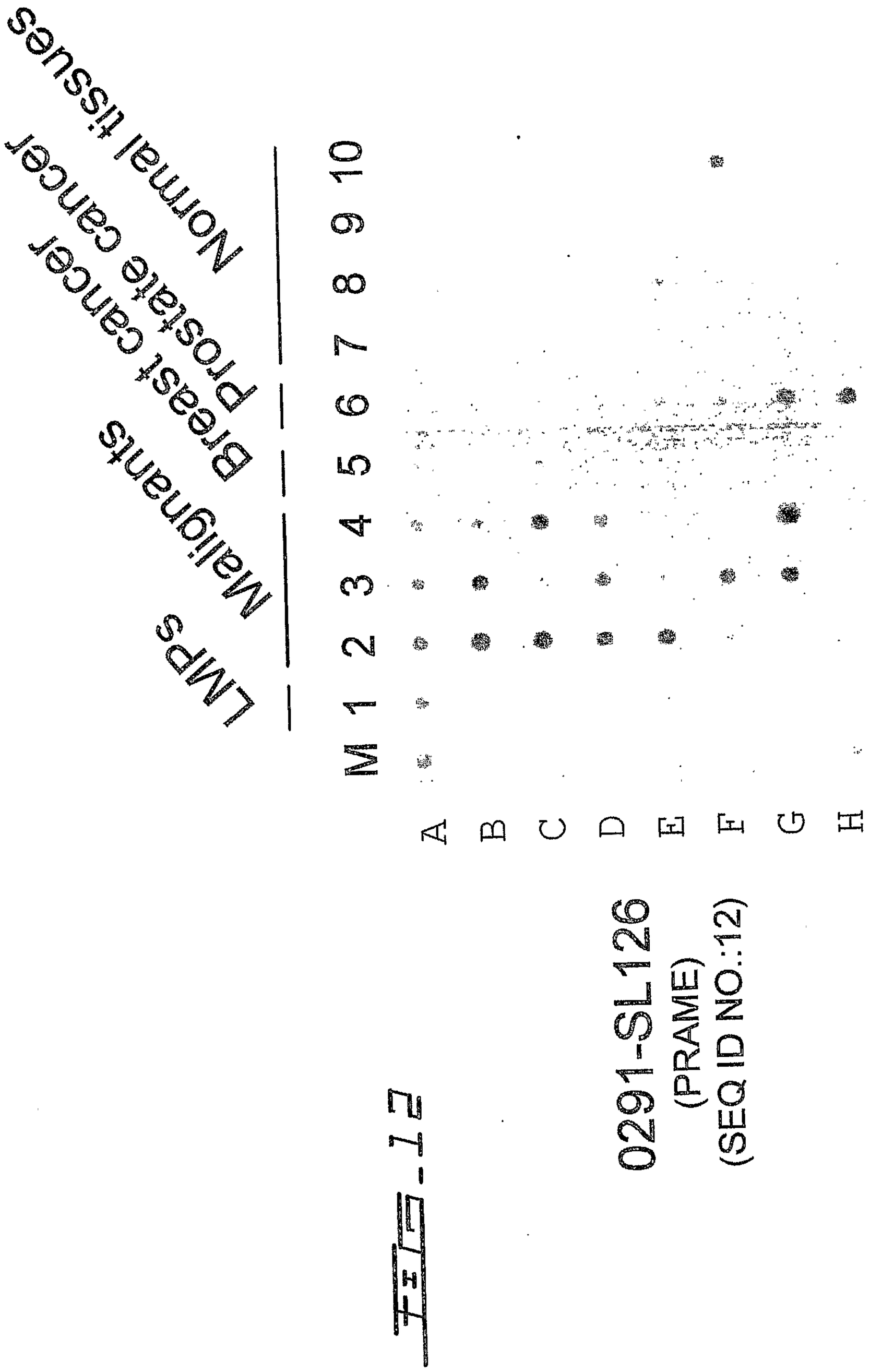
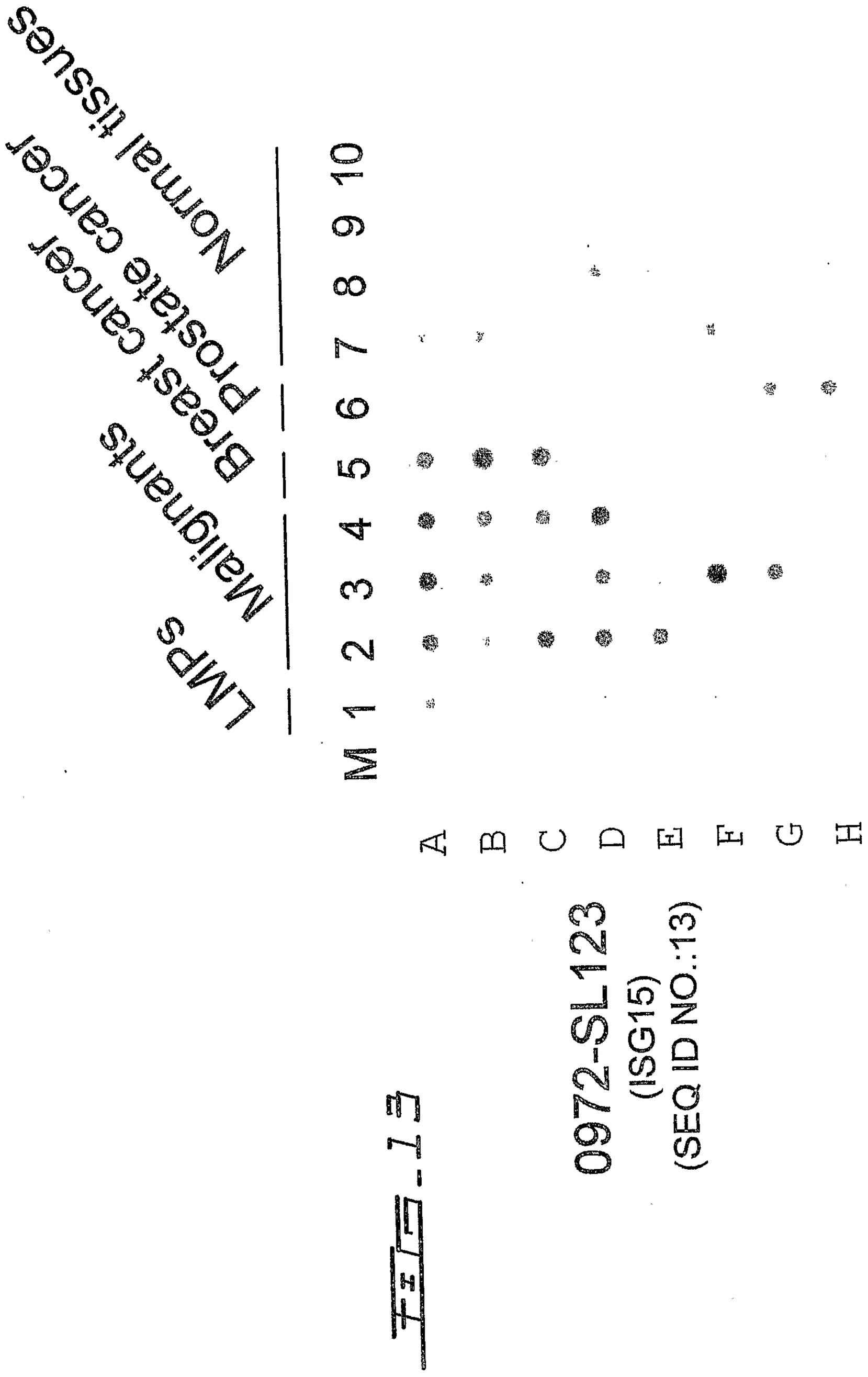

LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissue
M 1 2 3 4 5 6 7 8 9 10
A B C D E E G H
0059-SL125
(CDKN3)
(SEQ ID NO:10)

Fig. 10


sensitissues
Normal tissues
Prostate cancer
Breast cancer
Malignants
LMPs
M 1 2 3 4 5 6 7 8 9 10
A B C D E F G H
FIG. 11
0239-SL127
(CKS1B)
(SEQ ID NO.:11)


sensitivity
Normal tissues
Breast cancer
Prostate cancer
Malignants
LMPS
M 1 2 3 4 5 6 7 8 9 10
A
B
C
D
E
F
G
H
FIG-17
0291-SL126
(PRAME)
(SEQ ID NO:12)


Fig. 13
0972-SL123
(ISG15)
(SEQ ID NO.:13)
M 1 2 3 4 5 6 7 8 9 10
A
B
C
D
E
F
G
H
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues

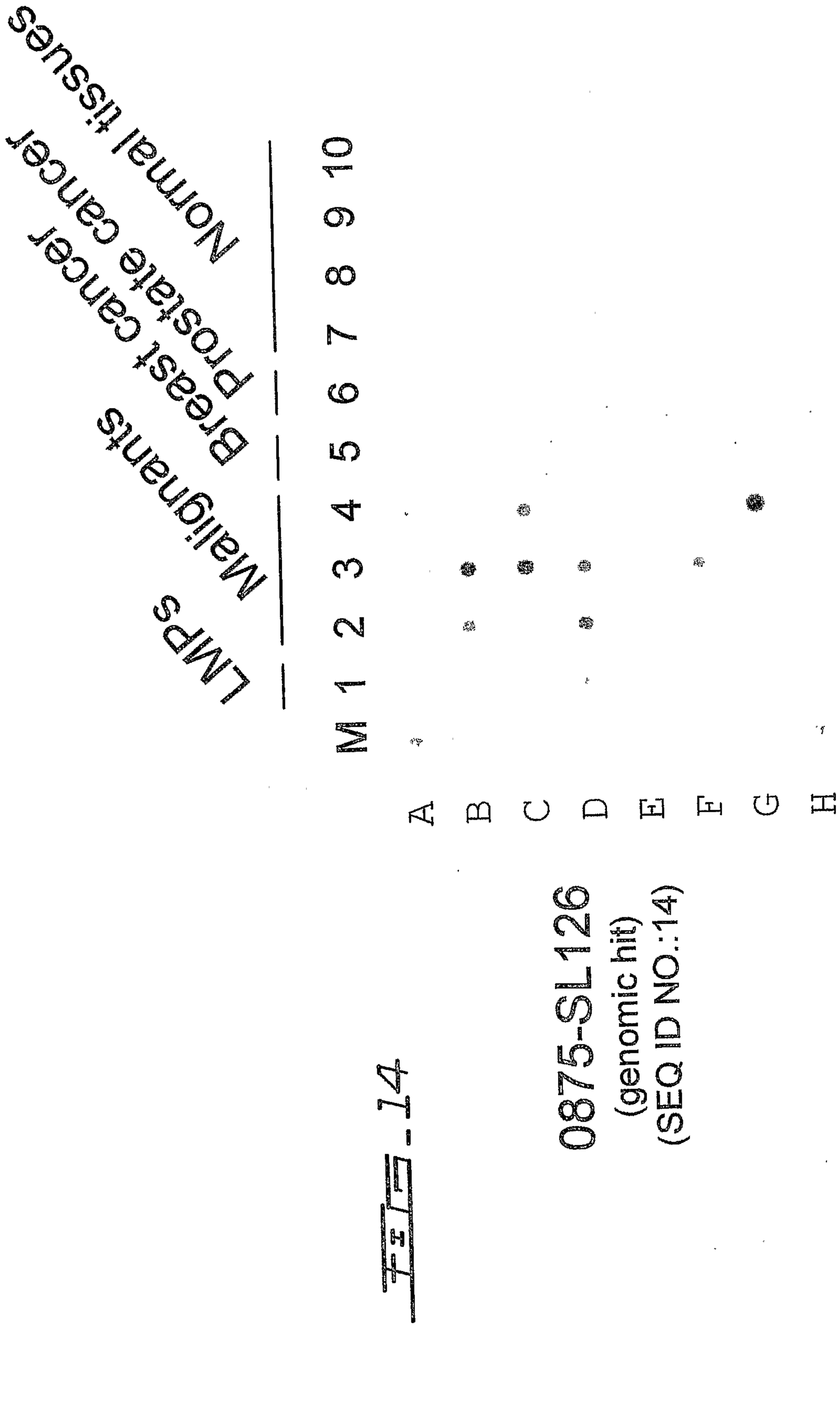
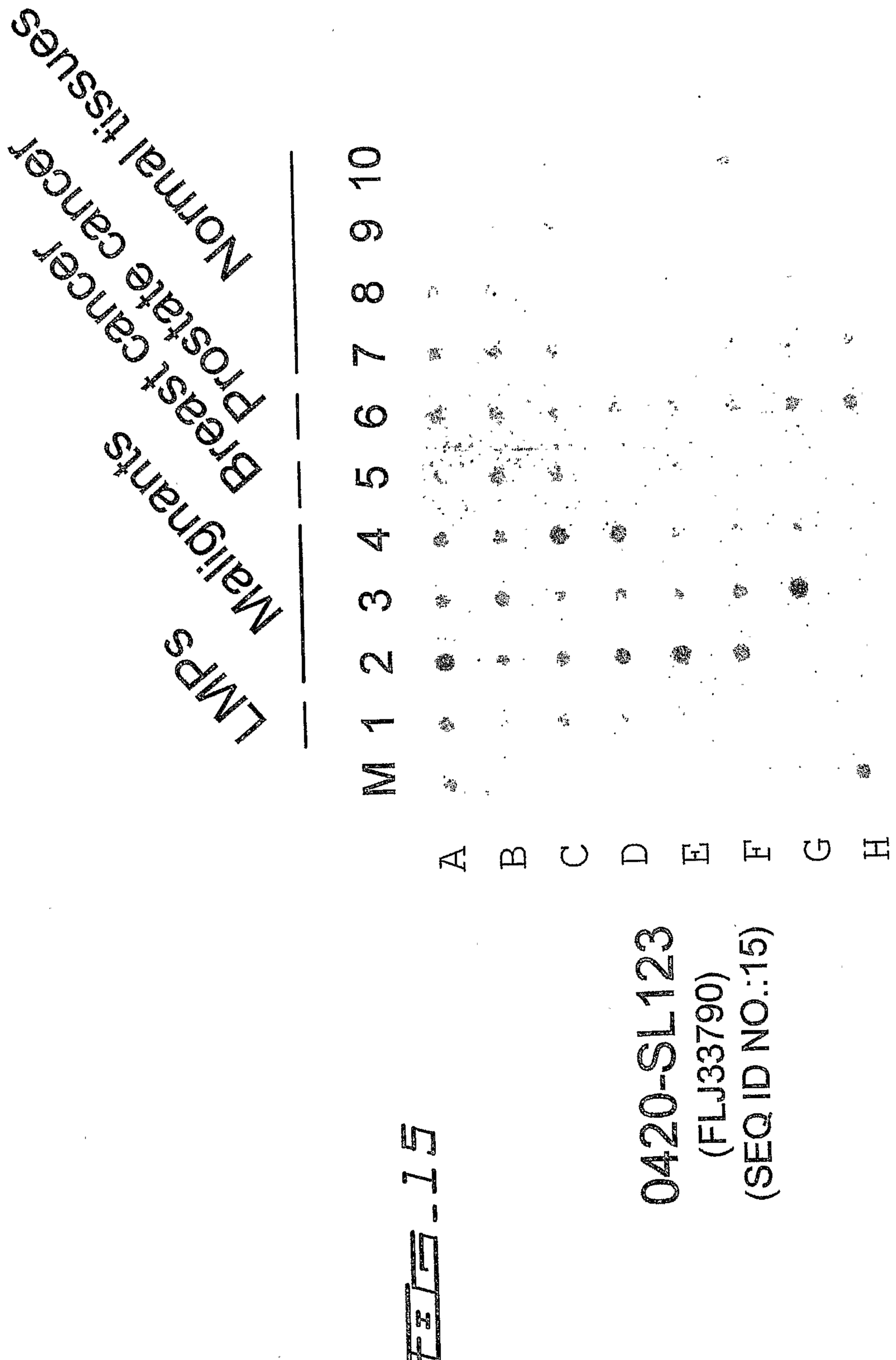
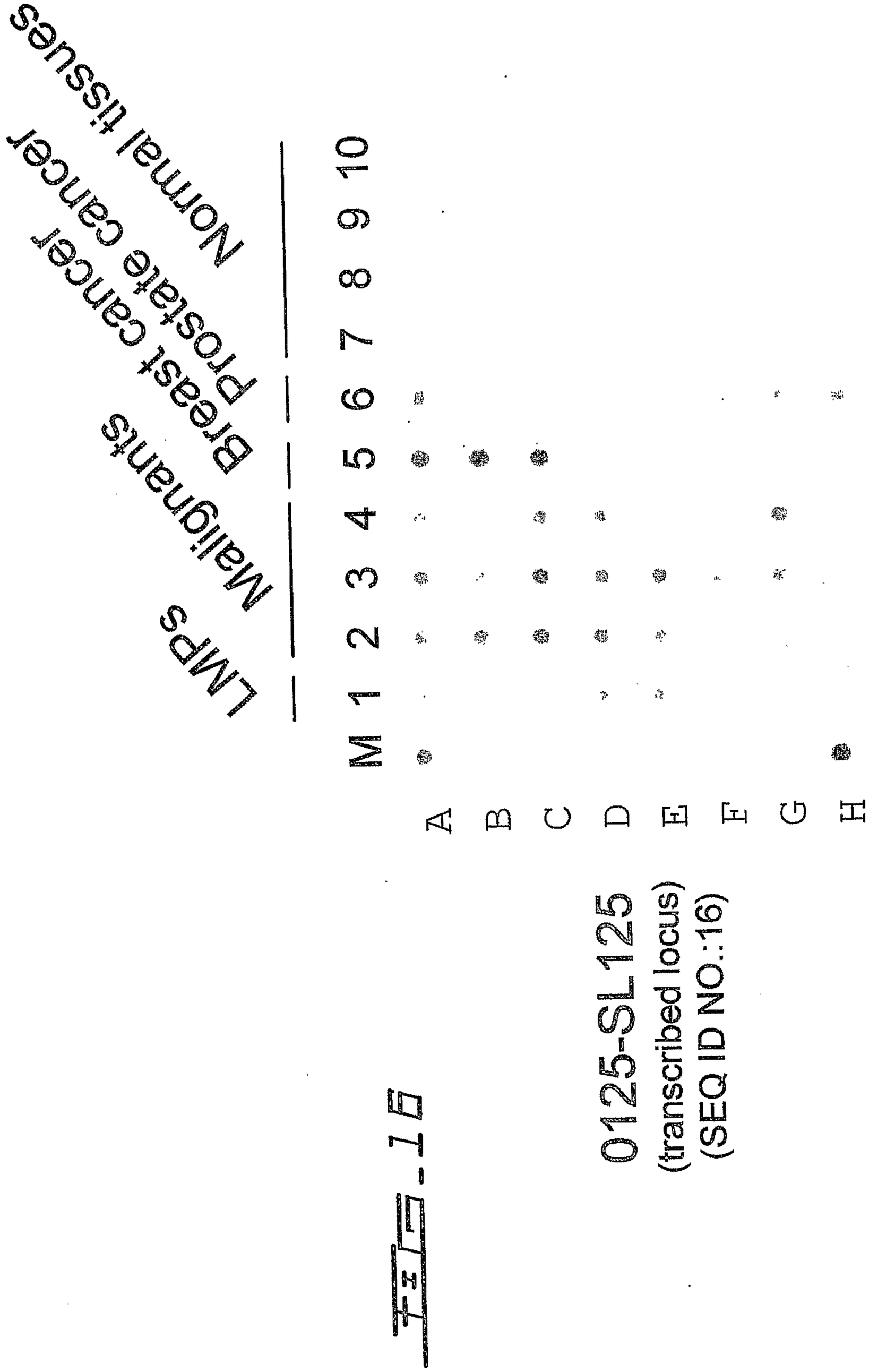

0875-SL126
(genomic hit)
(SEQ ID NO.:14)
A B C D E F G H
M 1 2 3 4 5 6 7 8 9 10
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues

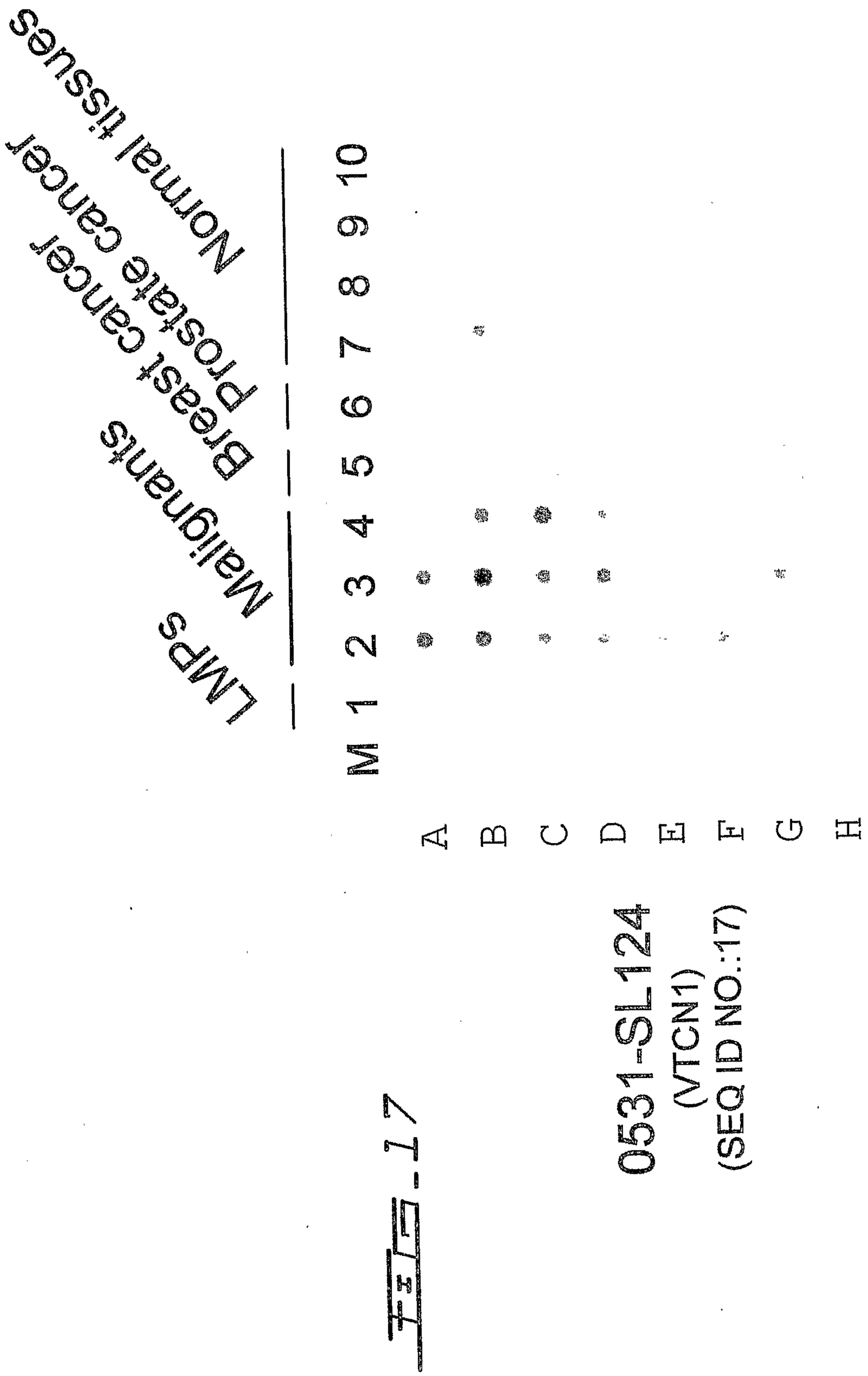
FIG - 14

FIG-15

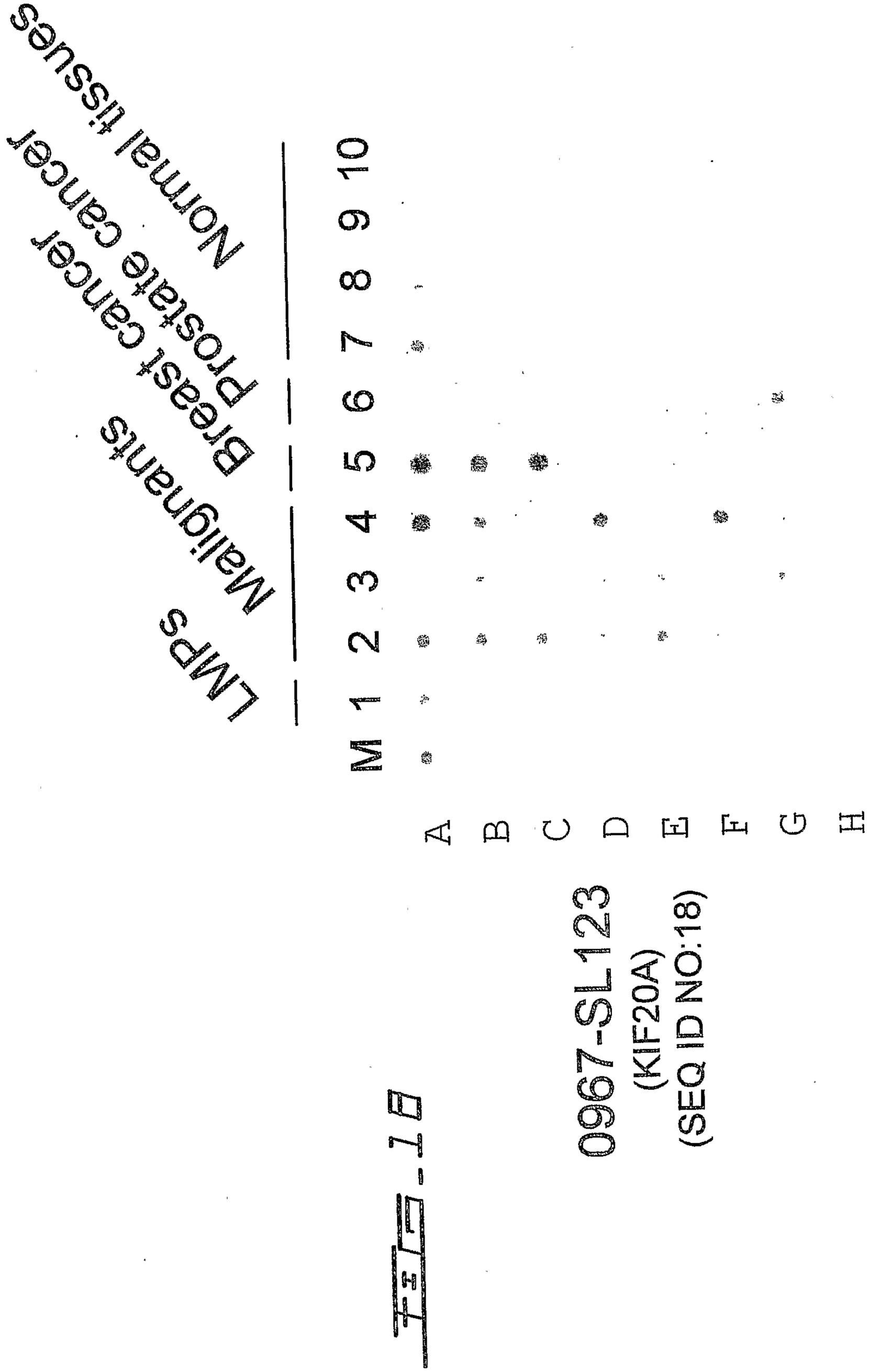
0420-SL123
(FLJ33790)
(SEQ ID NO:15)




sensitivity
Normal tissues
Prostate cancer
Breast cancer
Malignants
LMPS
1 2 3 4 5 6 7 8 9 10
M
A B C D E F G H
0125-SL125
(transcribed locus)
(SEQ ID NO.:16)
FIG. 16


sensit
LMPs
Malignants
Breast cancer
Prostate cancer
Normal th
1 2 3 4 5 6 7 8 9 10
M 1
A B C D E E G H
531-SL124
(VTCN1)
(SEQ ID NO.:17)
_17

FIG


FIG. 18
0967-SL123
(KIF20A)
(SEQ ID NO:18)
A B C D E F G H
M 1 2 3 4 5 6 7 8 9 10
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues

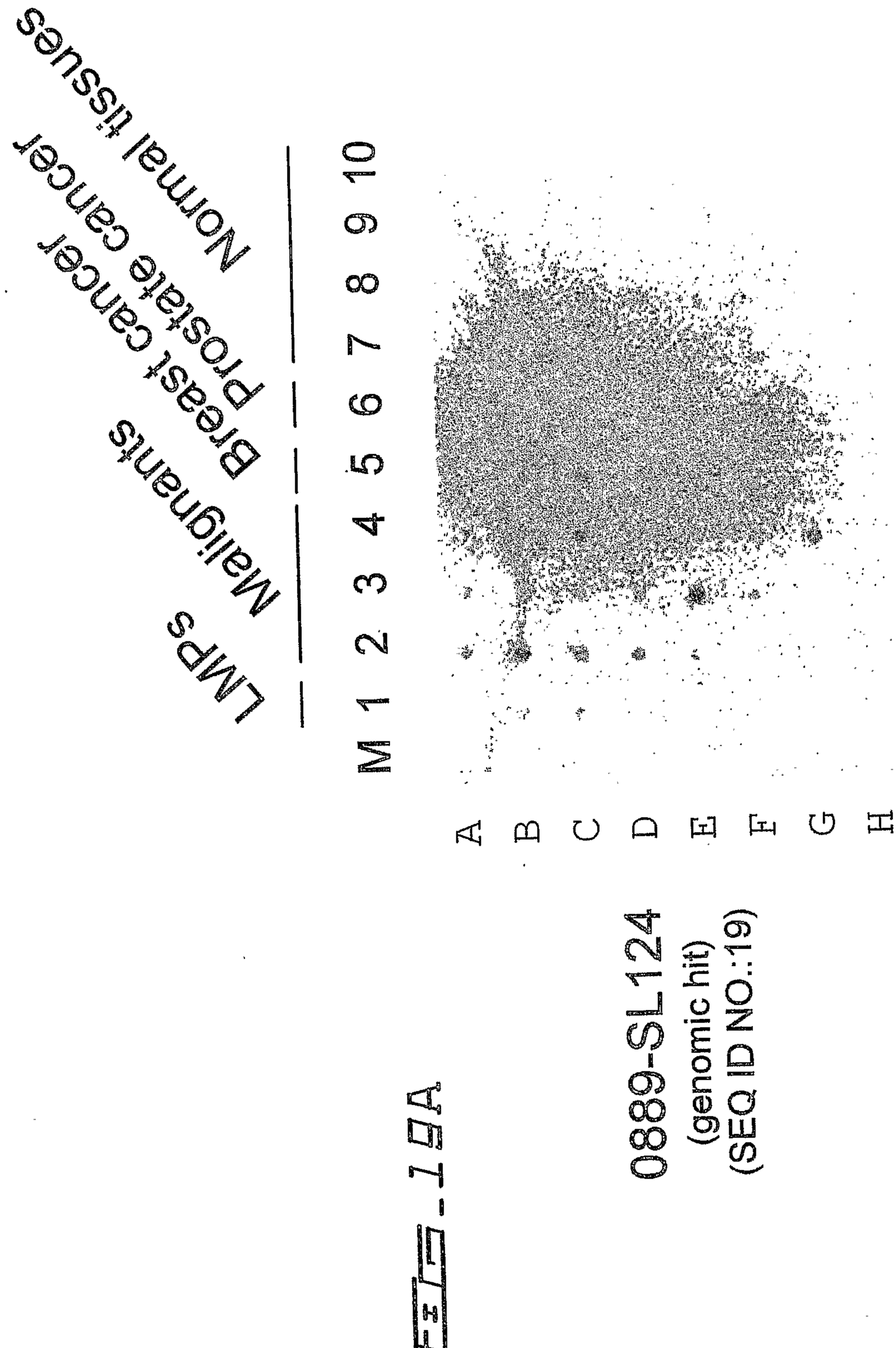
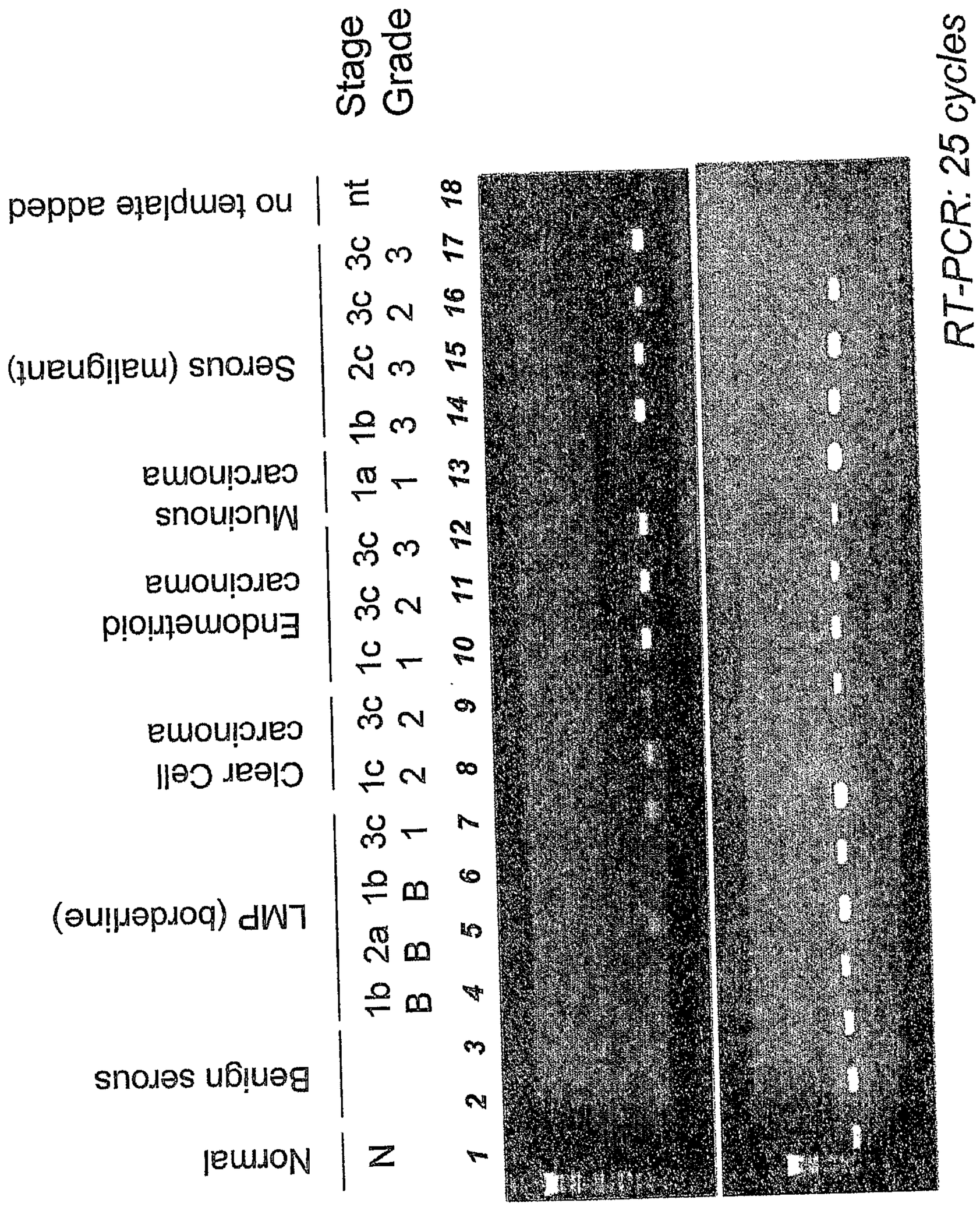


FIG. 19A

0889-SL124
(genomic hit)
(SEQ ID NO.:19)


Stage
Grade
Endometrioid carcinoma
Mucinous carcinoma
Serous (malignant)
no template added
Normal
Benign serous
LMP (borderline)
Clear Cell carcinoma
N
B
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
1c 3c 3c 1a 1b 2c 3c 3c nt
1b 2a 1b 3c 1c 3c
RT-PCR: 25 cycles
Panel A
SEQ. ID. NO. 19
0889-SL124
(Genomic hit)
Panel B
KCNMB2
(Hs.478368)
FIG - 19B

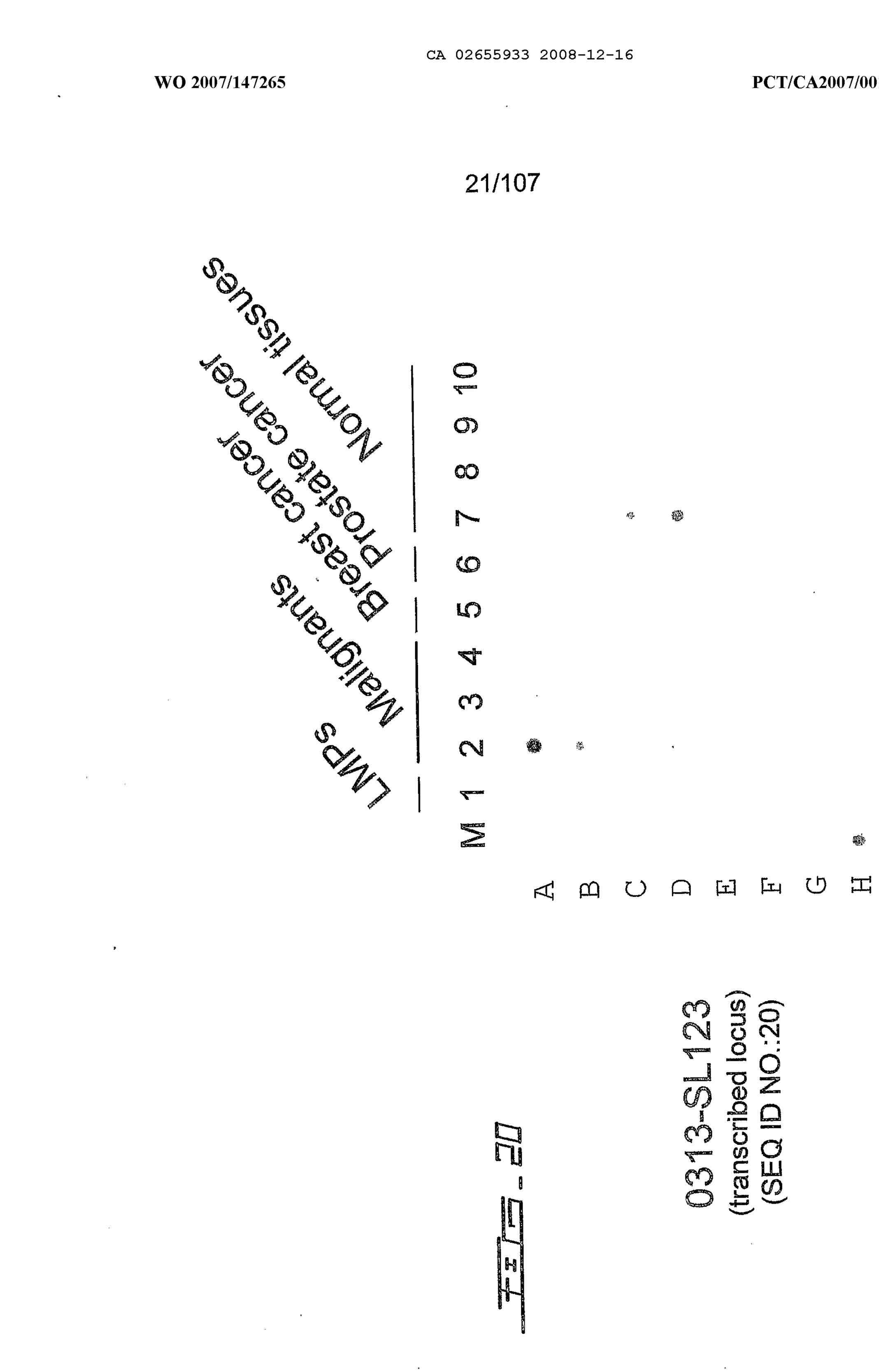
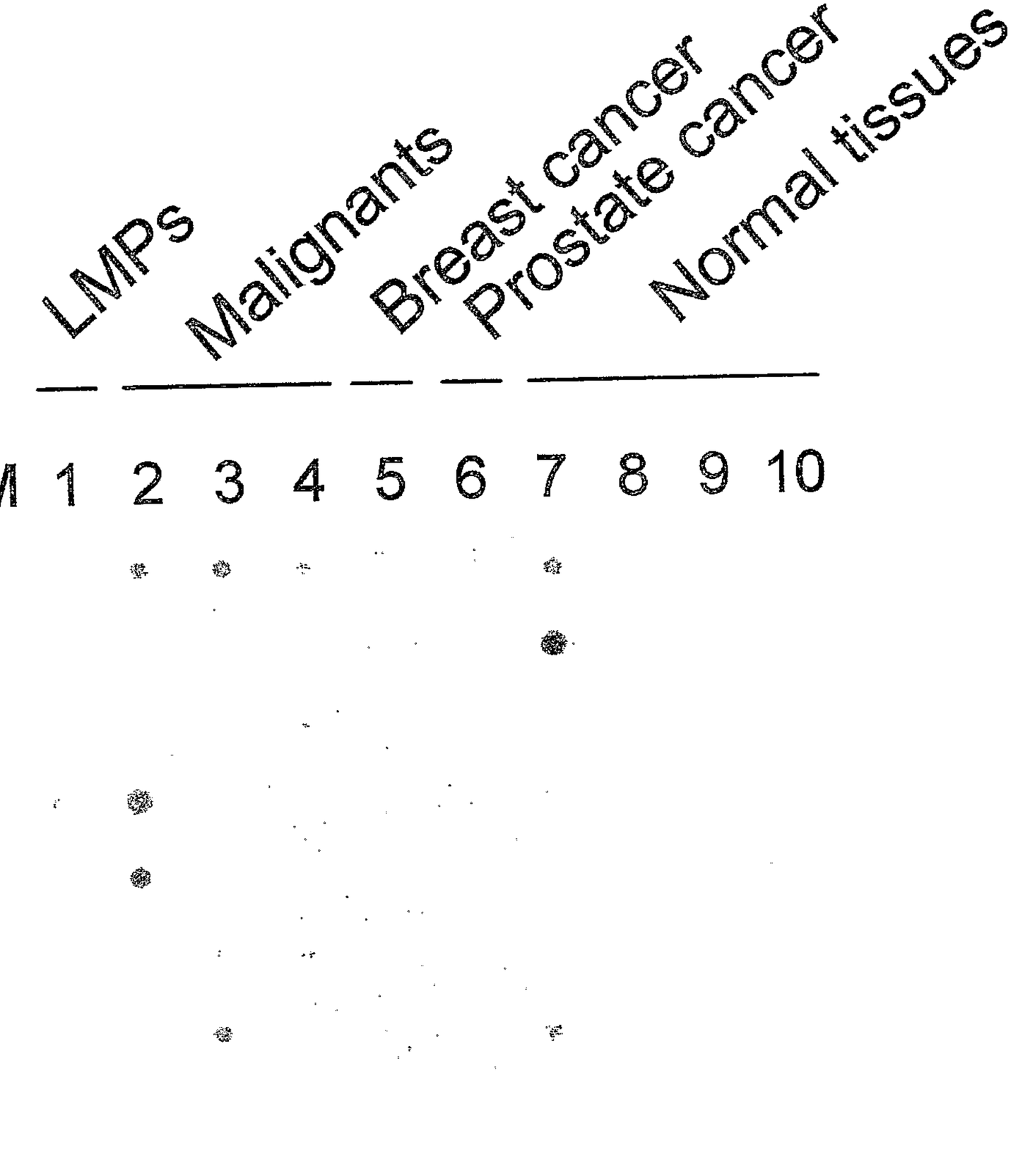

Fig. 20
0313-SL123
(transcribed locus)
(SEQ ID NO.:20)
A
B
C
D
E
F
G
H
1 2 3 4 5 6 7 8 9 10
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues

FIG_21



1134-SL126
(CXCL11)
(SEQ ID NO.:21)

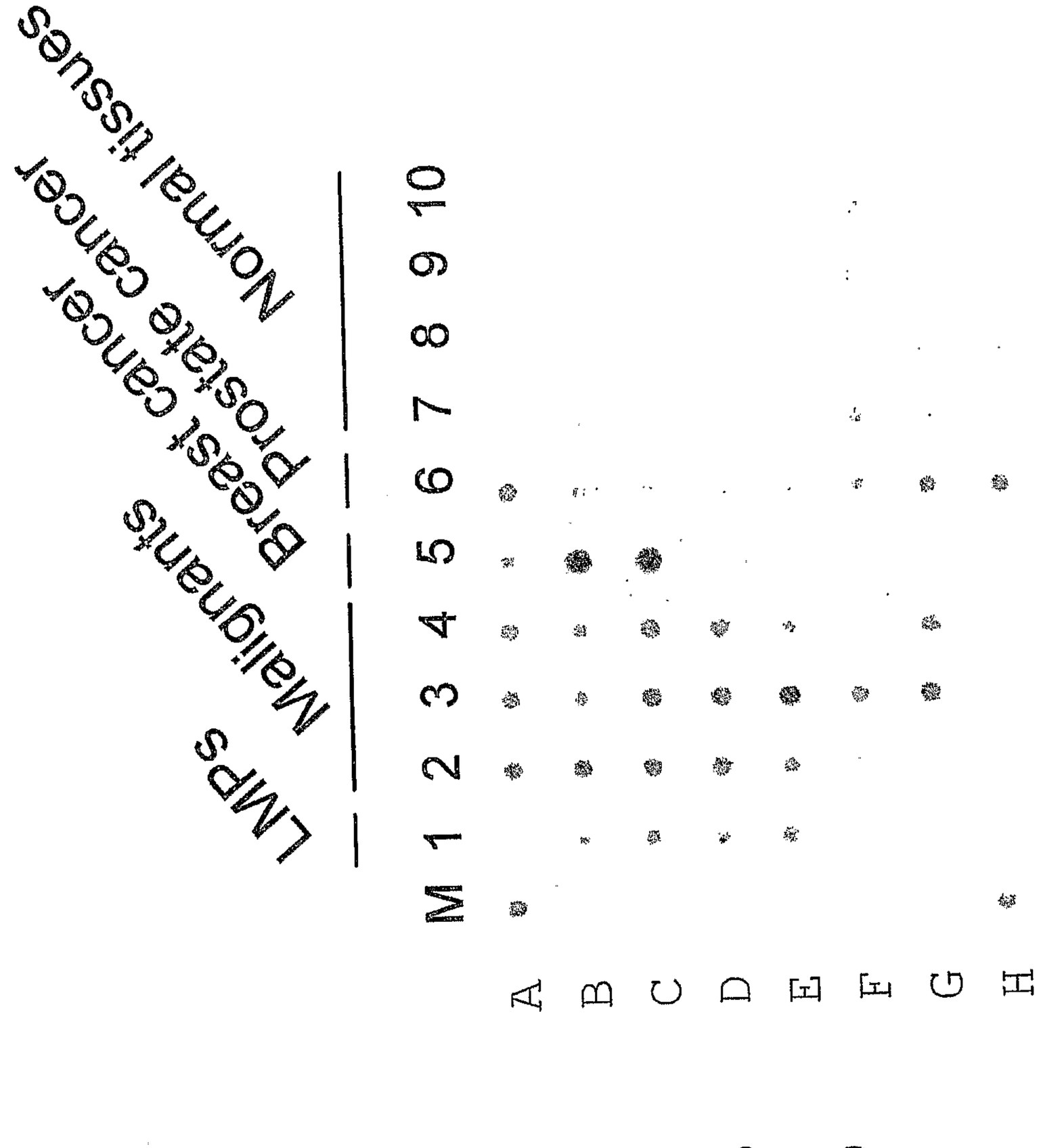

0488-SL123
(genomic hit)
(SEQ ID NO.:22)
Malignants
Breast cancer
Prostate cancer
Normal tissues
LMPs
1 2 3 4 5 6 7 8 9 10
A B C D E E G H
M

Fig. 22

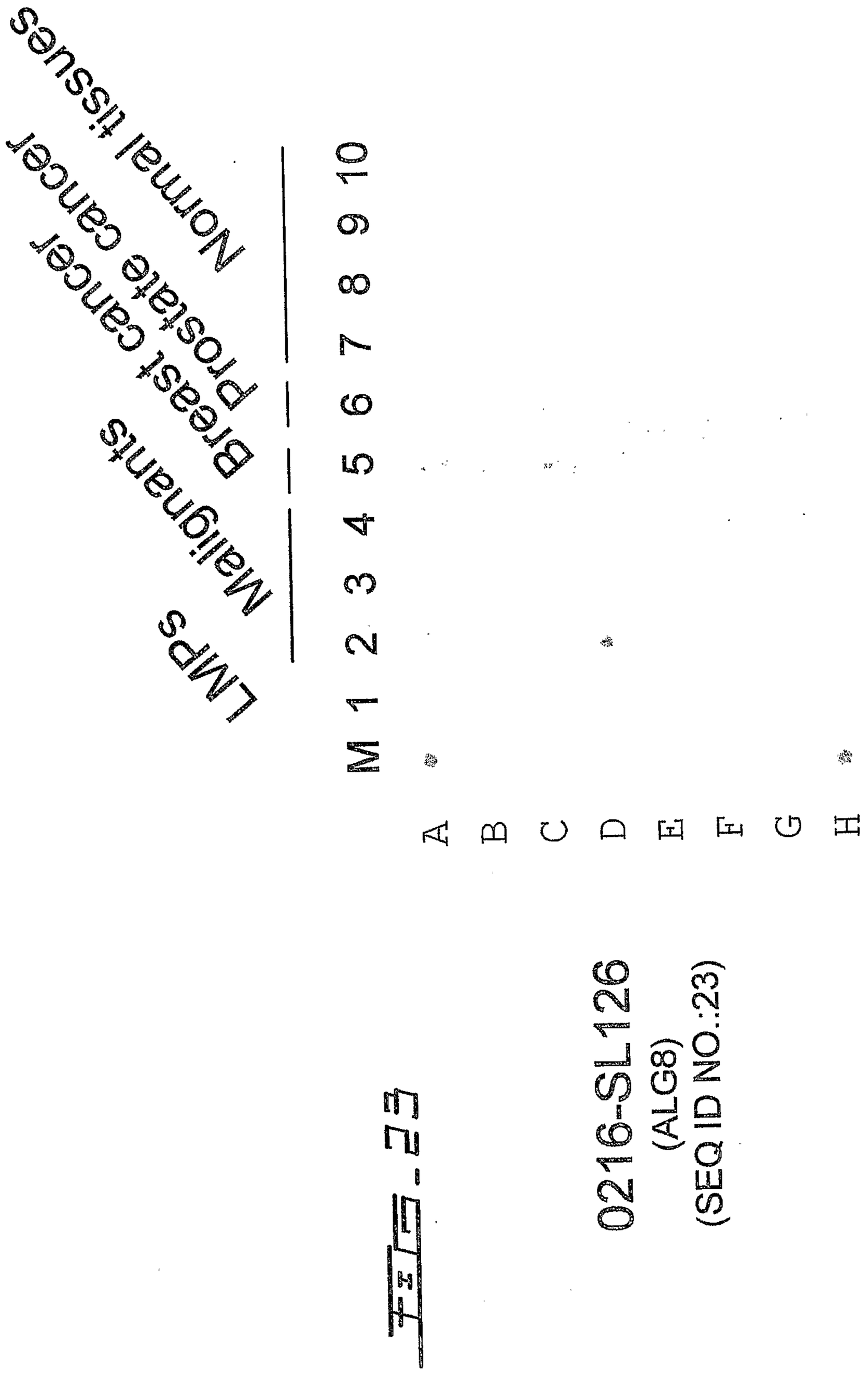


FIG. 23

021616-SL126
(ALG8)
(SEQ ID NO.:23)

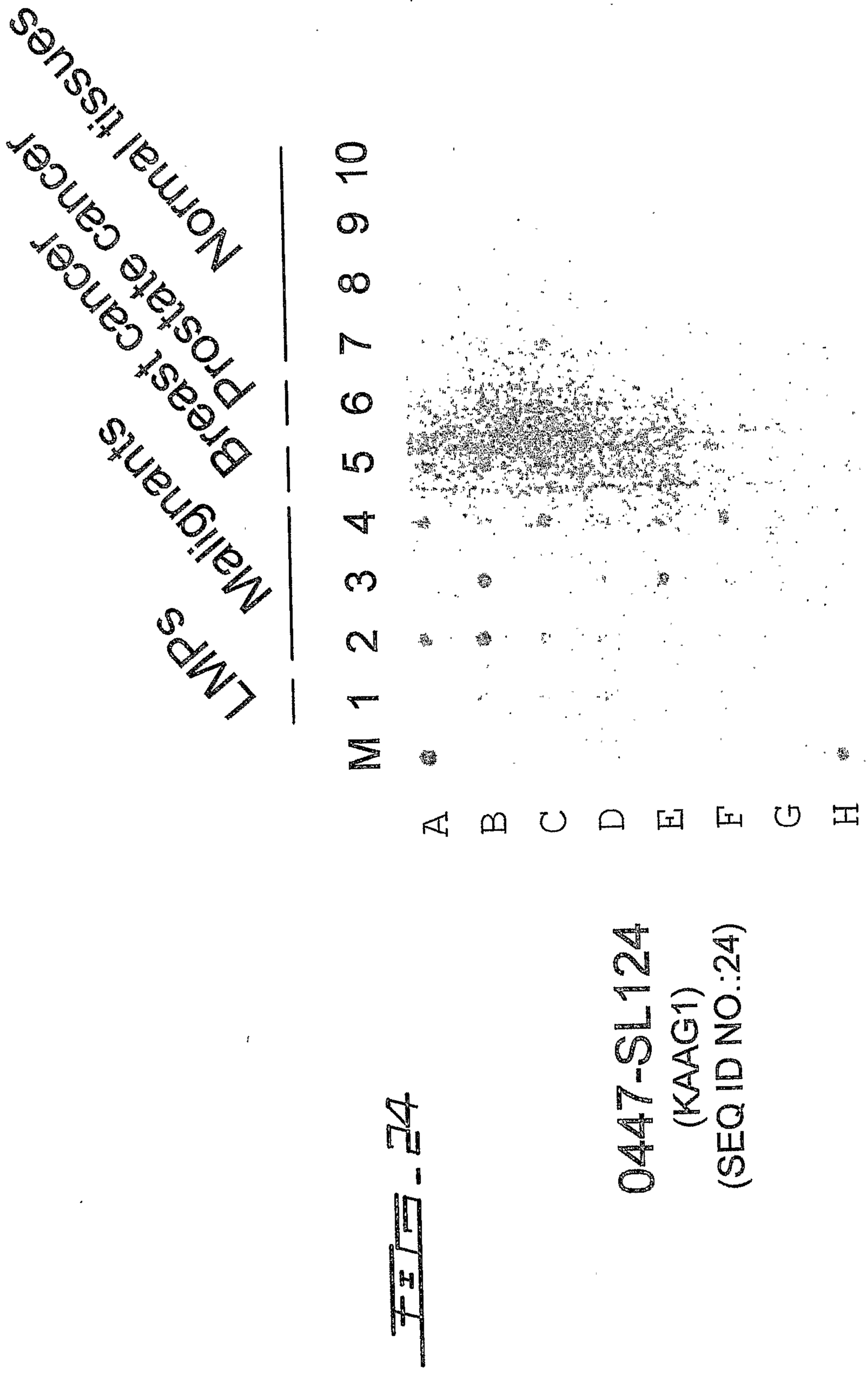
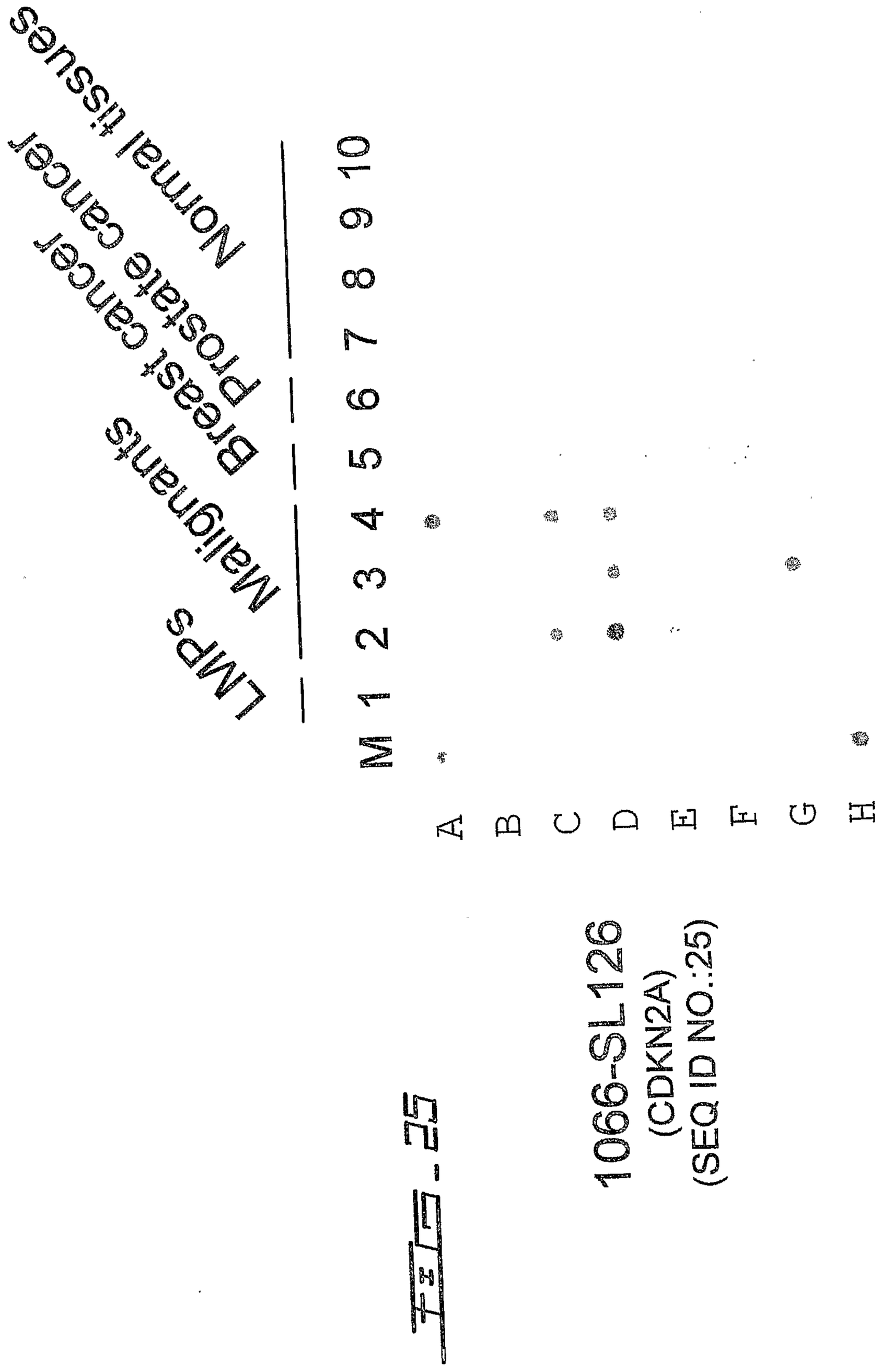


FIG. 24

04447-SL124
(KAAG1)
(SEQ ID NO.:24)

FIG - 25

1066-SL126
(CDKN2A)
(SEQ ID NO.:25)



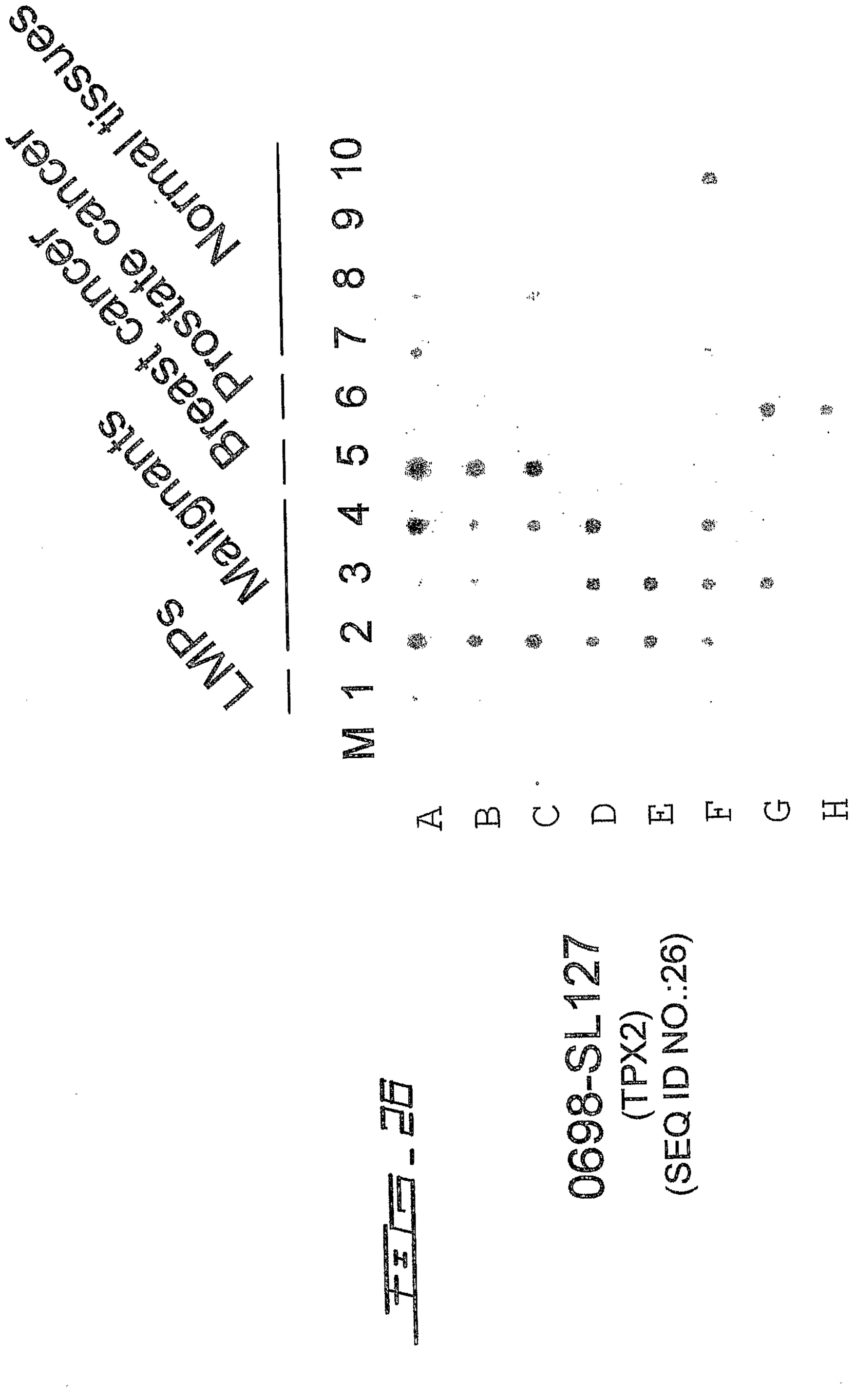


FIG - 2B

0698-SL127
(TPX2)
(SEQ ID NO.:26)

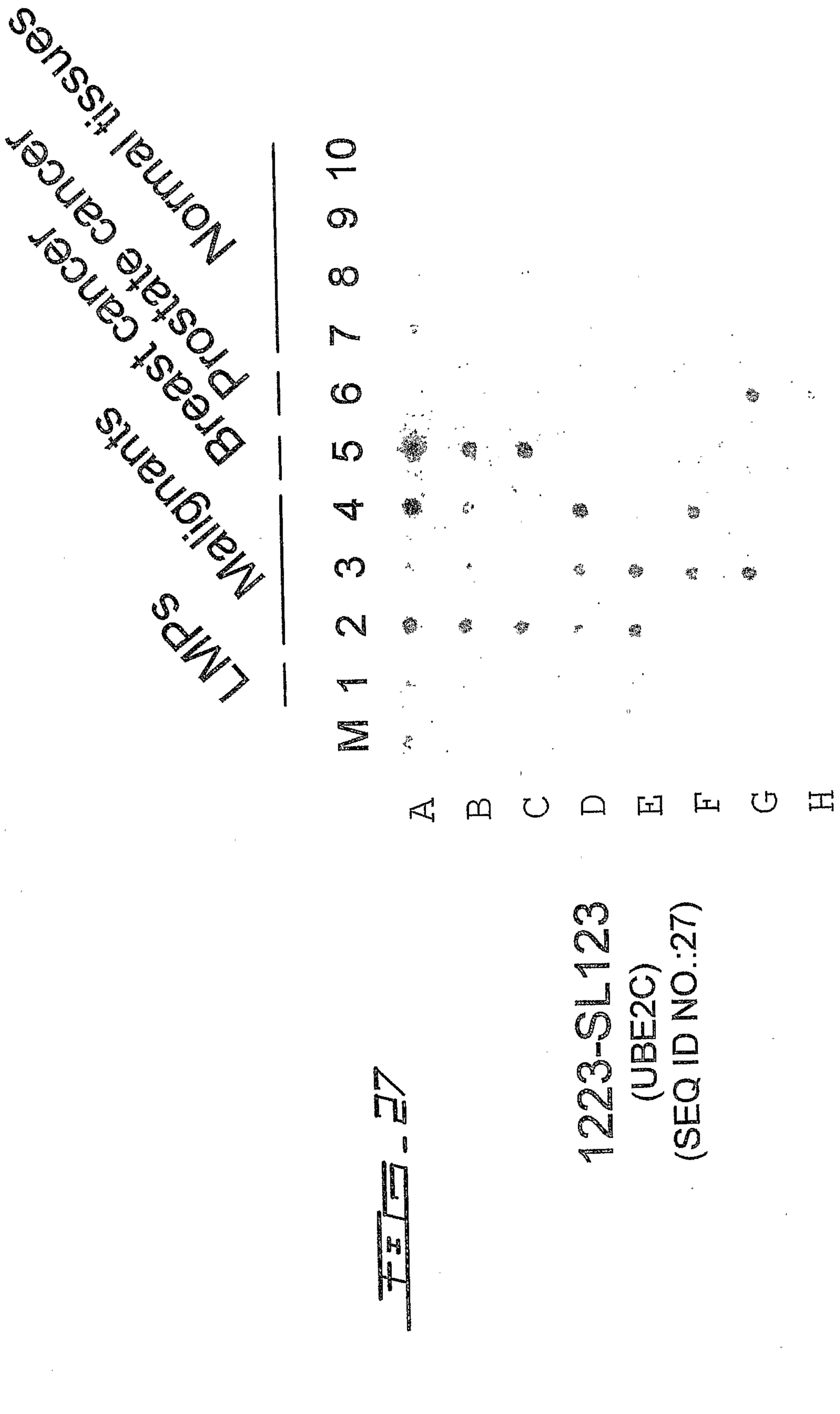

1223-SL123
(UBE2C)
(SEQ ID NO.:27)
Malignants
Breast cancer
Prostate cancer
Normal tissues
LMPS
M 1 2 3 4 5 6 7 8 9 10
A
B
C
D
E
F
G
H

FIG - 27

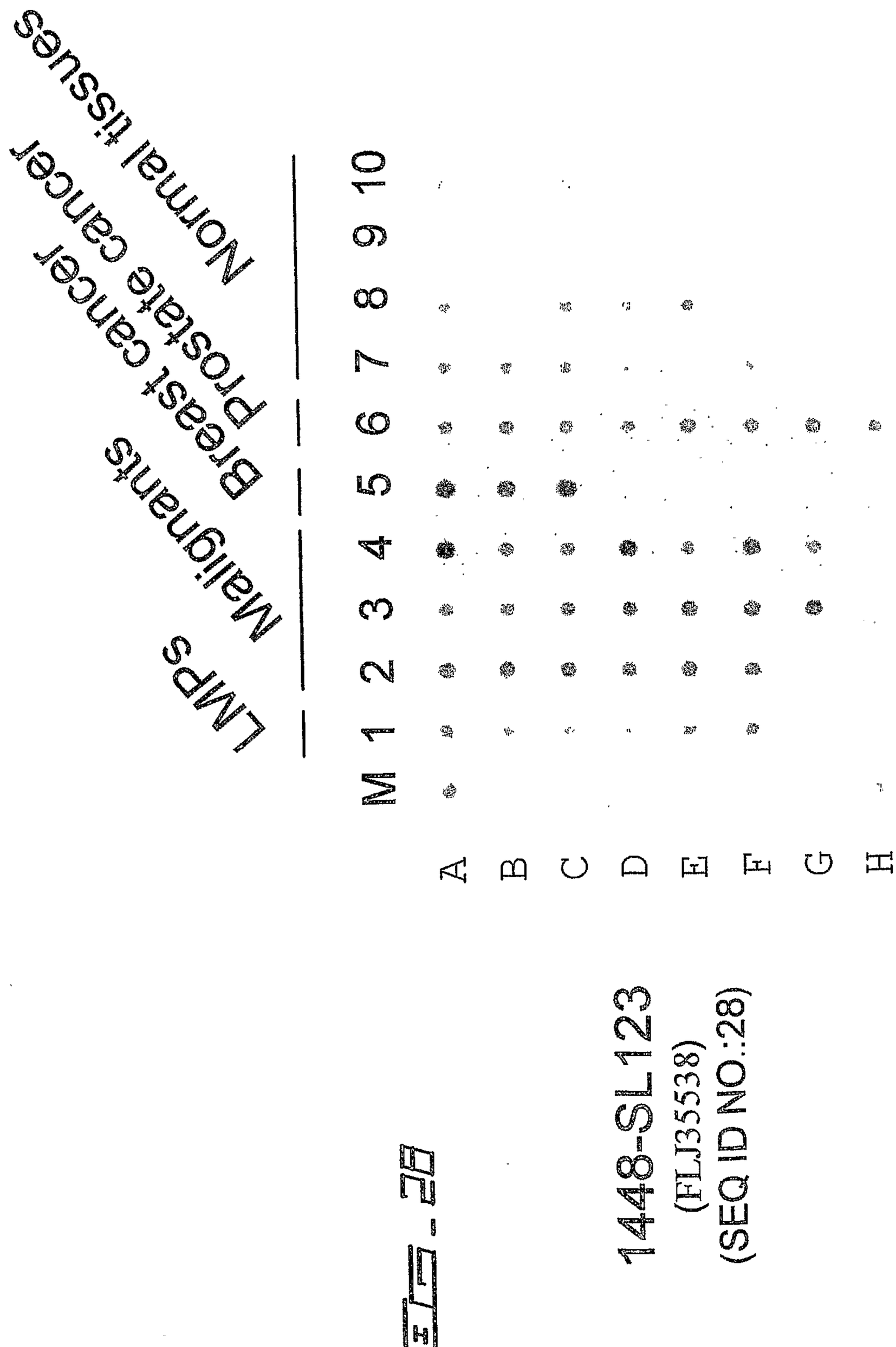


FIG. 28

1448-SL123
(FLJ35538)
(SEQ ID NO:28)

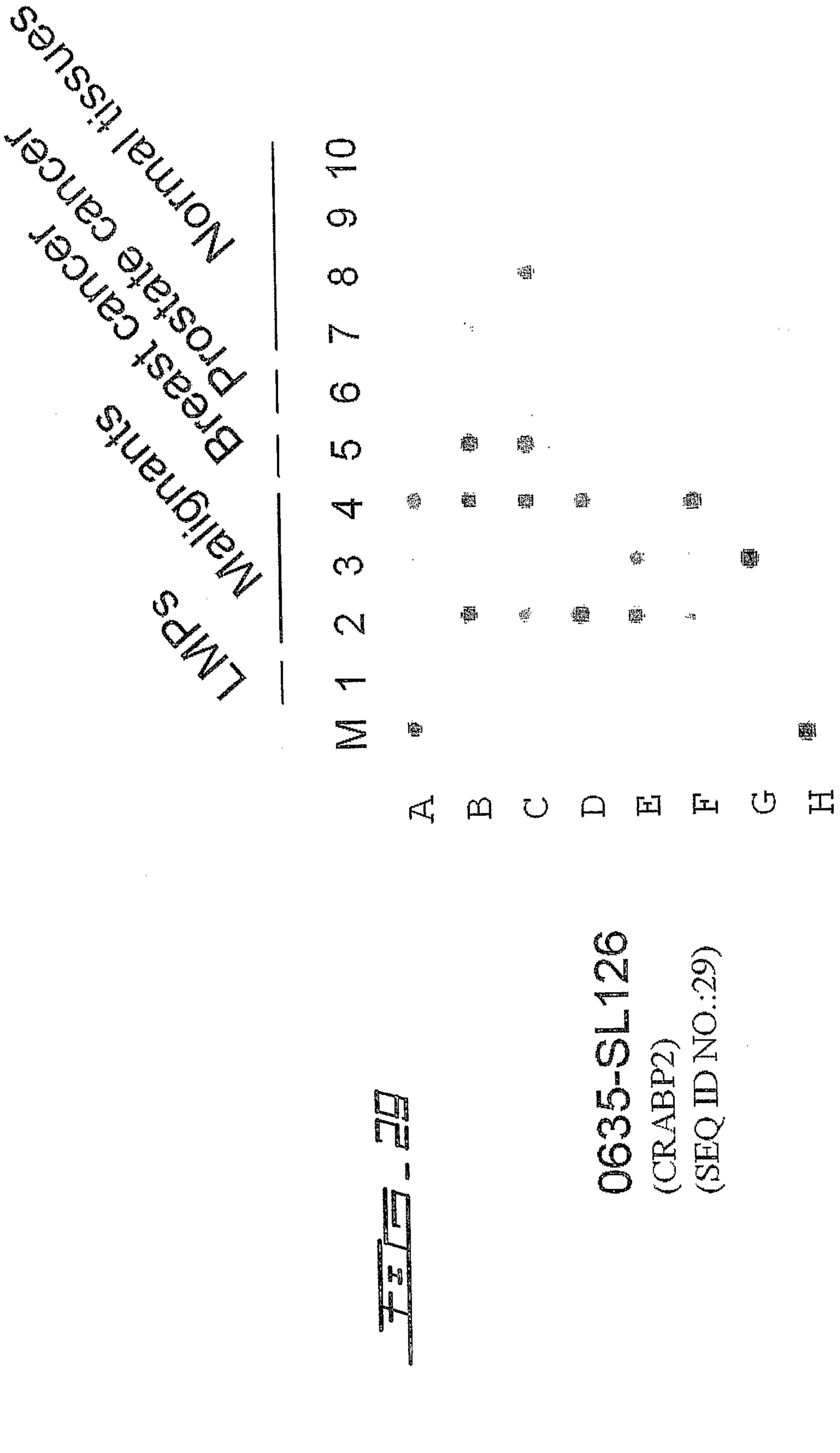
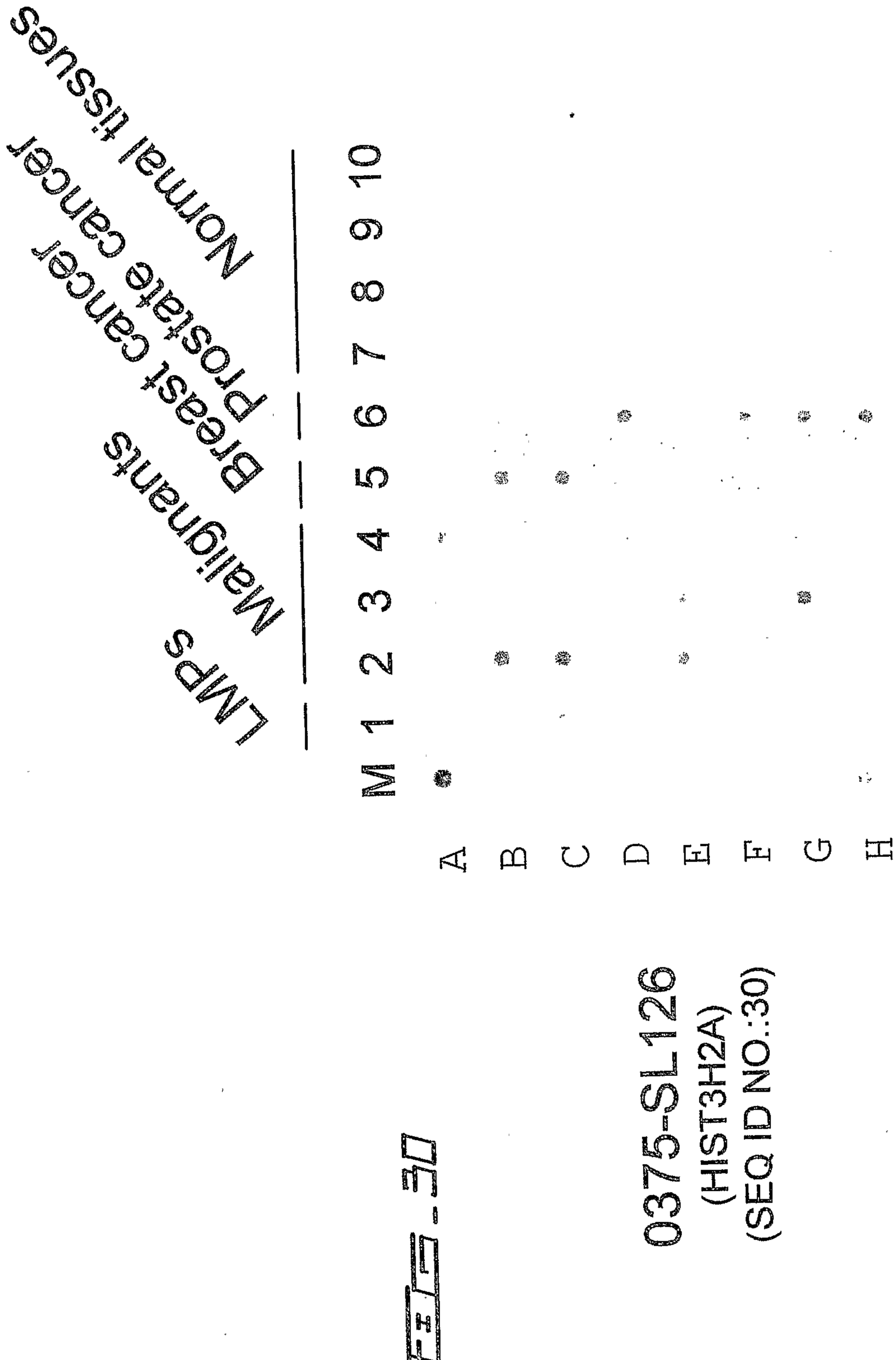

Sensitivity
Normal tissues
Prostate cancer
Breast cancer
Malignants
LMPs
M 1 2 3 4 5 6 7 8 9 10
A
B
C
D
E
F
G
H
0635-SL126
(CRABP2)
(SEQ ID NO:29)
FIG. 29

FIG. 31

0375-SL126
(HIST3H2A)
(SEQ ID NO.:30)



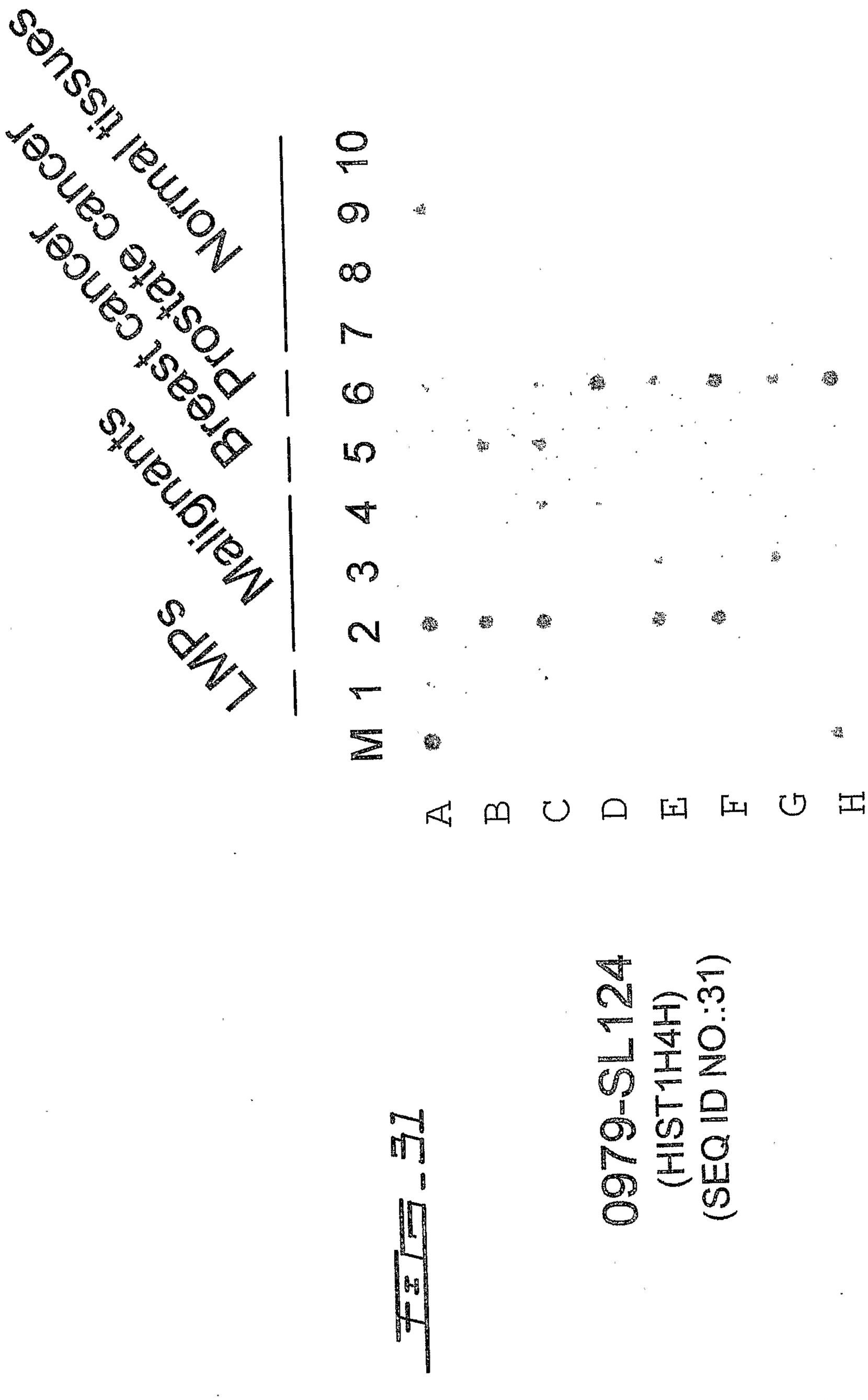

sensskuss
Normal tiss
Prostate cancer
Breast cancer
Malignants
LMPS
1 2 3 4 5 6 7 8 9 10
M
A
B
C
D
E
F
G
H
0979-SL124
(HIST1H4H)
(SEQ ID NO:31)

Fig. 31

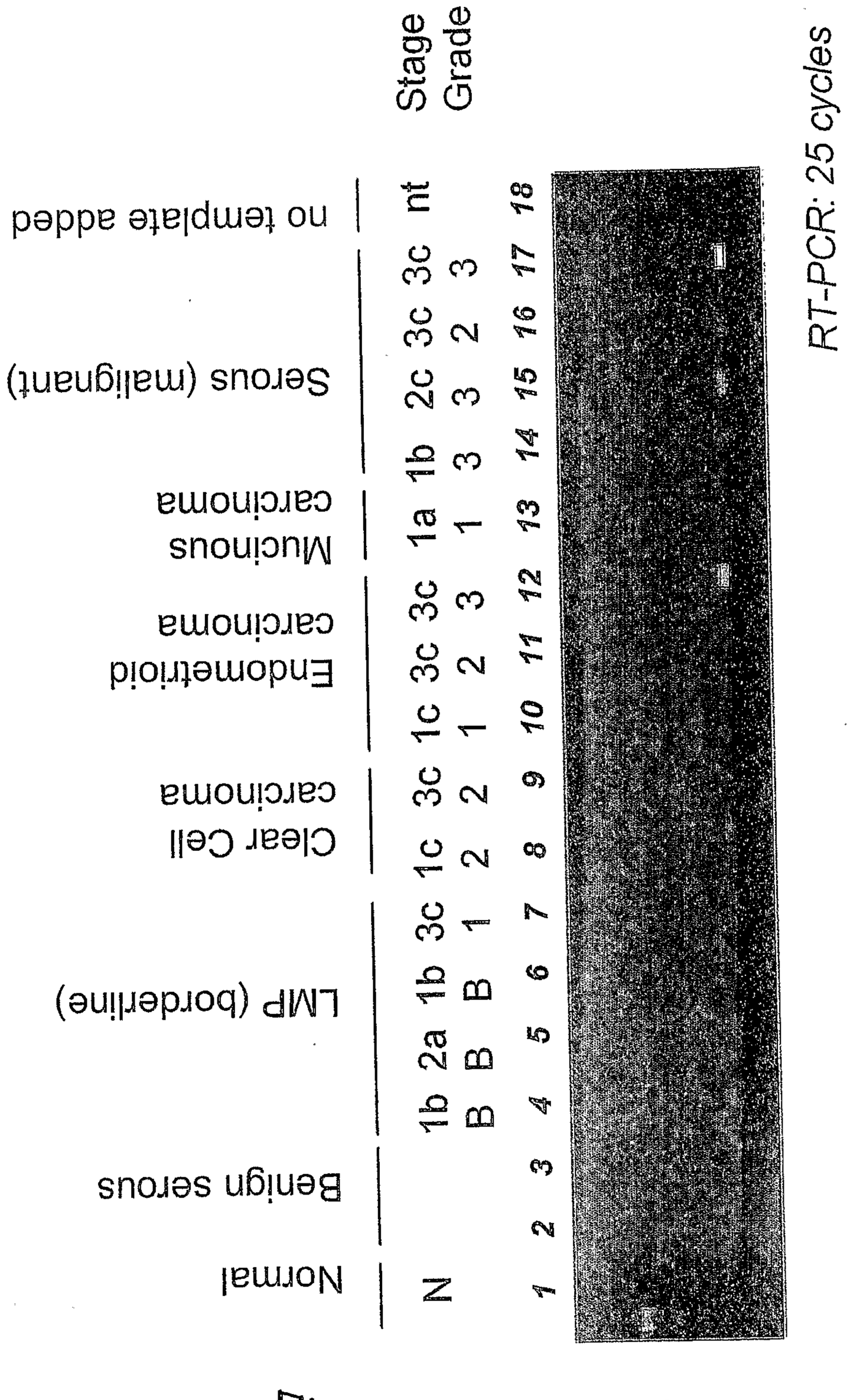


FIG - 32

1133-SL127
(HOX D3)

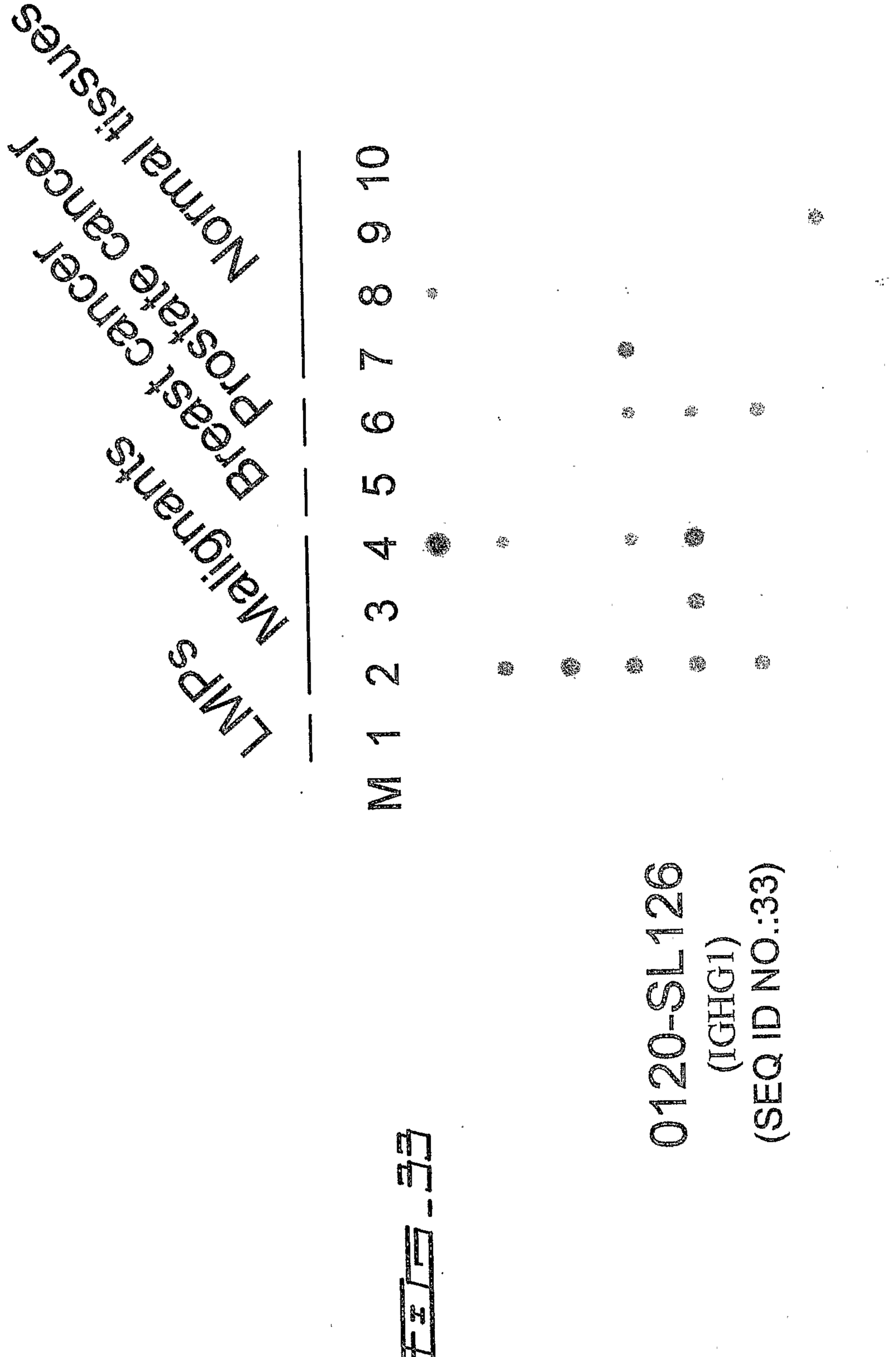

sensitivity
Normal tissues
Prostate cancer
Breast cancer
Malignants
LMPS
M 1 2 3 4 5 6 7 8 9 10
O120-SL126
(IGHG1)
(SEQ ID NO.:33)

FIG. 33

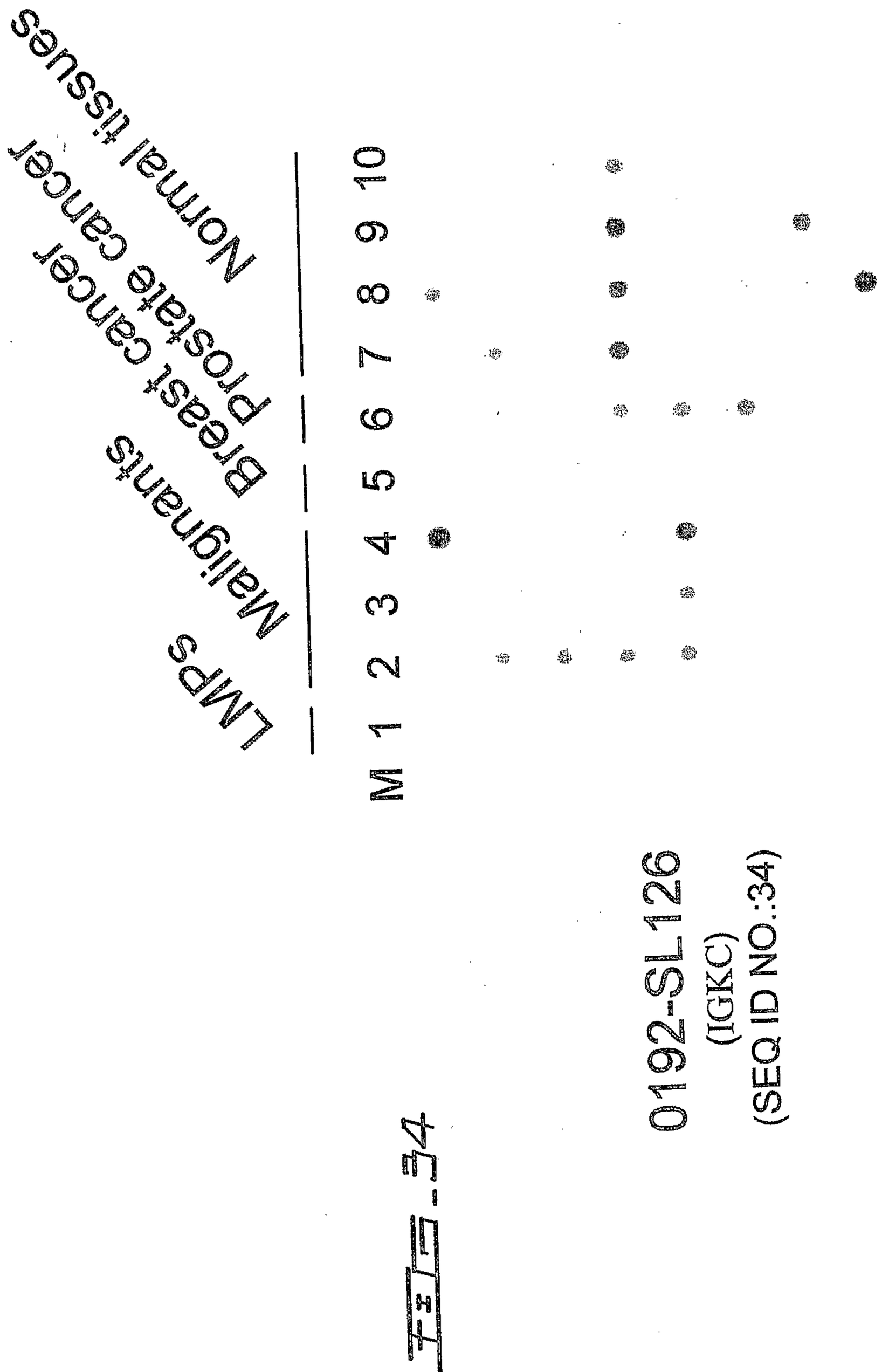
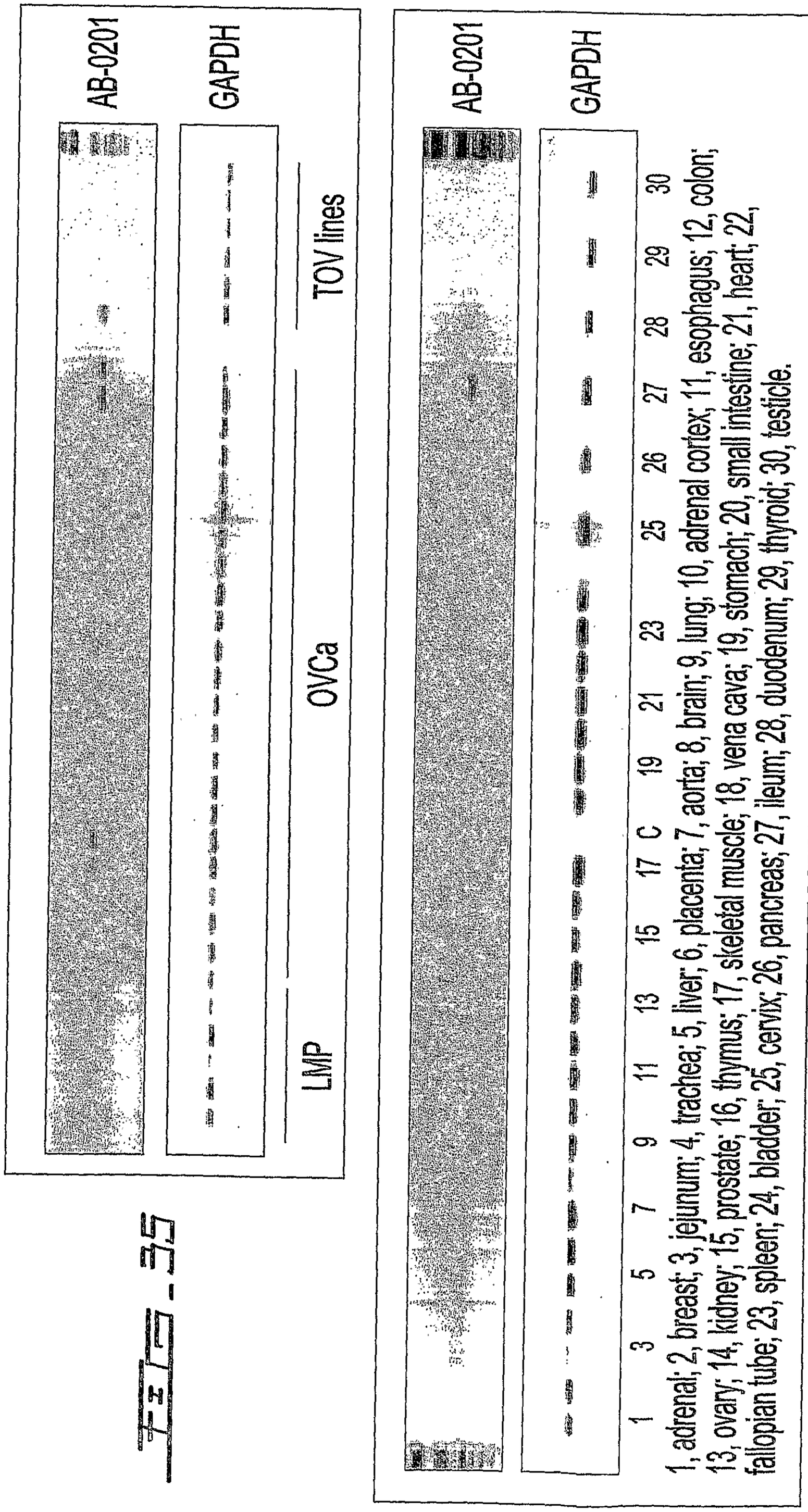

LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues
M 1 2 3 4 5 6 7 8 9 10
0192-SL126
(IGKC)
(SEQ ID NO.:34)

FIG. 4



Ovarian cancer expression analysis using PCR
0201-SL125 (Chr10orf38)
(SEQ ID NO.:35)

FIG - 35

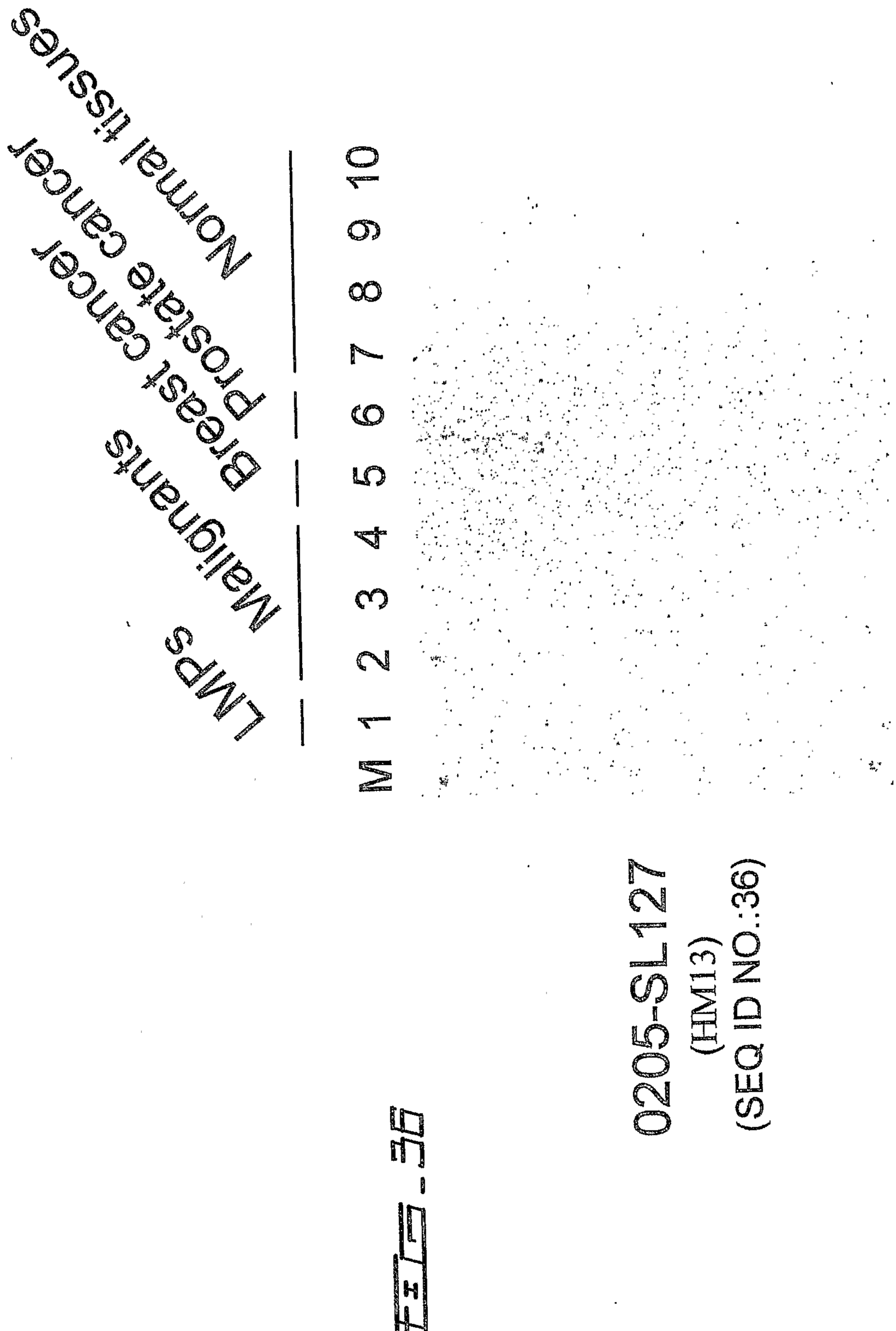


FIG. 37

0205-SL127
(HM13)
(SEQ ID NO.:36)

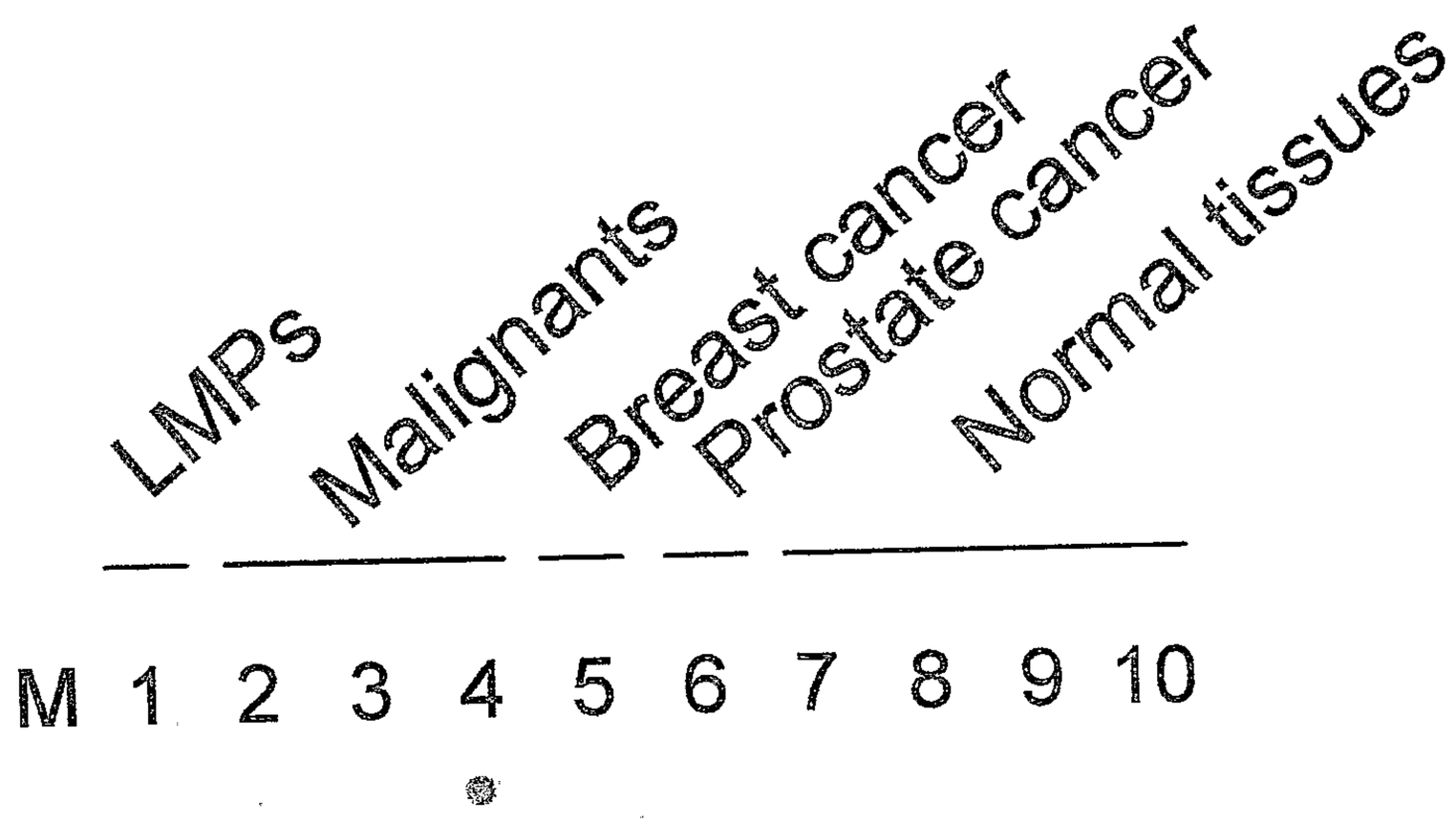
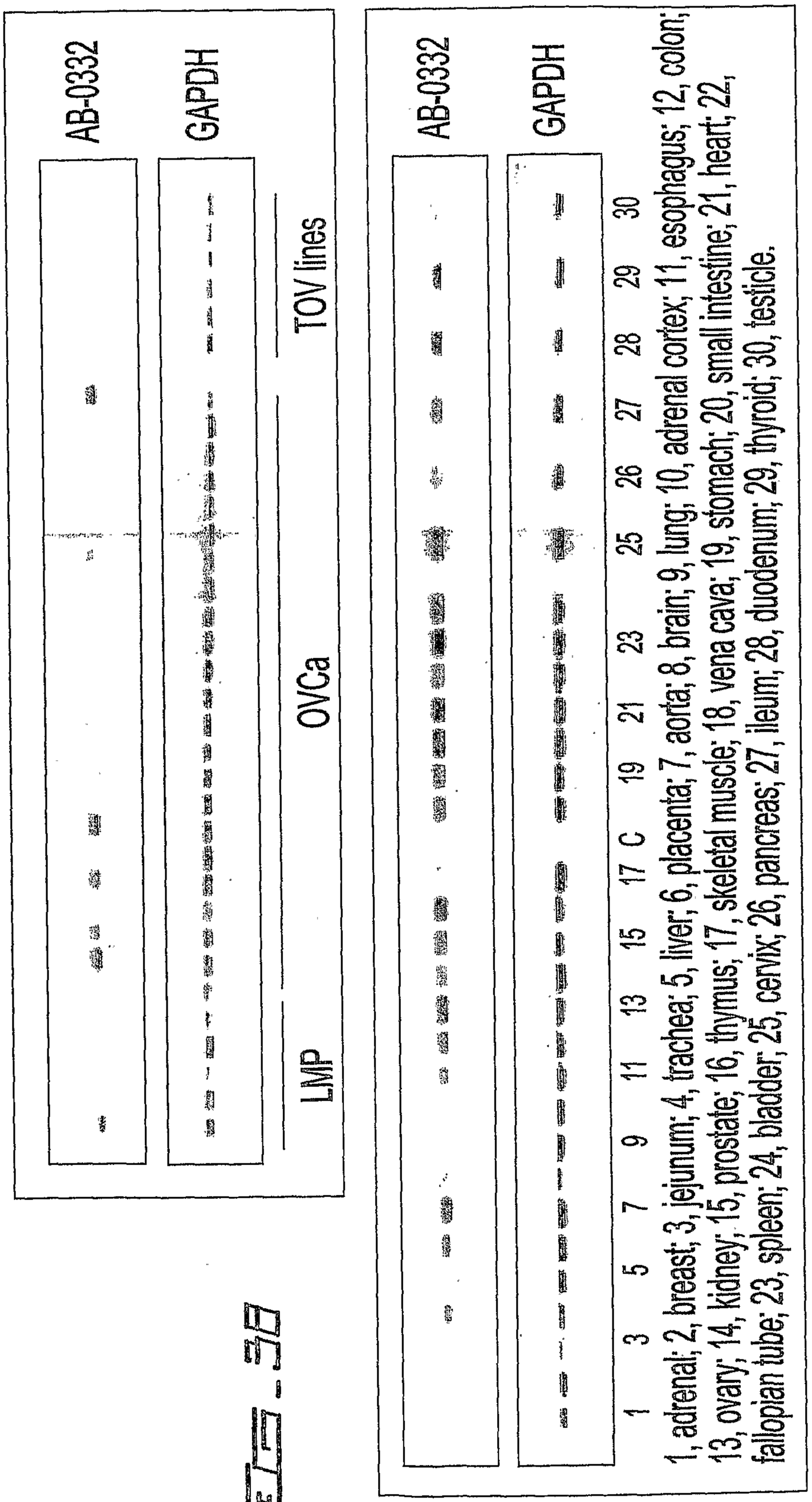


FIG-37

0319-SL124
(Novel genomic hit)
(SEQ ID NO.:37)



Ovarian cancer expression analysis using PCR
0332-SL 126 (FRZB)
(SEQ ID NO:38)

Fig. 39

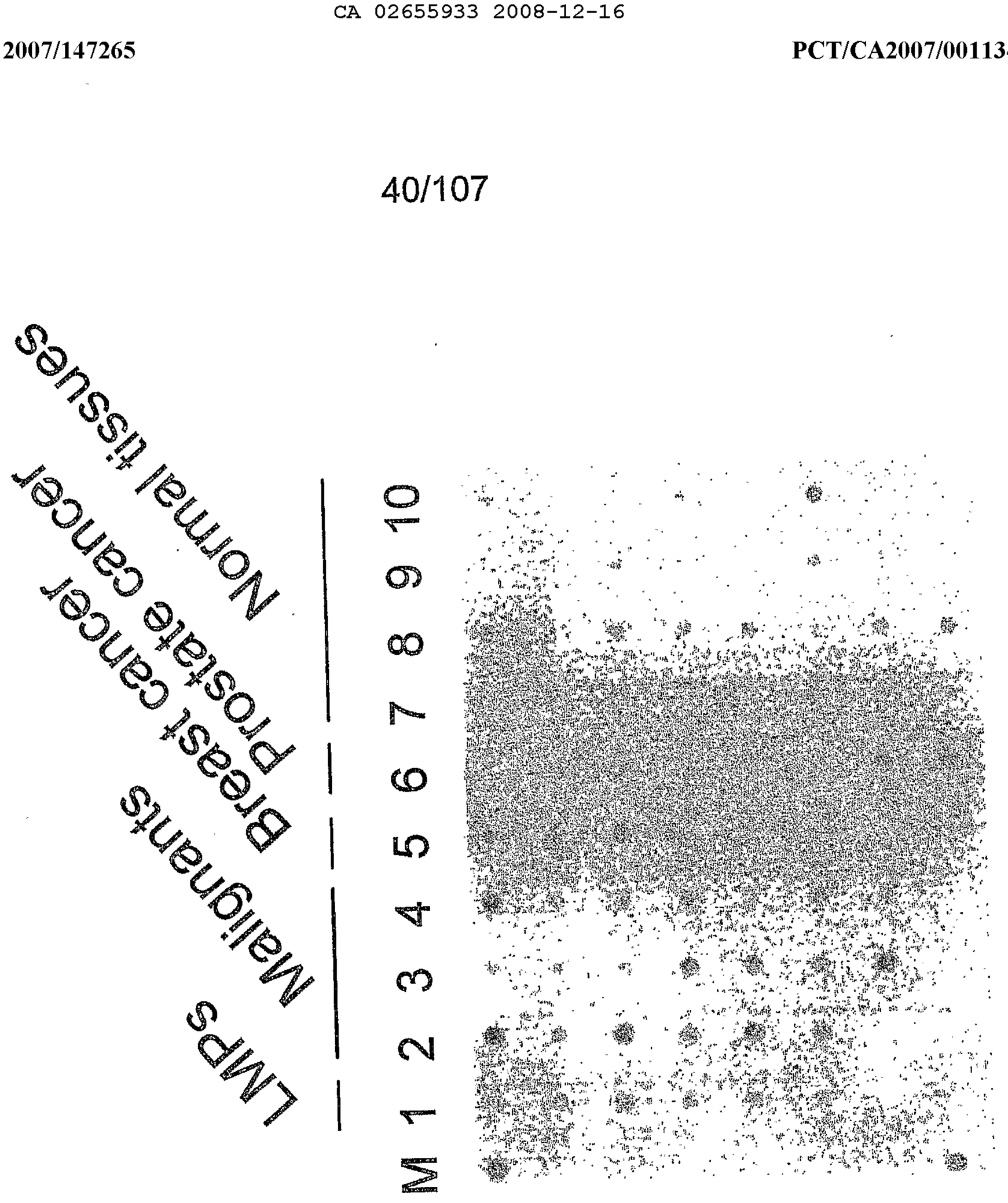


FIG. 39
0344-SL127
(FOXM1)
(SEQ ID NO.:39)

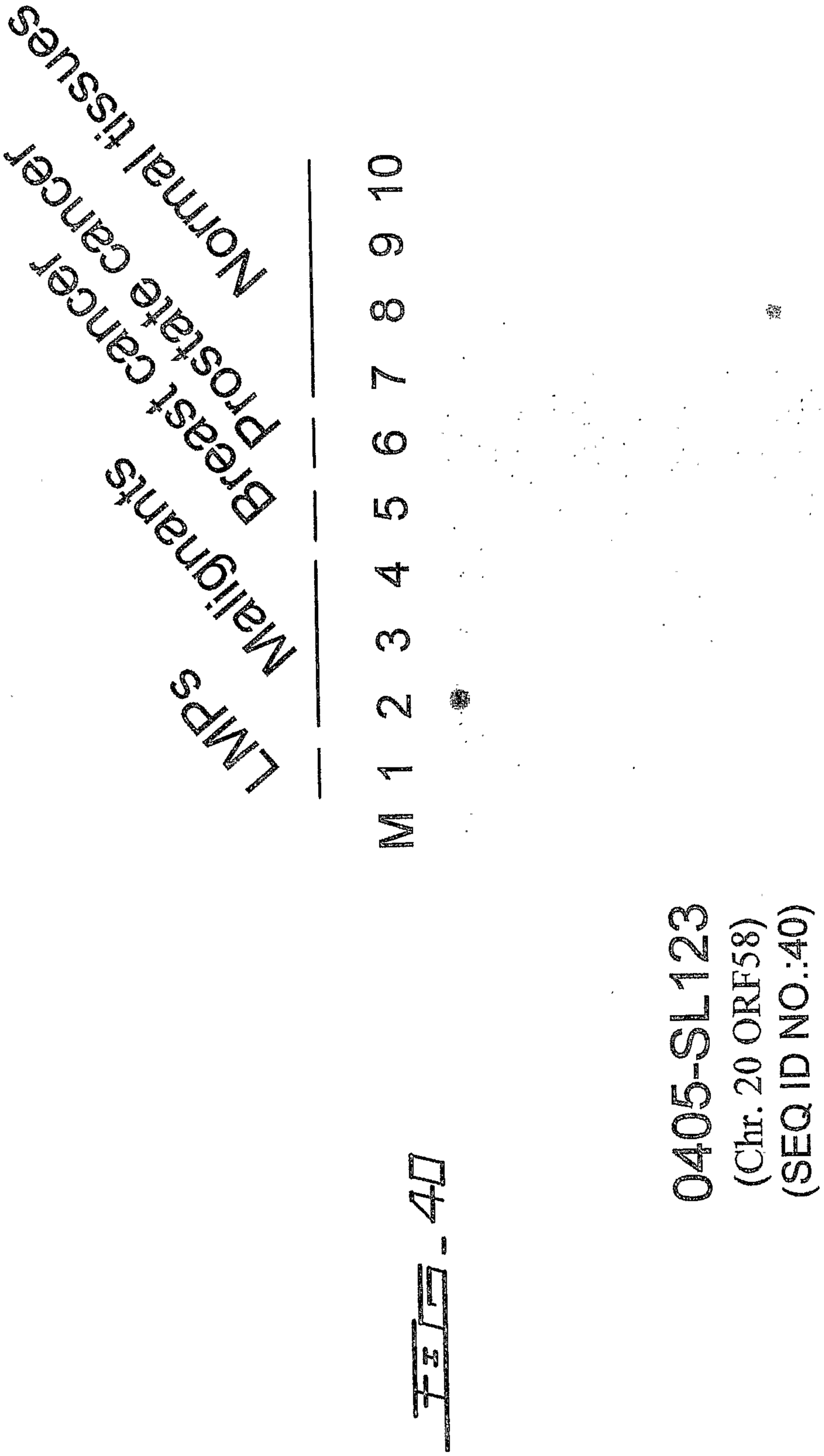


FIG. 40

0405-SL123
(Chr. 20 ORF58)
(SEQ ID NO.:40)

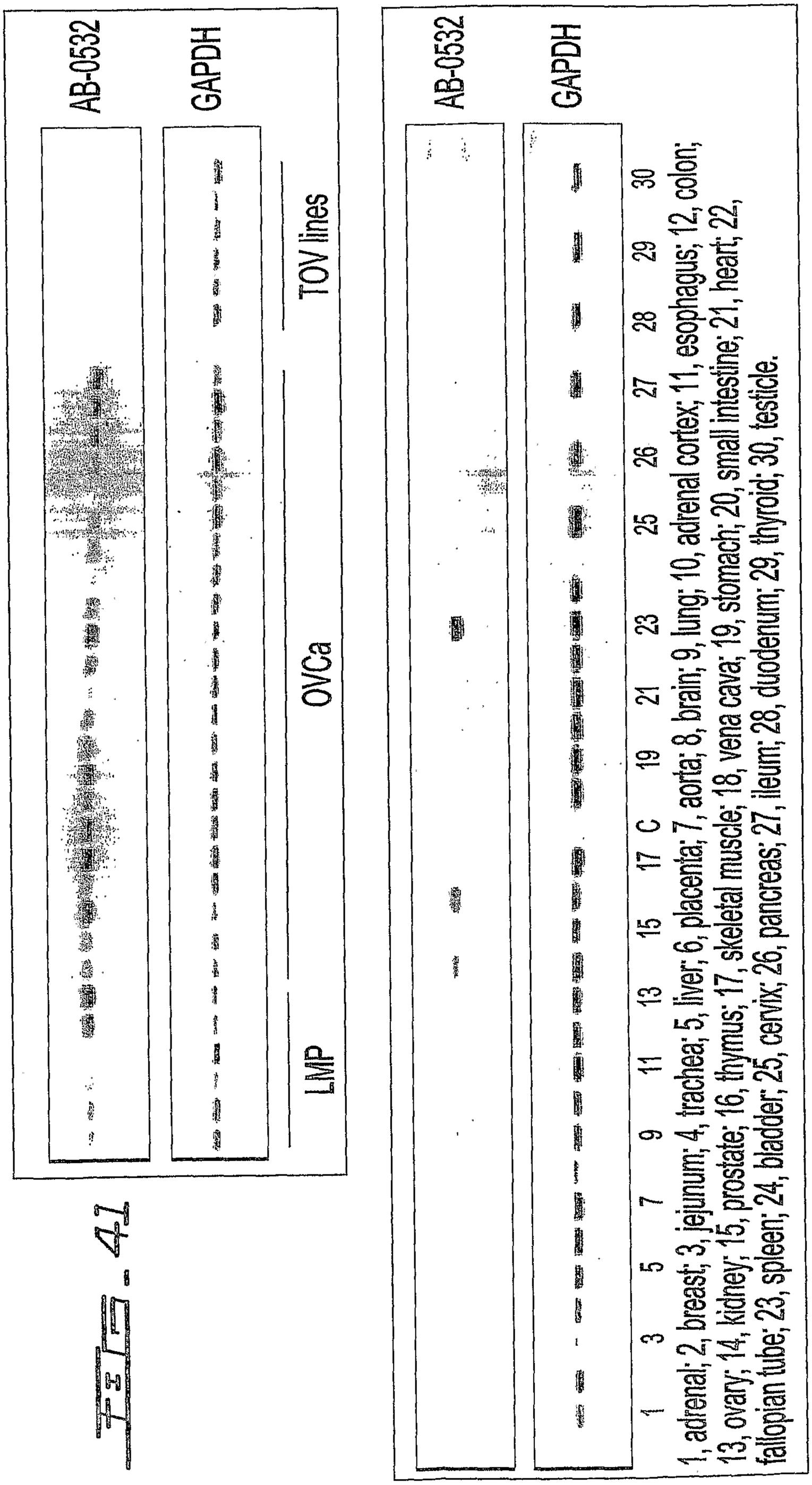

Ovarian cancer expression analysis using PCR
0532-SL124 (novel genomic hit)
(SEQ ID NO:41)
AB-0532
GAPDH
OVCa
TOV lines
LMP
1, adrenal; 2, breast; 3, jejunum; 4, trachea; 5, liver; 6, placenta; 7, aorta; 8, brain; 9, lung; 10, adrenal cortex; 11, esophagus; 12, colon; 13, ovary; 14, kidney; 15, prostate; 16, thymus; 17, skeletal muscle; 18, vena cava; 19, stomach; 20, small intestine; 21, heart; 22, fallopian tube; 23, spleen; 24, bladder; 25, cervix; 26, pancreas; 27, ileum; 28, duodenum; 29, thyroid; 30, testicle.

Fig. 41

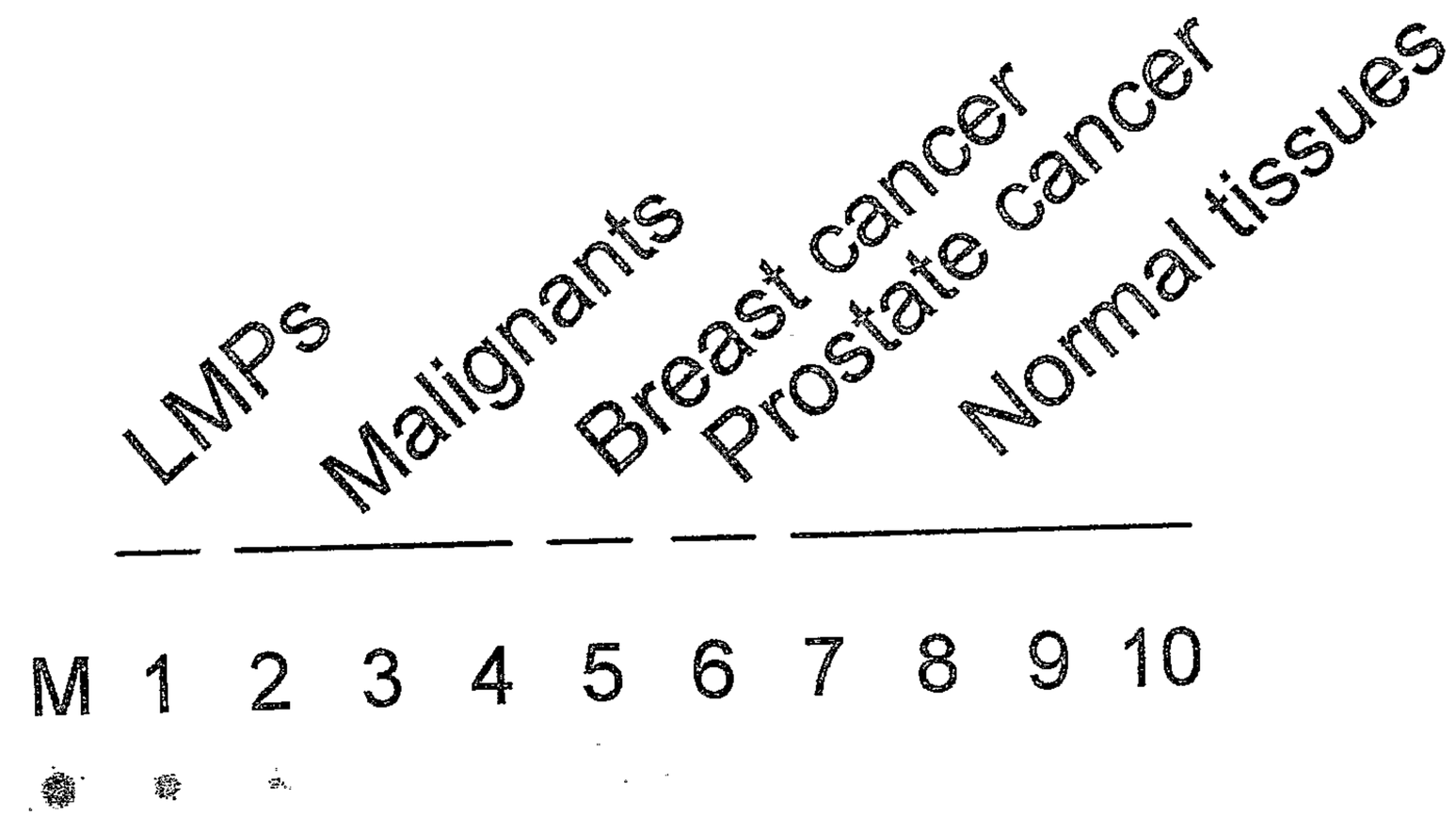


FIG. 42

0567-SL123
(Chr. 16 ORF74)
(SEQ ID NO.:42)

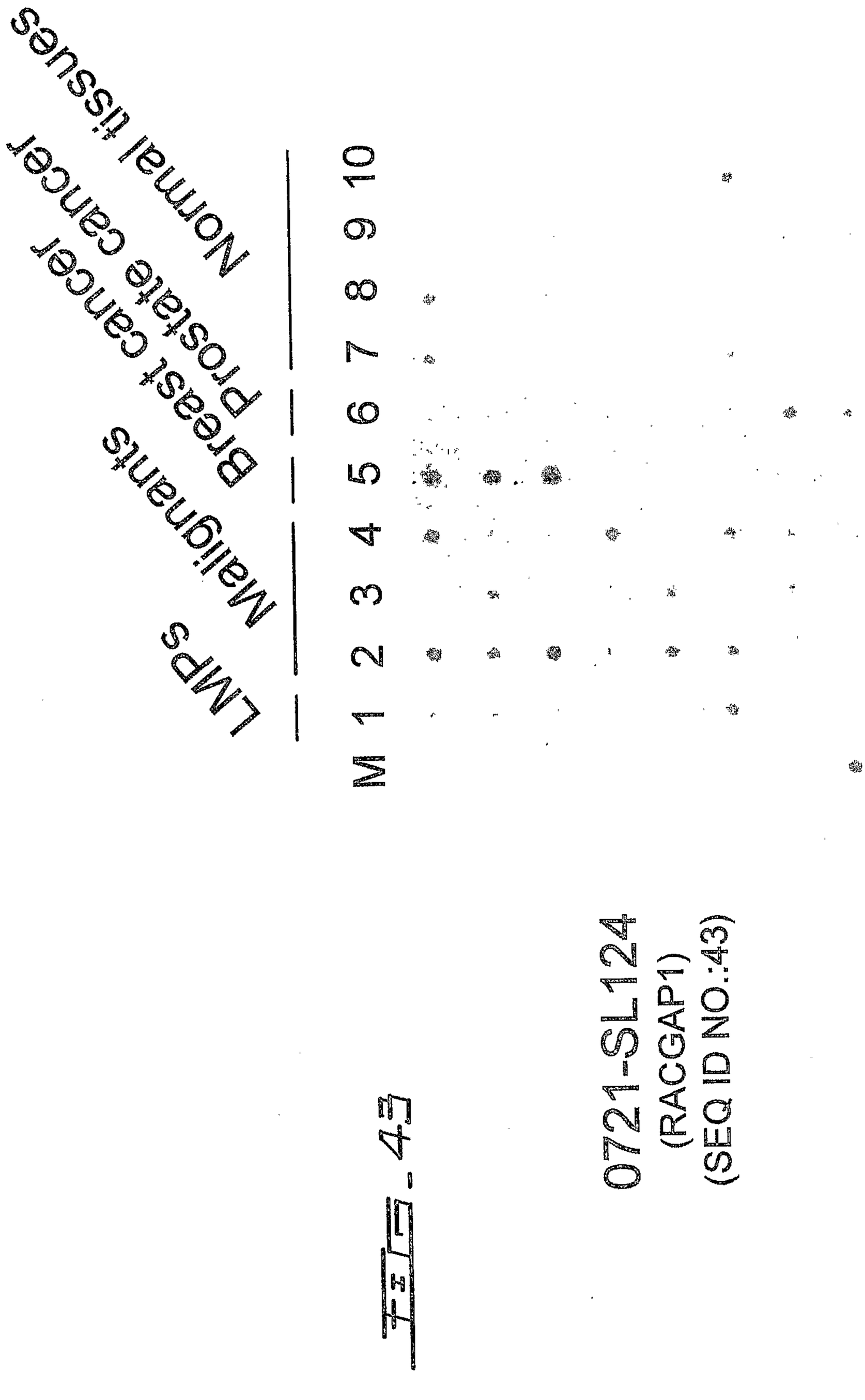


FIG - 43

0721-SL124
(RACGAP1)
(SEQ ID NO:43)

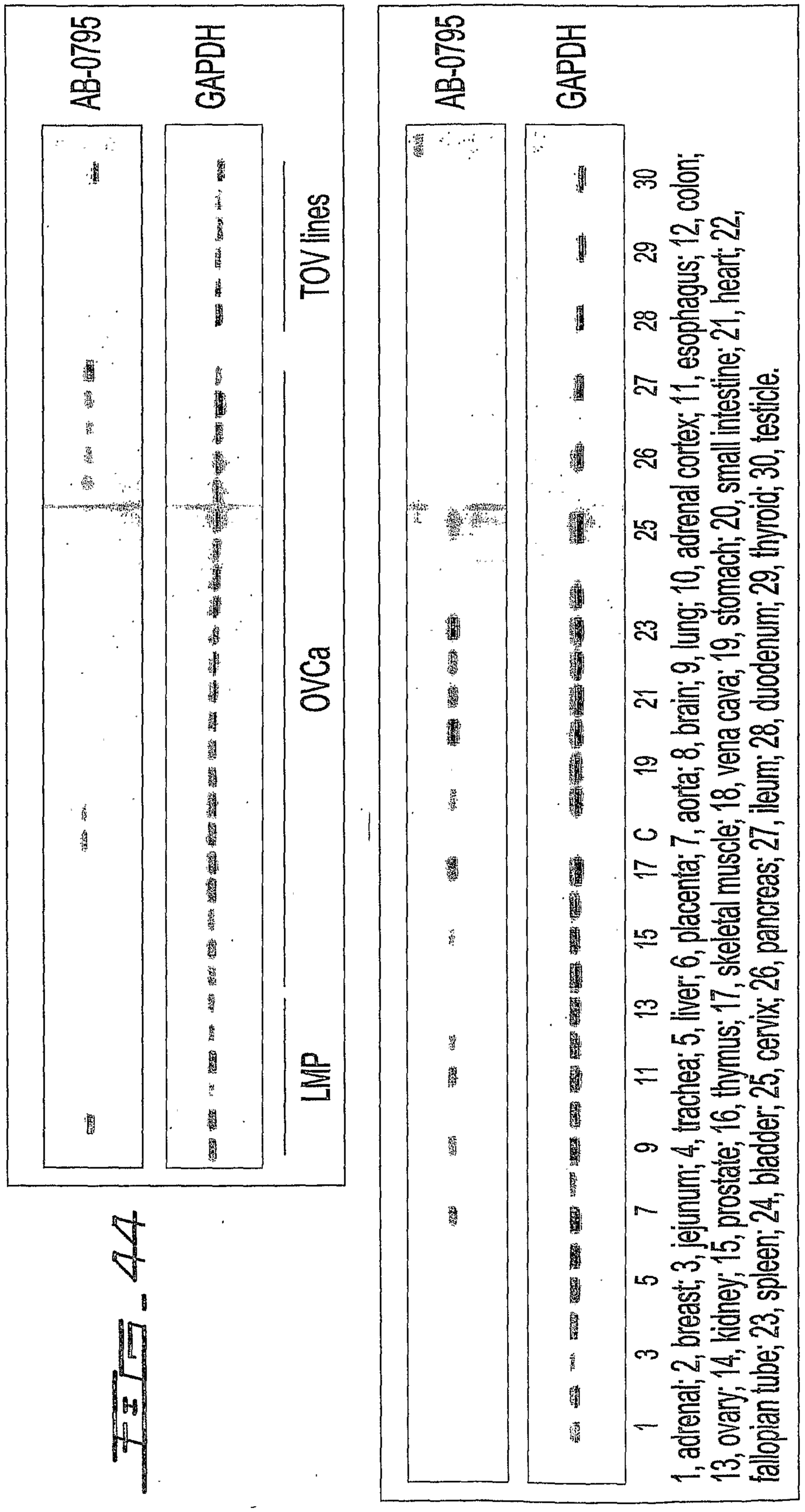

AB-0795
GAPDH
AB-0795
GAPDH
Ovarian cancer expression analysis using PCR
0795-SL125 (RACGAP1)
(SEQ ID NO:44)
OVCa
TOV lines
LMP
1, adrenal; 2, breast; 3, jejunum; 4, trachea; 5, liver; 6, placenta; 7, aorta; 8, brain; 9, lung; 10, adrenal cortex; 11, esophagus; 12, colon; 13, ovary; 14, kidney; 15, prostate; 16, thymus; 17, skeletal muscle; 18, vena cava; 19, stomach; 20, small intestine; 21, heart; 22, fallopian tube; 23, spleen; 24, bladder; 25, cervix; 26, pancreas; 27, ileum; 28, duodenum; 29, thyroid; 30, testicle.

FIG - 44

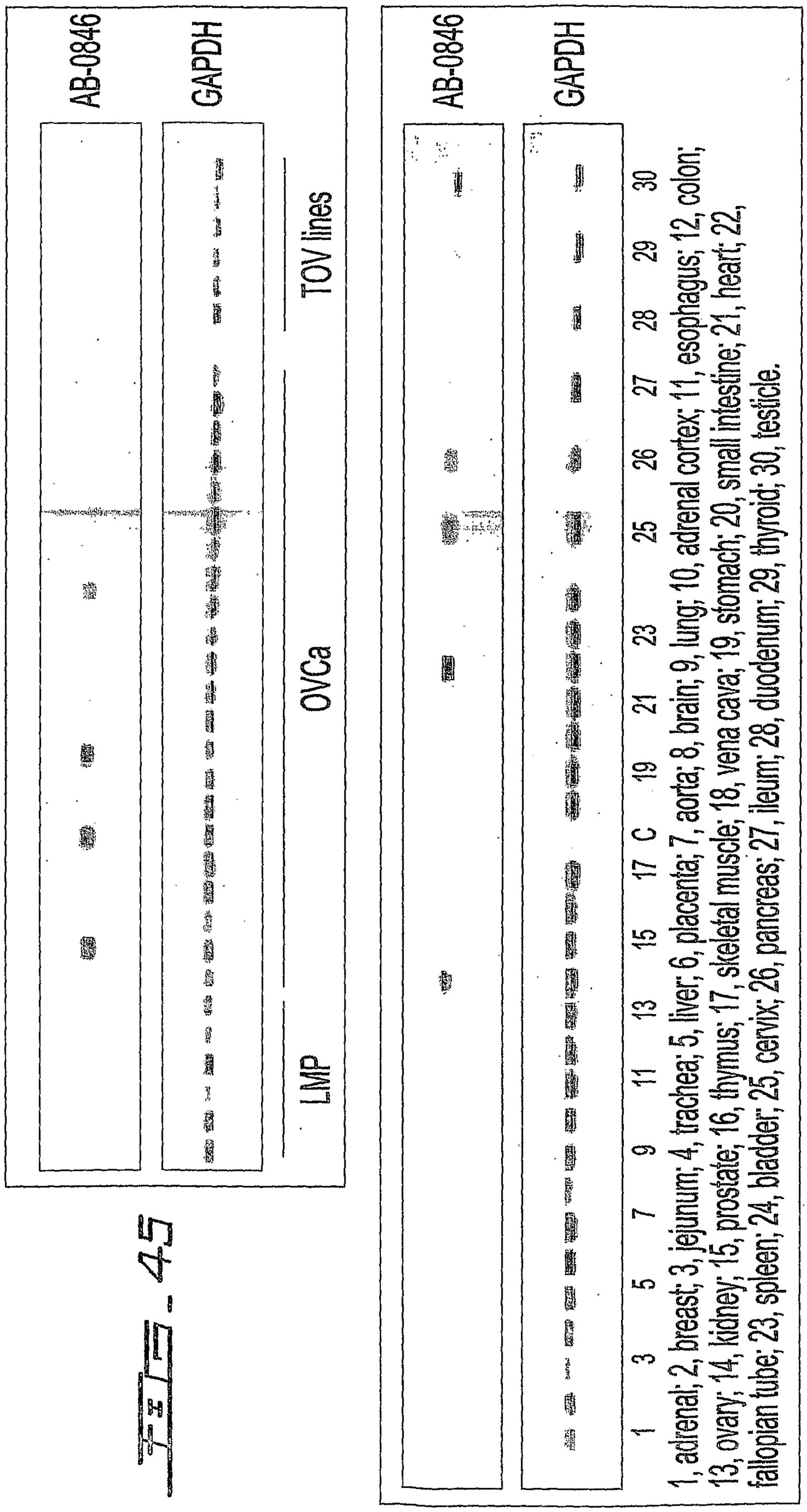
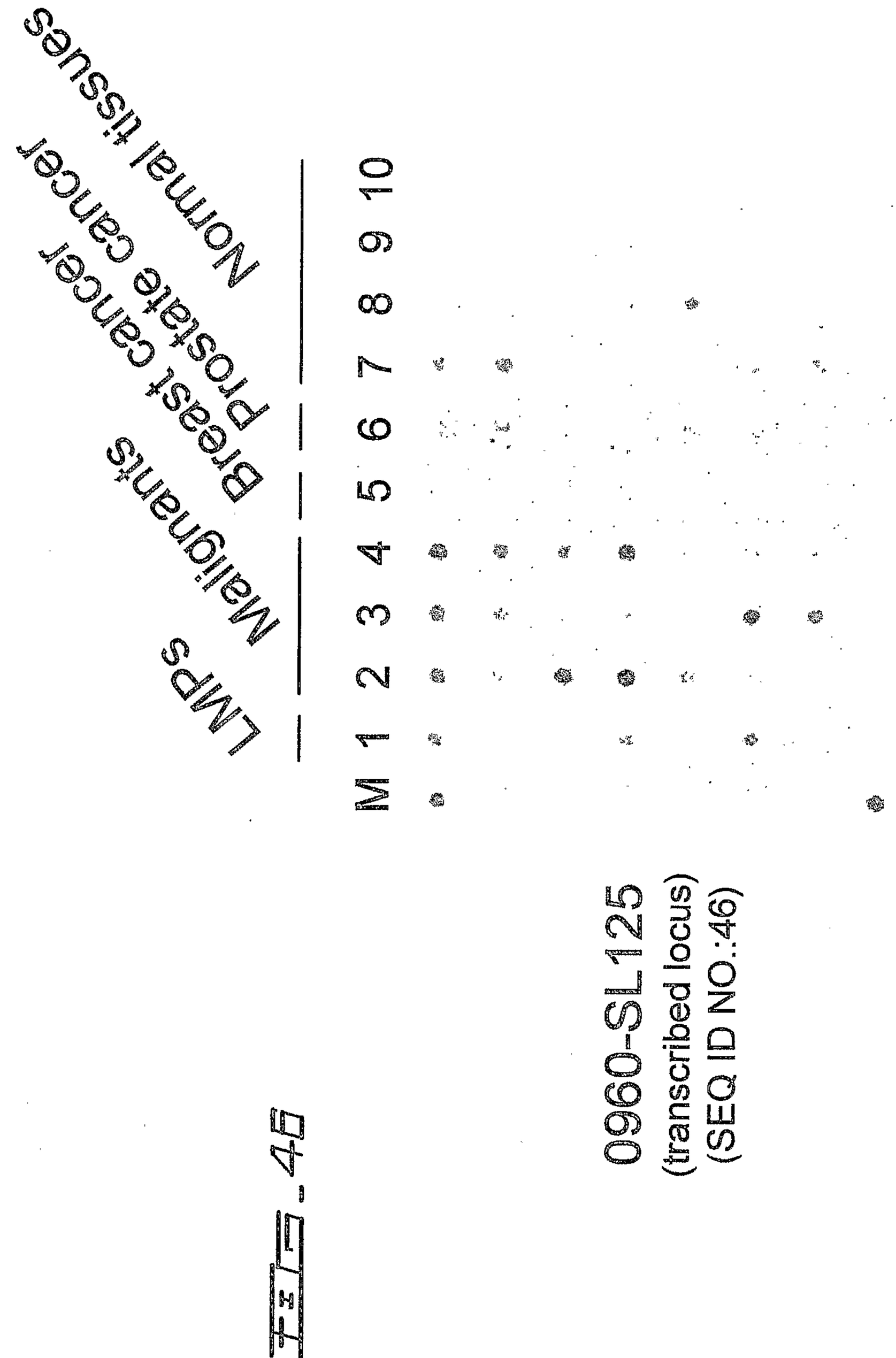
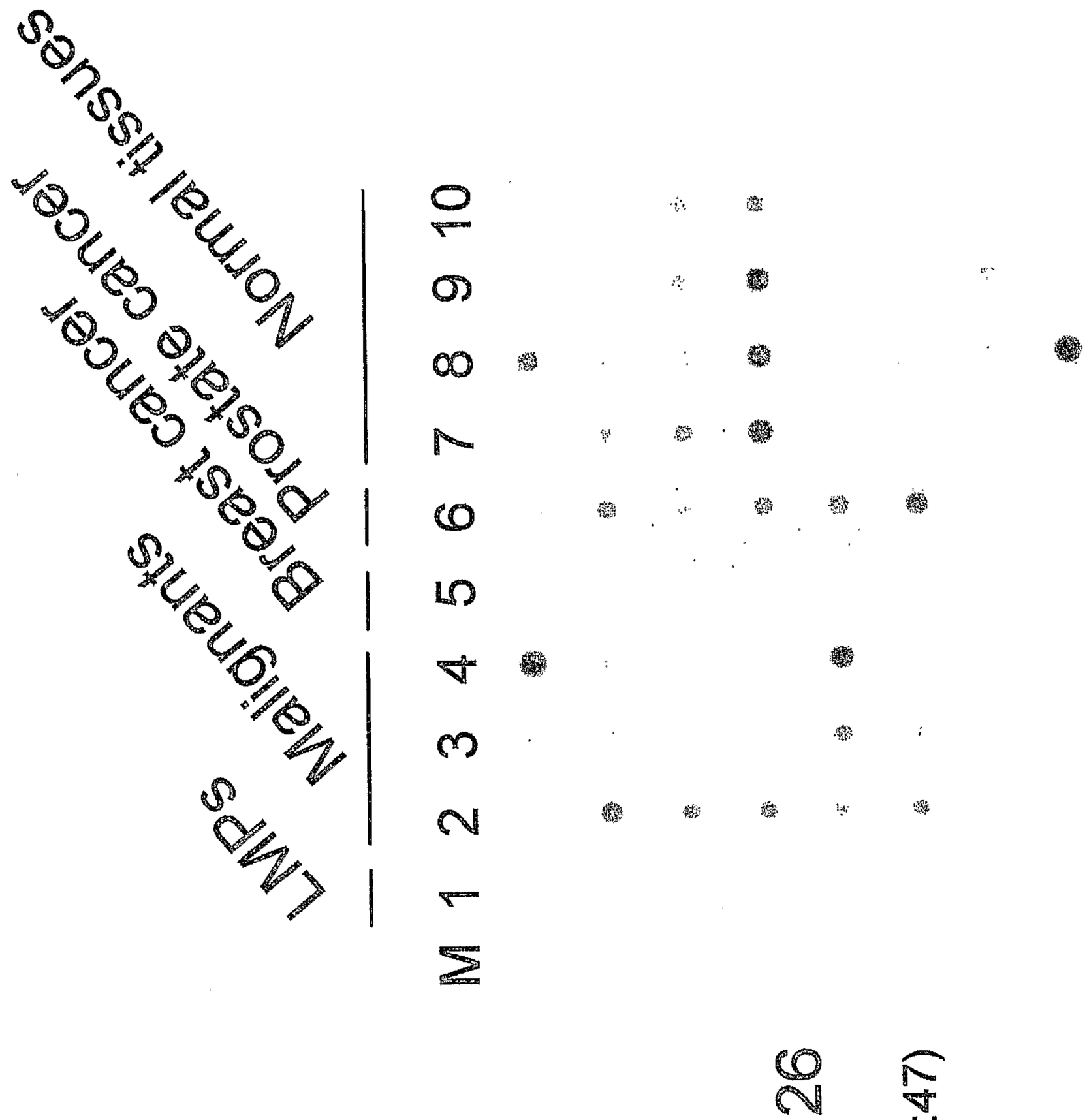
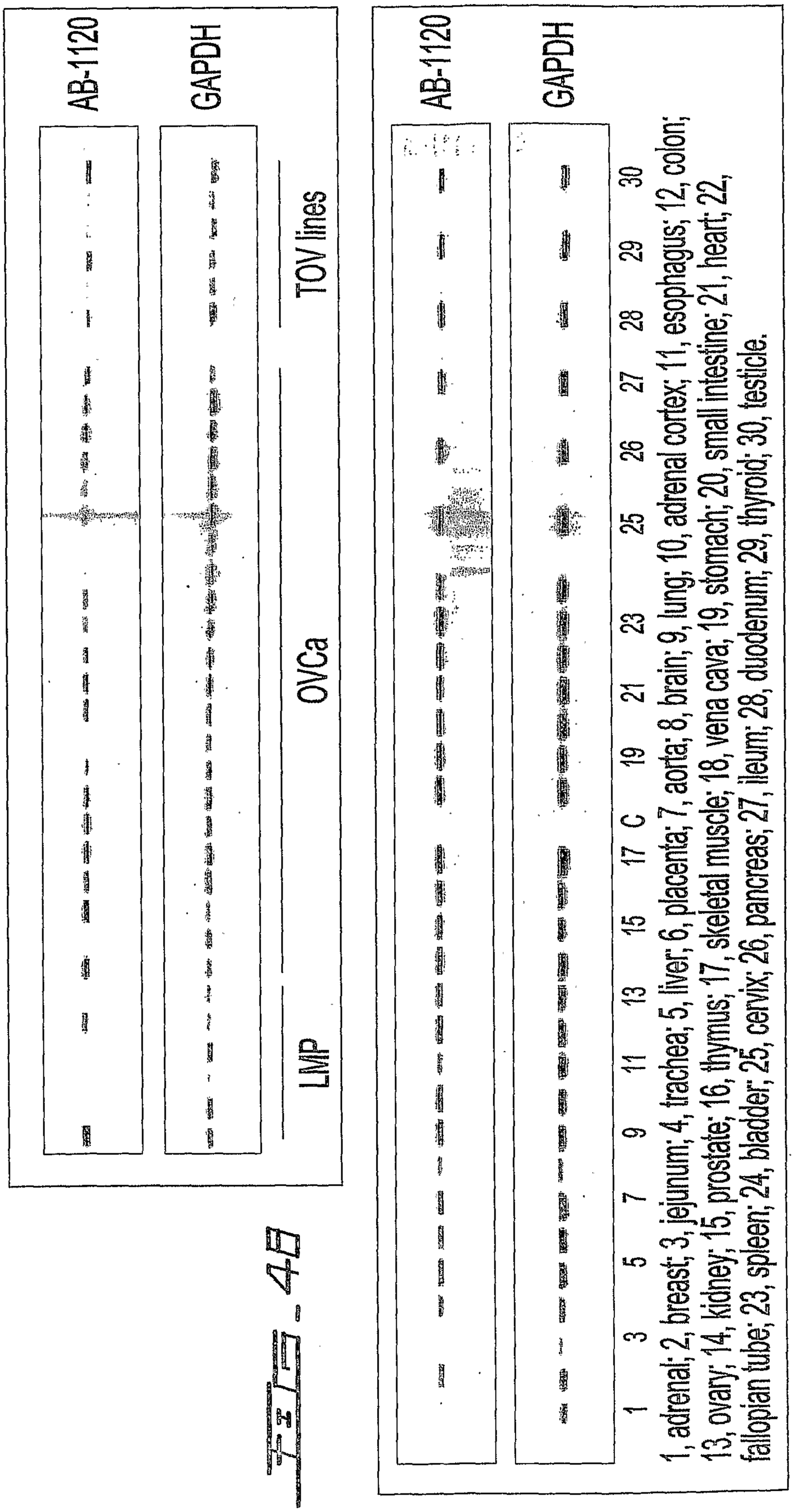

AB-0846
GAPDH
OVCa
TOV lines
LMP
Ovarian cancer expression analysis using PCR
0846-SL125 (novel genomic hit)
(SEQ ID NO:45)
1 3 5 7 9 11 13 15 17 C 19 21 23 25 26 27 28 29 30
1, adrenal; 2, breast; 3, jejunum; 4, trachea; 5, liver; 6, placenta; 7, aorta; 8, brain; 9, lung; 10, adrenal cortex; 11, esophagus; 12, colon; 13, ovary; 14, kidney; 15, prostate; 16, thymus; 17, skeletal muscle; 18, vena cava; 19, stomach; 20, small intestine; 21, heart; 22, fallopian tube; 23, spleen; 24, bladder; 25, cervix; 26, pancreas; 27, ileum; 28, duodenum; 29, thyroid; 30, testicle.

FIG. 45


Normal tissues
Prostate cancer
Breast cancer
Malignants
LMPs
M 1 2 3 4 5 6 7 8 9 10
0960-SL125
(transcribed locus)
(SEQ ID NO.:46)
FIG. 45


sensspt tissue
Normal tissue
Prostate cancer
Breast cancer
Malignants
LMPS
M 1 2 3 4 5 6 7 8 9 10
1083-SL126
(IGLV@)
(SEQ ID NO:47)
47



Ovarian cancer expression analysis using PCR
1120-SL123 (SCAMP3)
(SEQ ID NO:48)

FIG - 48

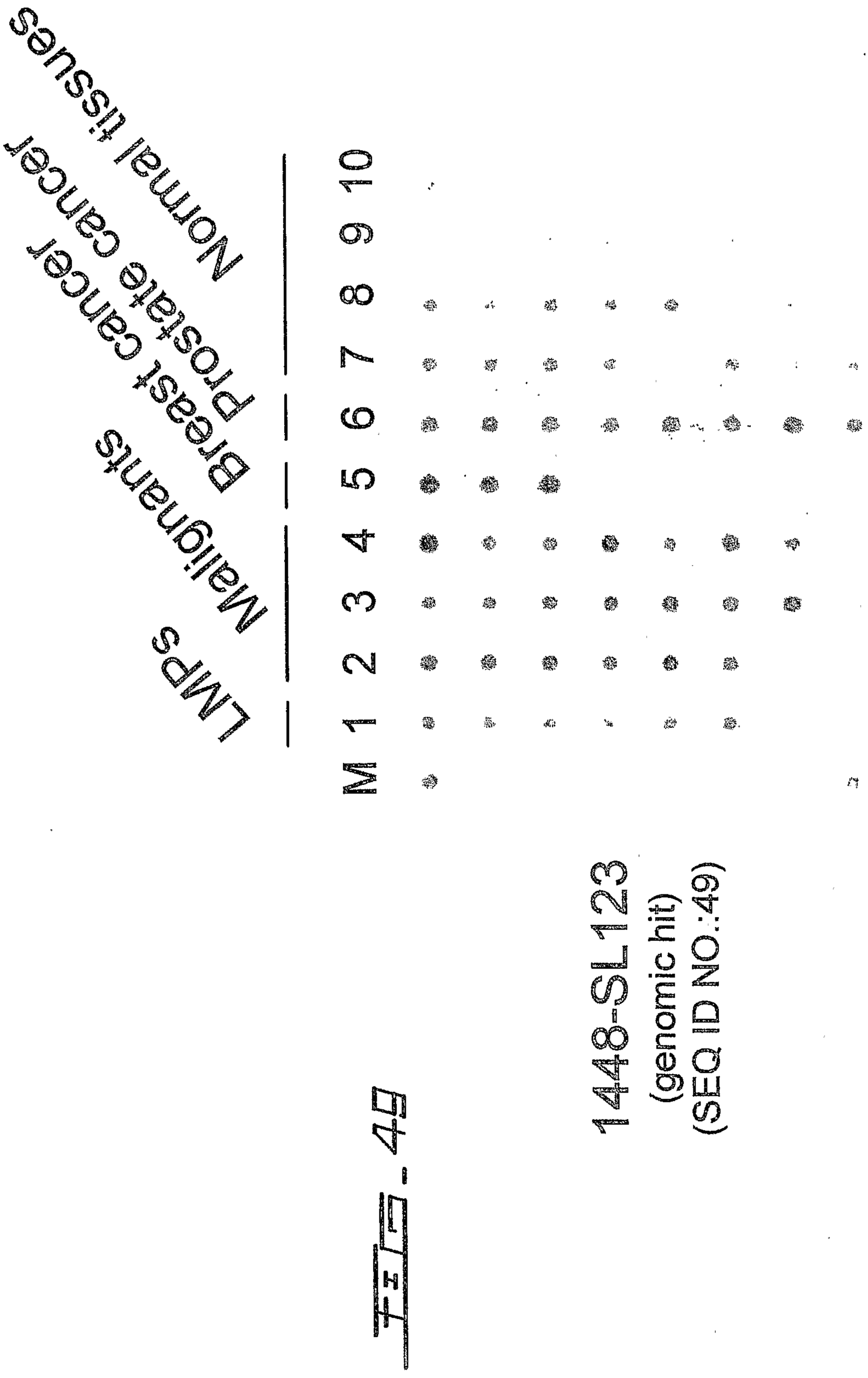
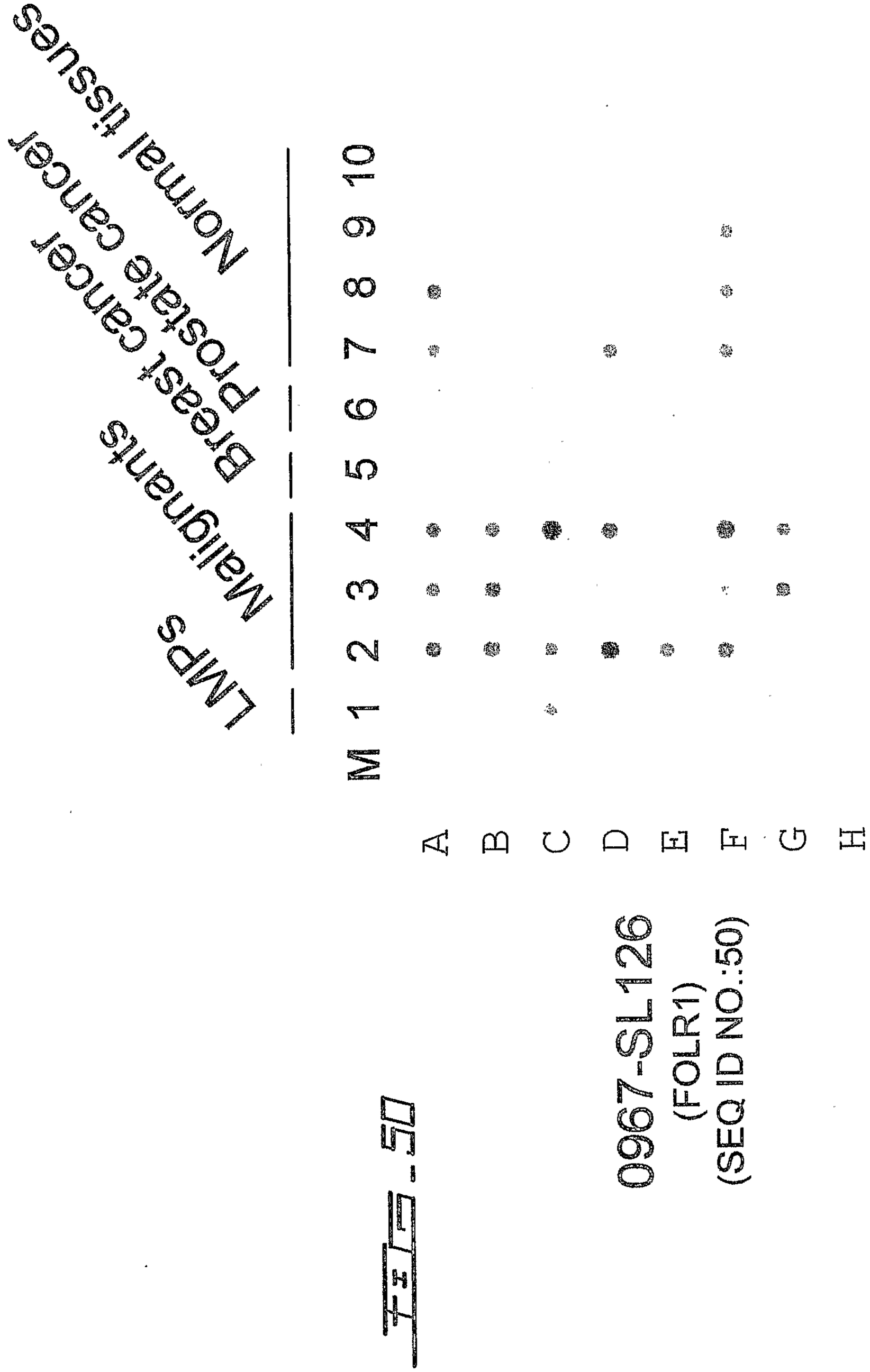


FIG. 49

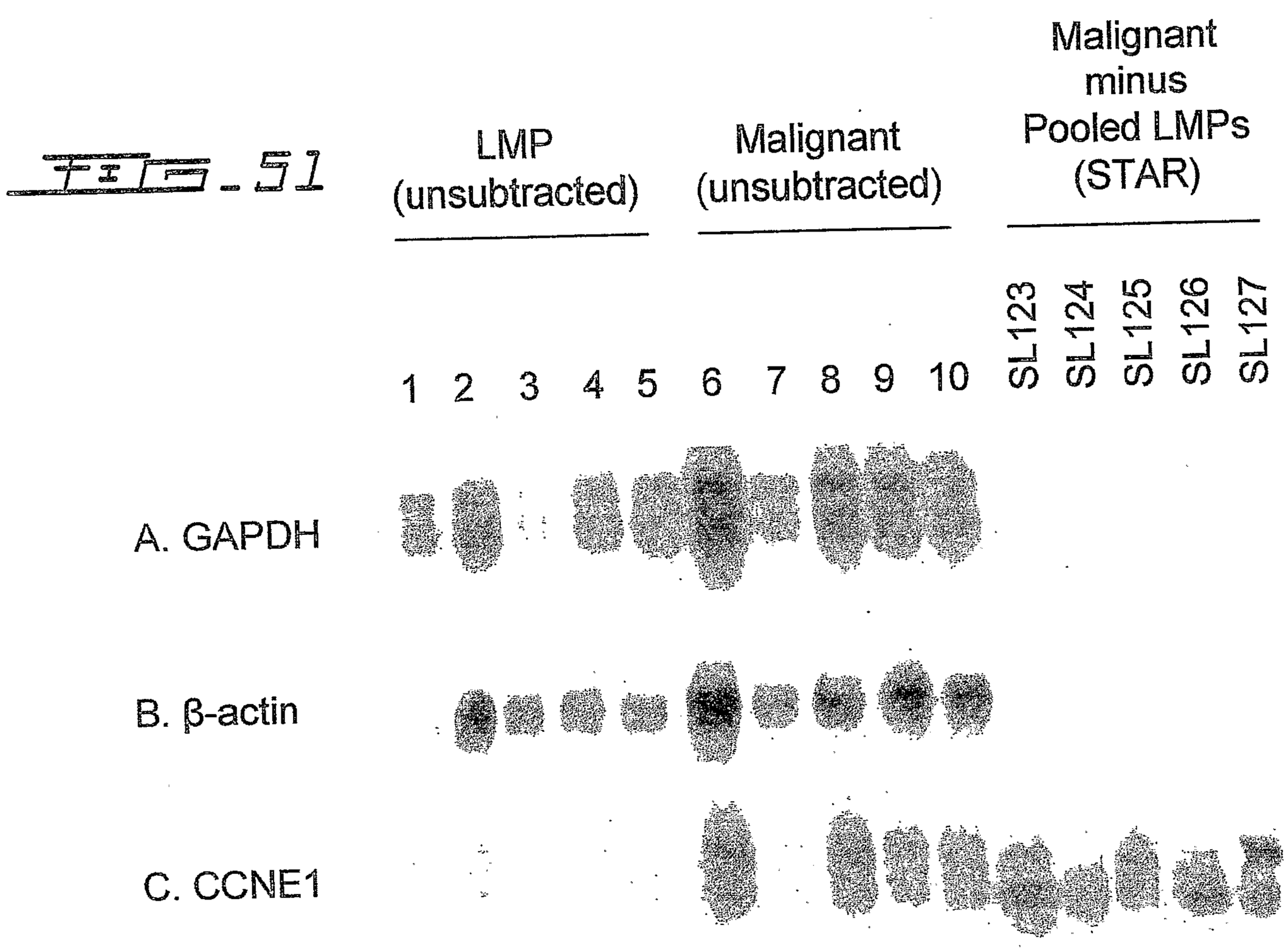
1448-SL123
(genomic hit)
(SEQ ID NO:49)


SEQ ID NO:50
0967-SL126
(FOLR1)
(SEQ ID NO:50)
A B C D E F G H
M 1 2 3 4 5 6 7 8 9 10
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissues

SUBSTITUTE SHEET (RULE 26)

Fig. 51

Example of Subtraction Using STAR for Ovarian Samples



Effect of shRNAs on Expression of SEQ.ID. Nos. 1 and 3

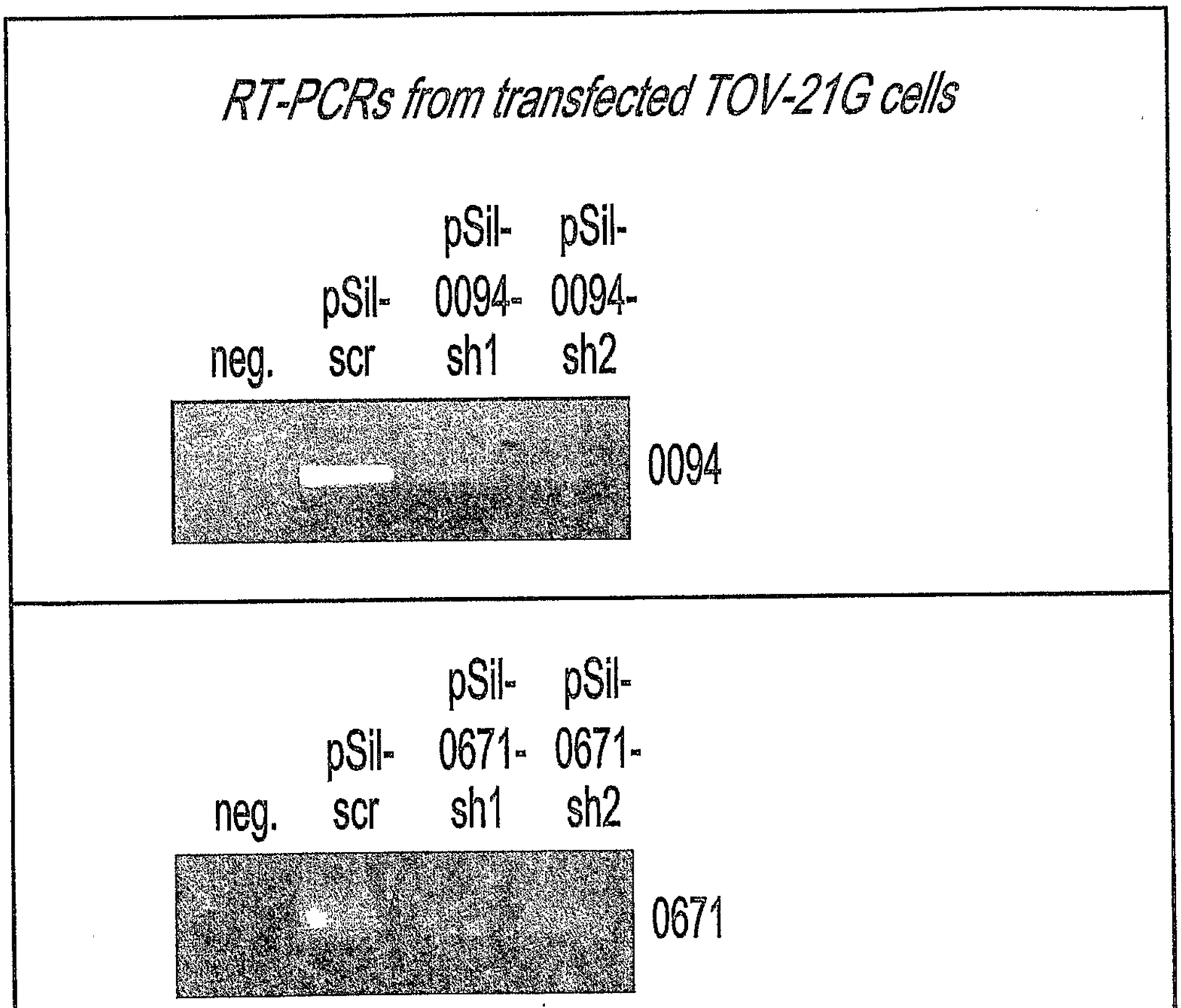


Fig. 52

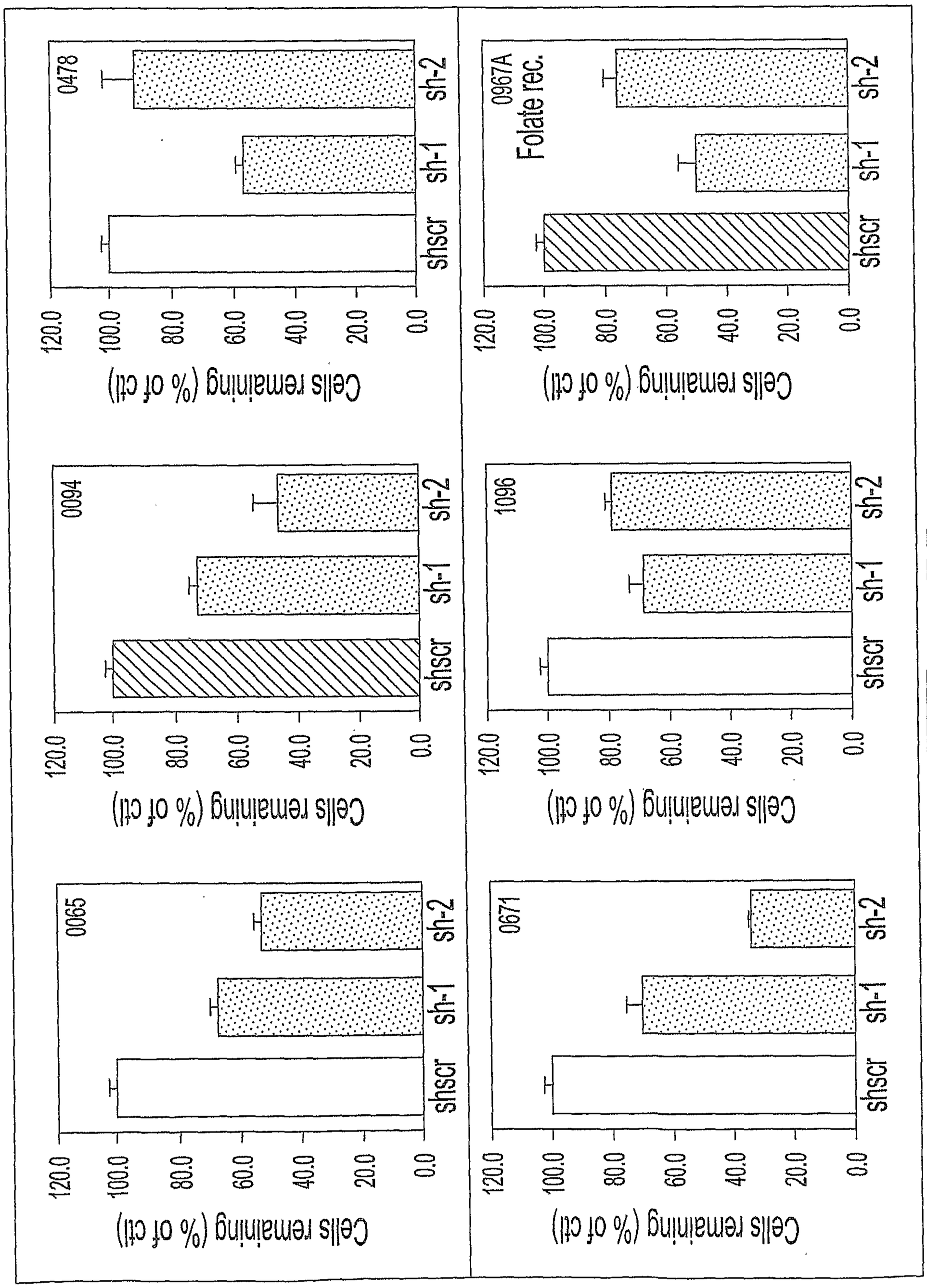

0478
0967A
Folate rec.
0094
1096
0065
0671
Cells remaining (% of ctl)
120.0
100.0
80.0
60.0
40.0
20.0
0.0
shscr
sh-1
sh-2

Fig. 57

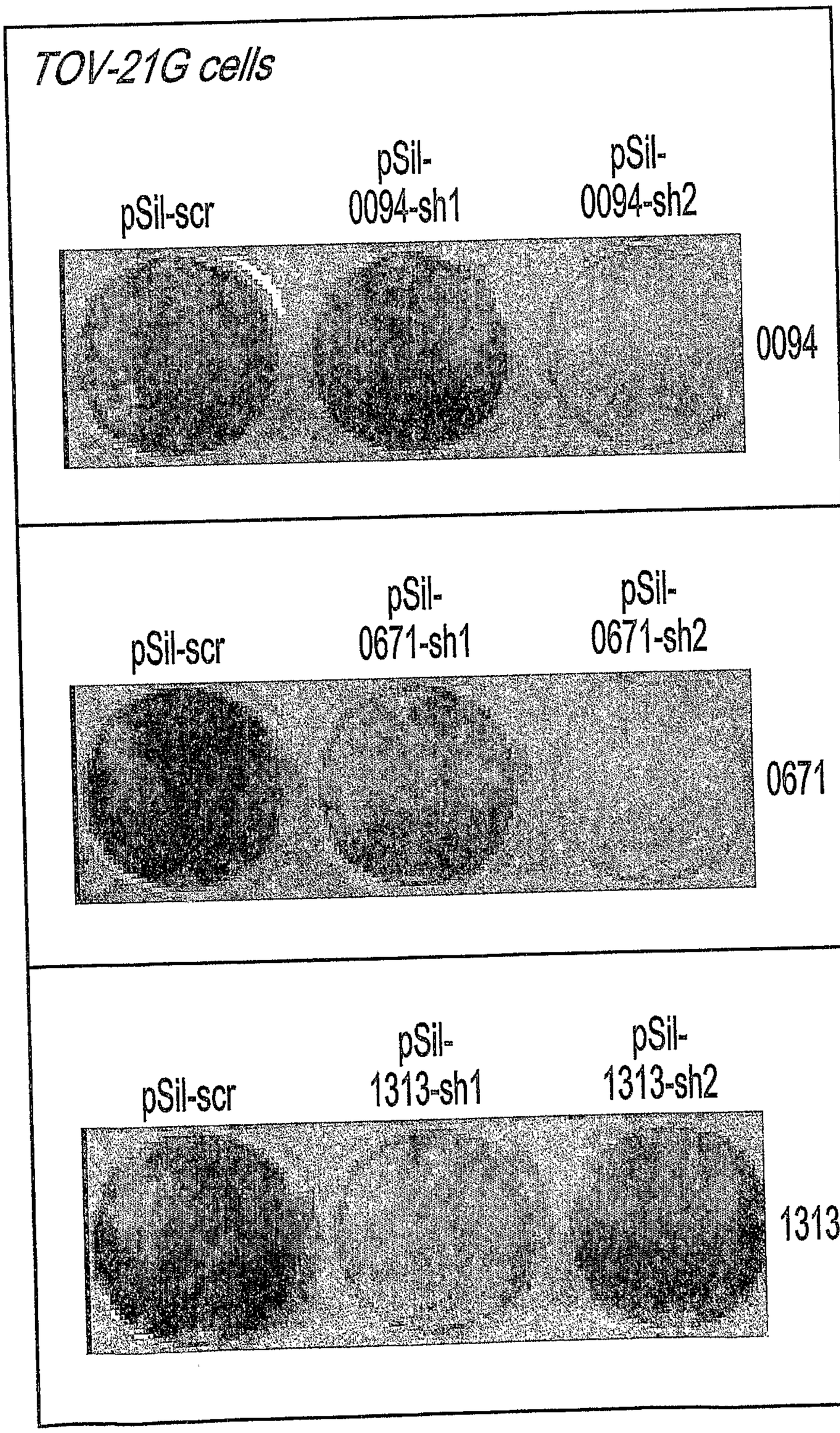

TOV-21G cells
pSil-scr
pSil-0094-sh1
pSil-0094-sh2
0094
pSil-scr
pSil-0671-sh1
pSil-0671-sh2
0671
pSil-scr
pSil-1313-sh1
pSil-1313-sh2
1313

FIG. 54

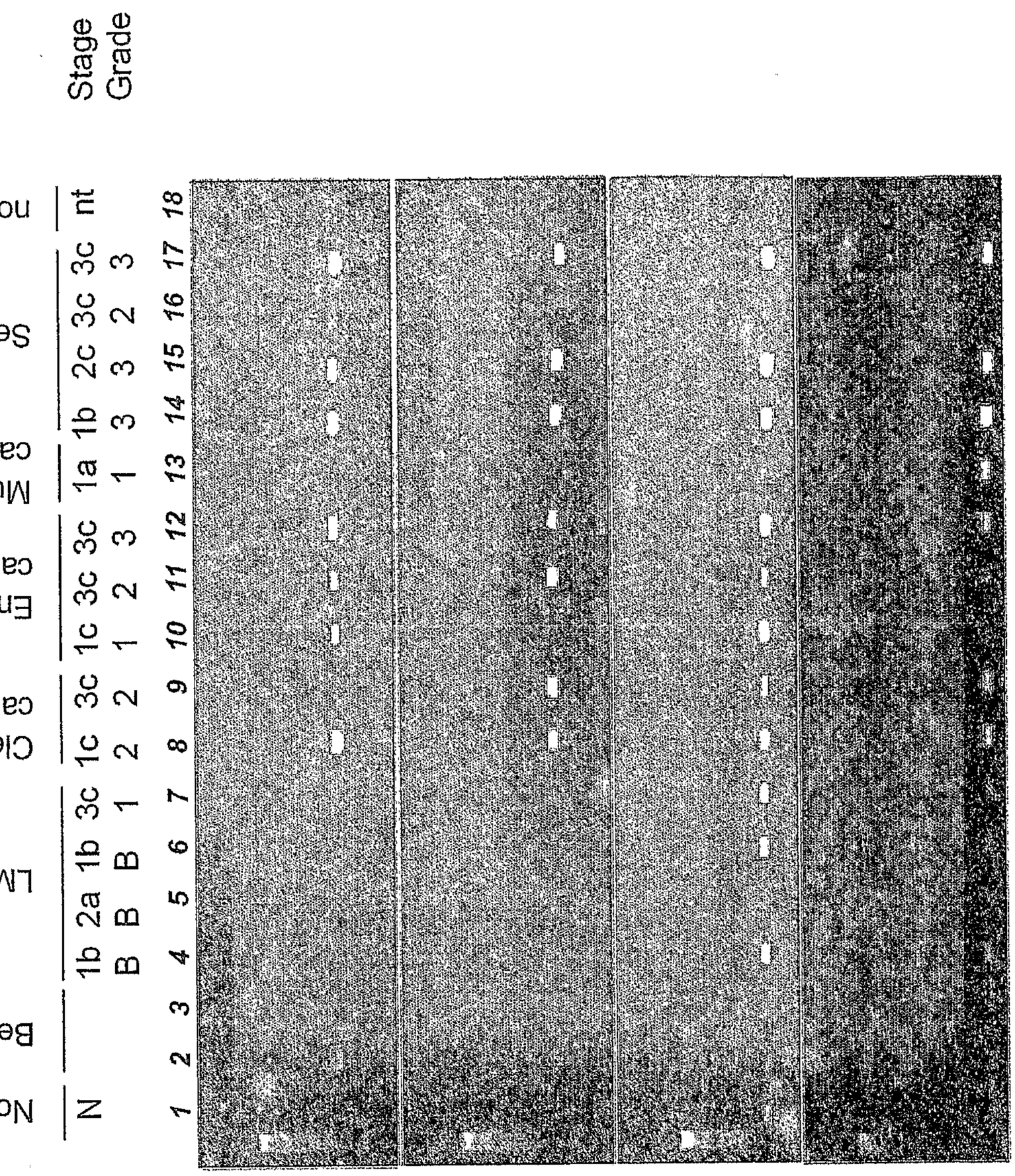


FIG. 5A

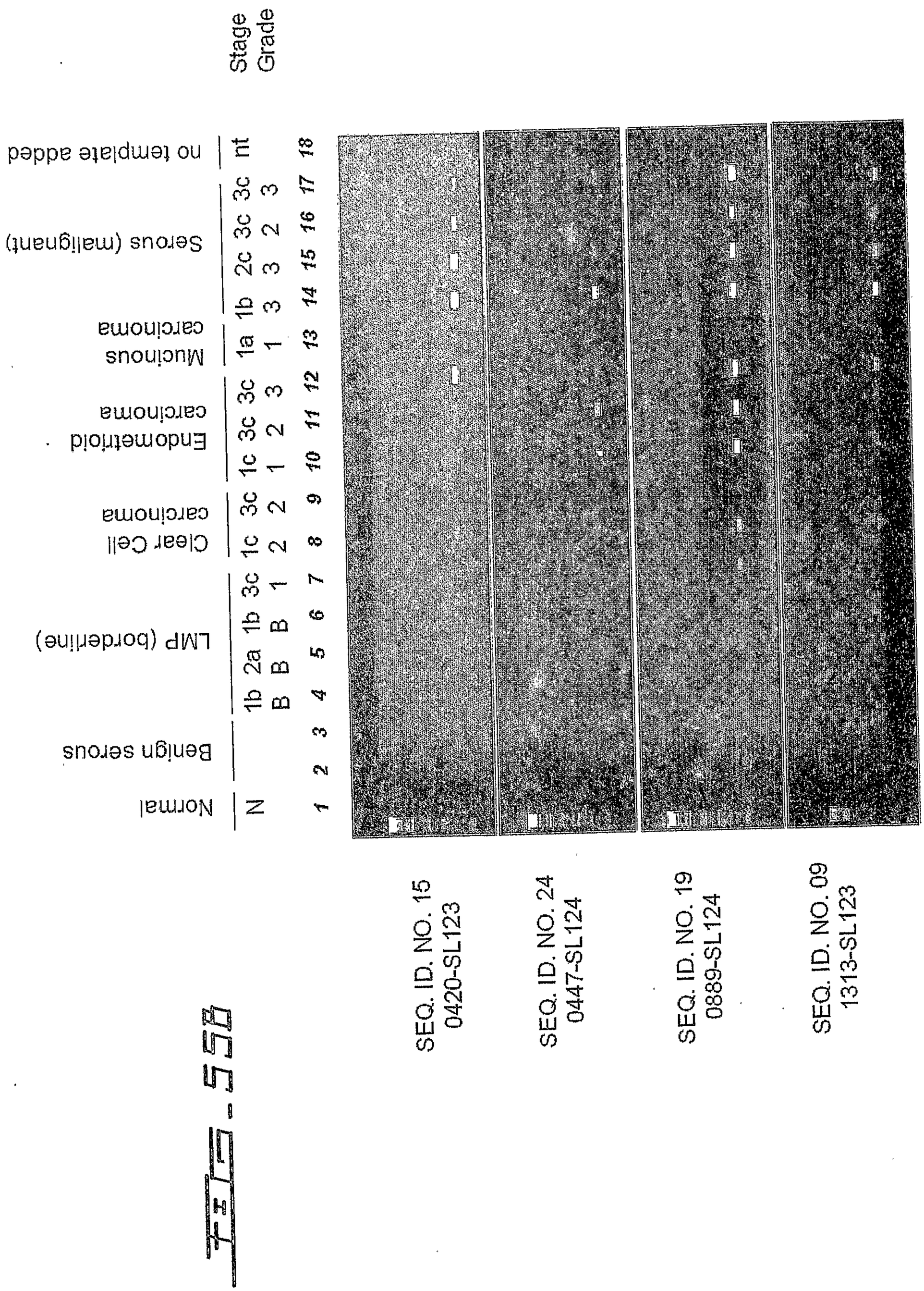
SEQ. ID. NO. 17
0531-SL124

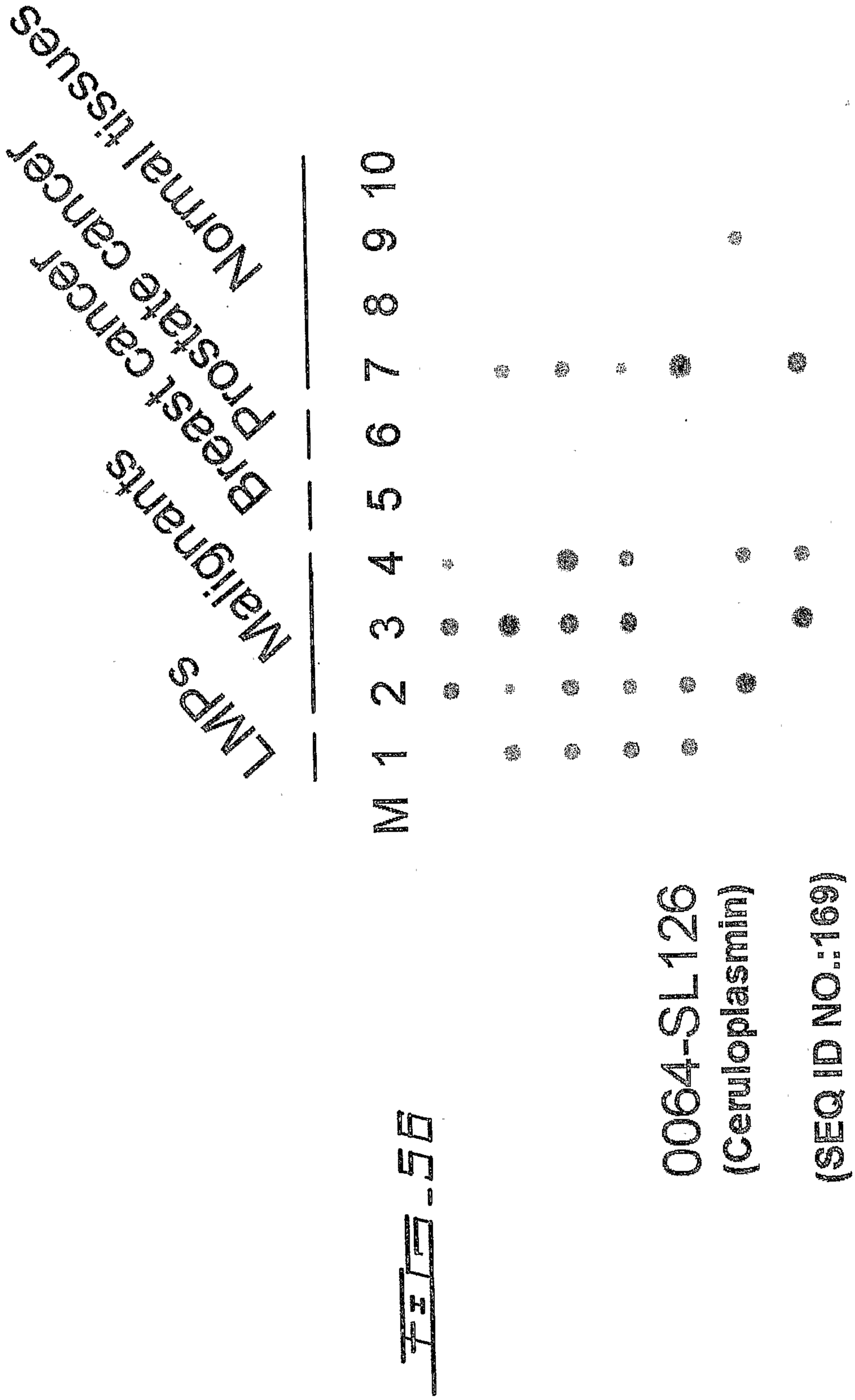
SEQ. ID. NO. 01
0094-SL126

SEQ. ID. NO. 12
0291-SL126

SEQ. ID. NO. 20
0313-SL126

Fig. 5B


Stage
Grade
Normal
N
Benign serous
1b
2a
1b
3c
LMP (borderline)
B
B
B
1
Clear Cell
carcinoma
1c
3c
2
2
Endometrioid
carcinoma
1c
3c
1
2
3c
3
Mucinous
carcinoma
1a
1
1b
3
2c
3
Serous (malignant)
3c
2
3c
3
nt
no template added
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
SEQ. ID. NO. 15
0420-SL123
SEQ. ID. NO. 24
0447-SL124
SEQ. ID. NO. 19
0889-SL124
SEQ. ID. NO. 09
1313-SL123


SEQ ID NO:56
0064-SL126
(cerulean mini)
(SEQ ID NO:169)
LMPS
Malignants
Breast cancer
Prostate cancer
Normal tissue
M 1 2 3 4 5 6 7 8 9 10

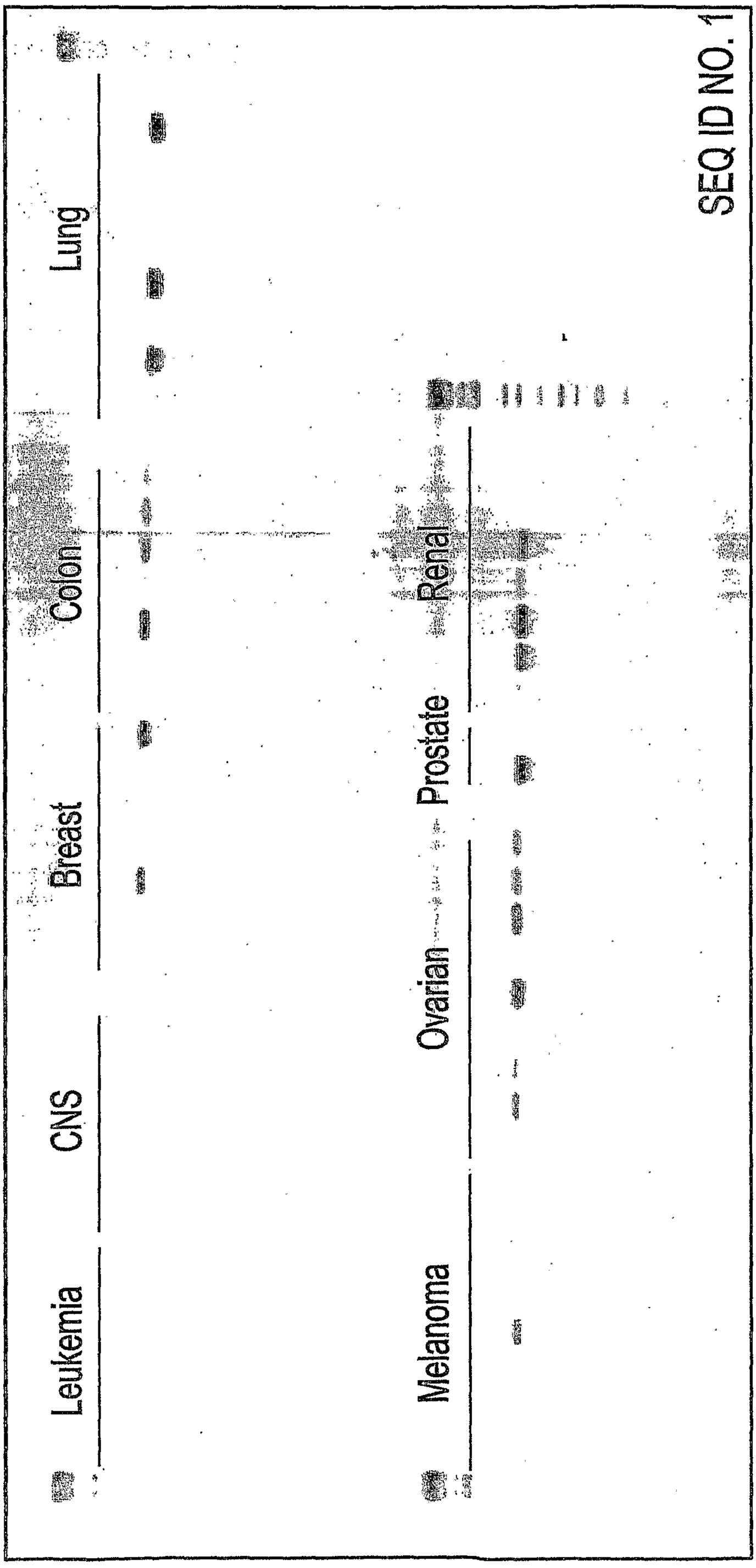

SEQ ID NO. 1
Lung
Colon
Renal
Prostate
Ovarian
Breast
CNS
Melanoma
Leukemia
SEQ ID NO 1/009094-SL123

FIG. 57

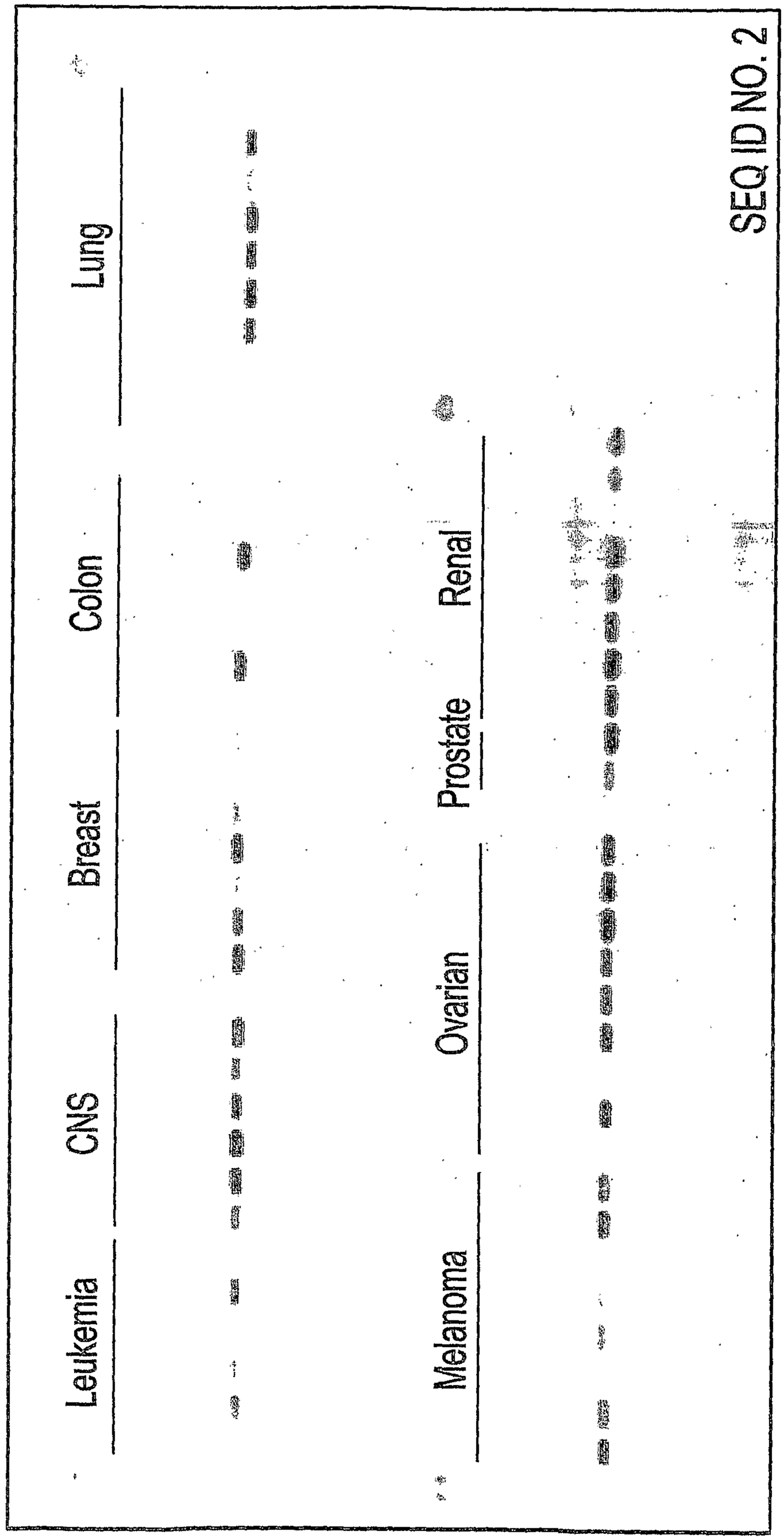
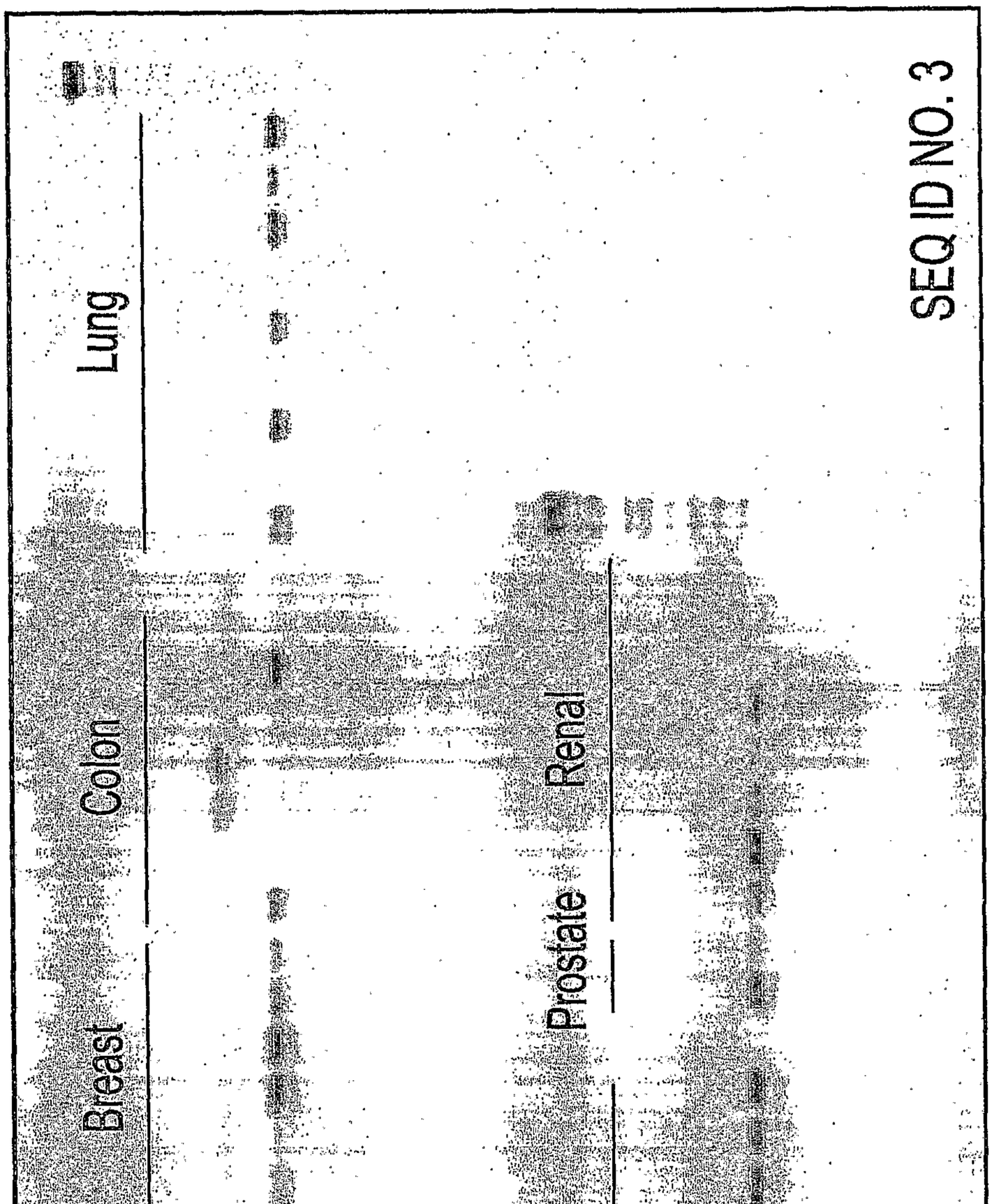
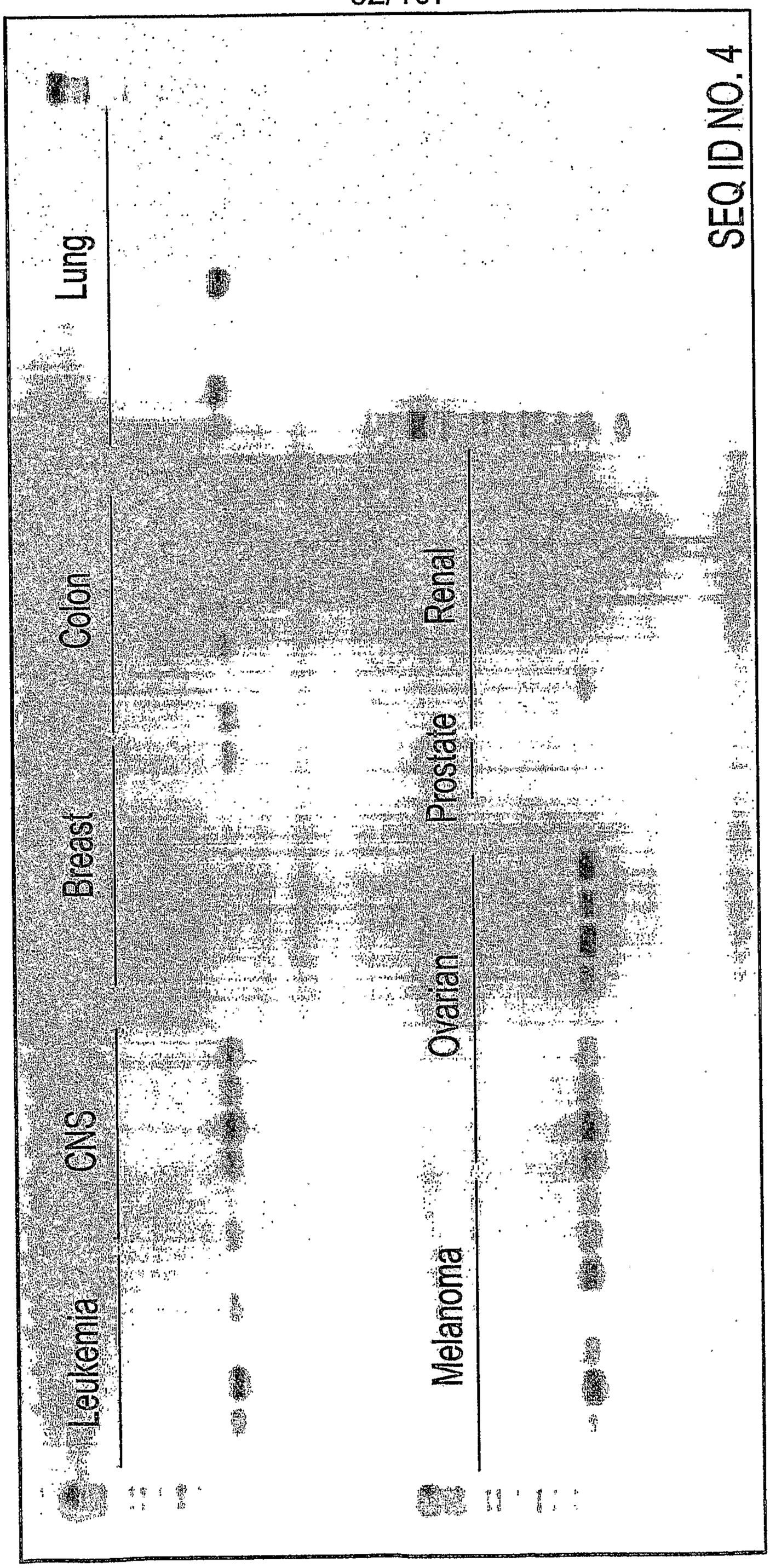

SEQ ID NO 2/0478-SL126
SEQ ID NO. 2
Colon
Lung
CNS
Breast
Renal
Prostate
Ovarian
Leukemia
Melanoma

FIG. 58


SEQ ID NO 3/071-SL126
Leukemia
CNS
Breast
Lung
Colon
Renal
Melanoma
Ovarian
Prostate
SEQ ID NO. 3


SEQ ID NO 4/0851-SL126
SEQ ID NO. 4
Colon
Lung
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia
FIG - 60

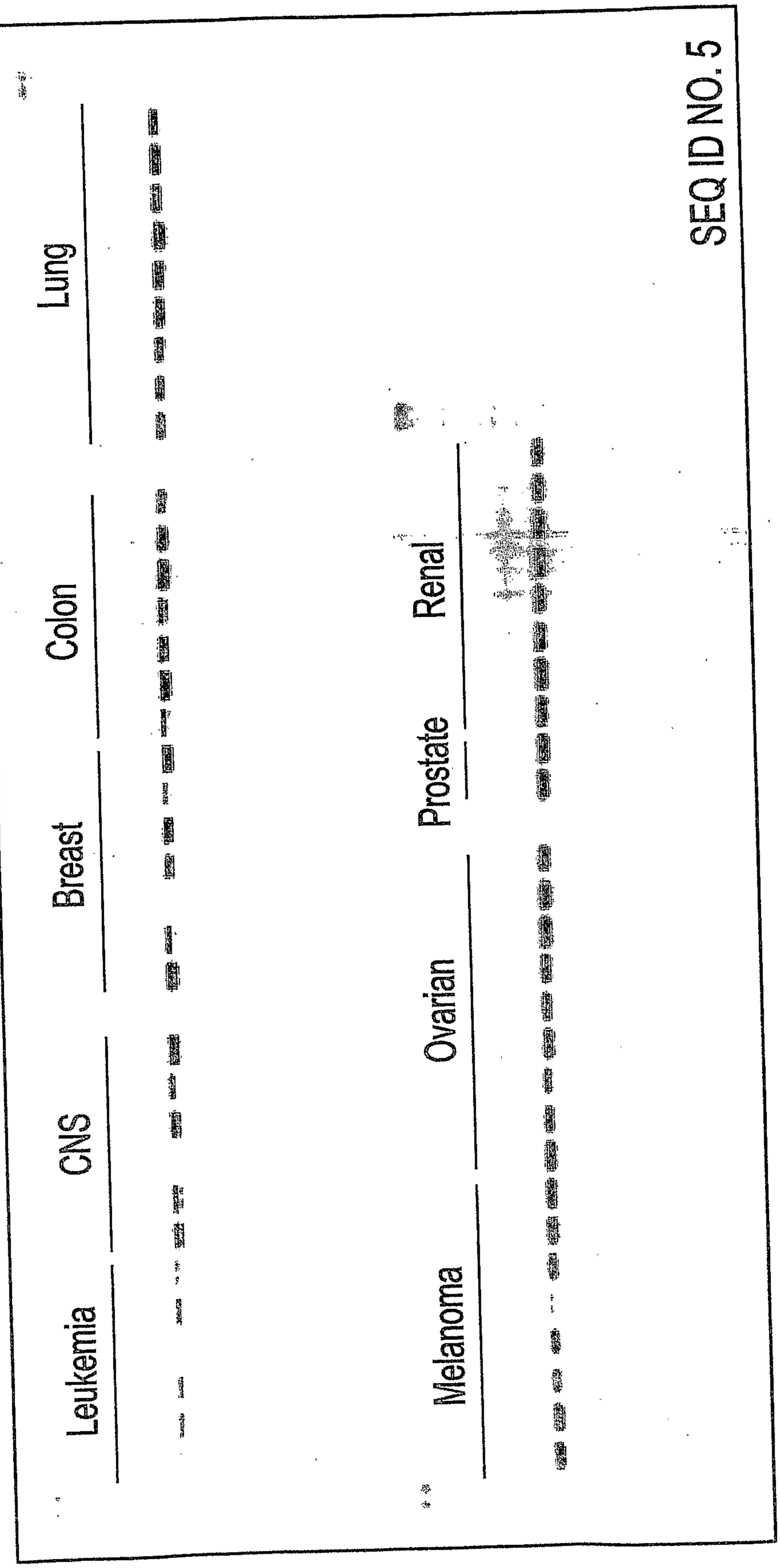

SEQ ID NO 5/713-SL126
SEQ ID NO.5
CNS
Colon
Lung
Breast
Renal
Ovarian
Prostate
Leukemia
Melanoma

FIG. 63

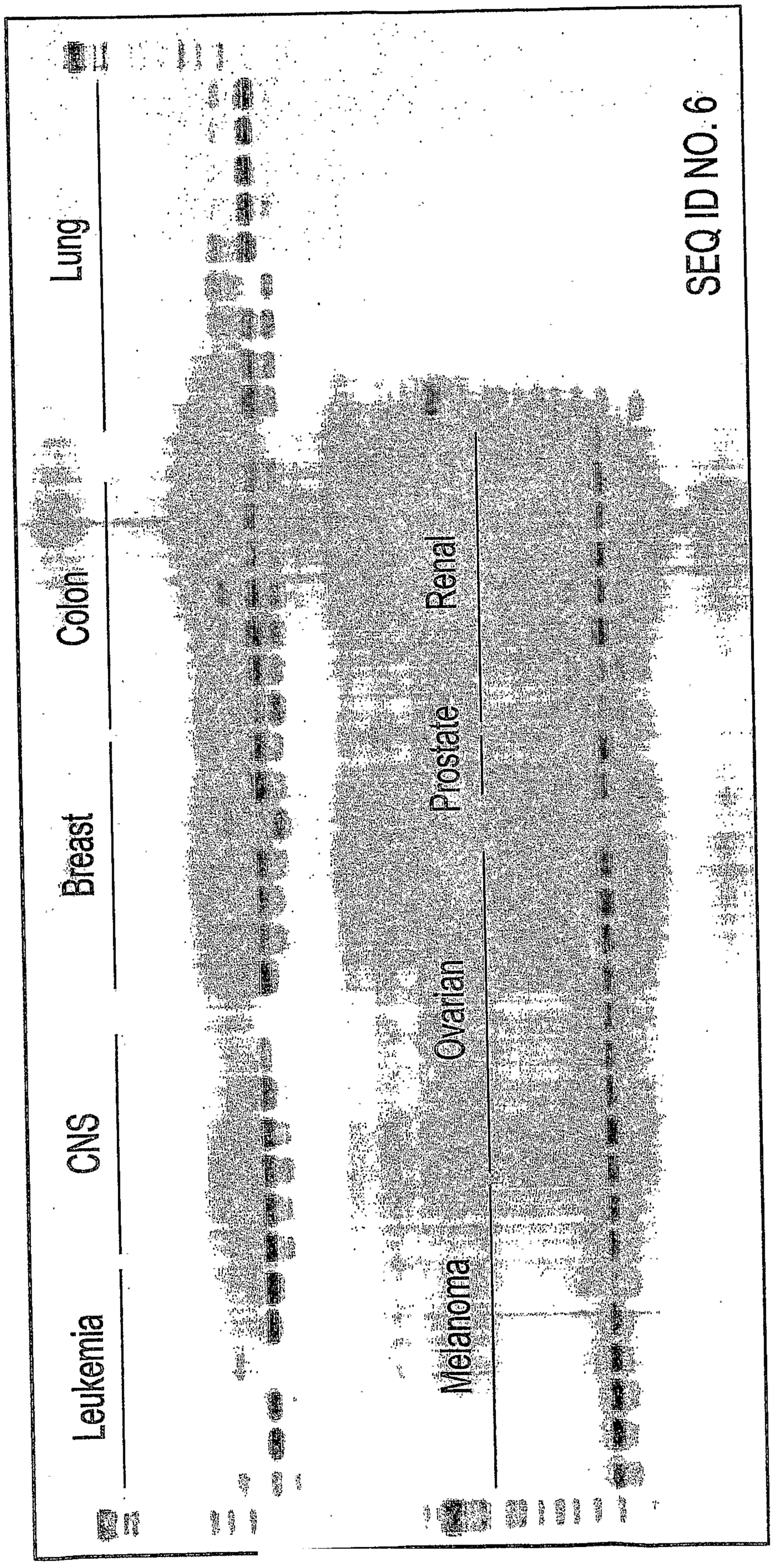

SEQ ID NO 6/106-SL126
SEQ ID NO.6
Colon
Lung
Breast
CNS
Renal
Prostate
Ovarian
Leukemia
Melanoma

FIG. 62

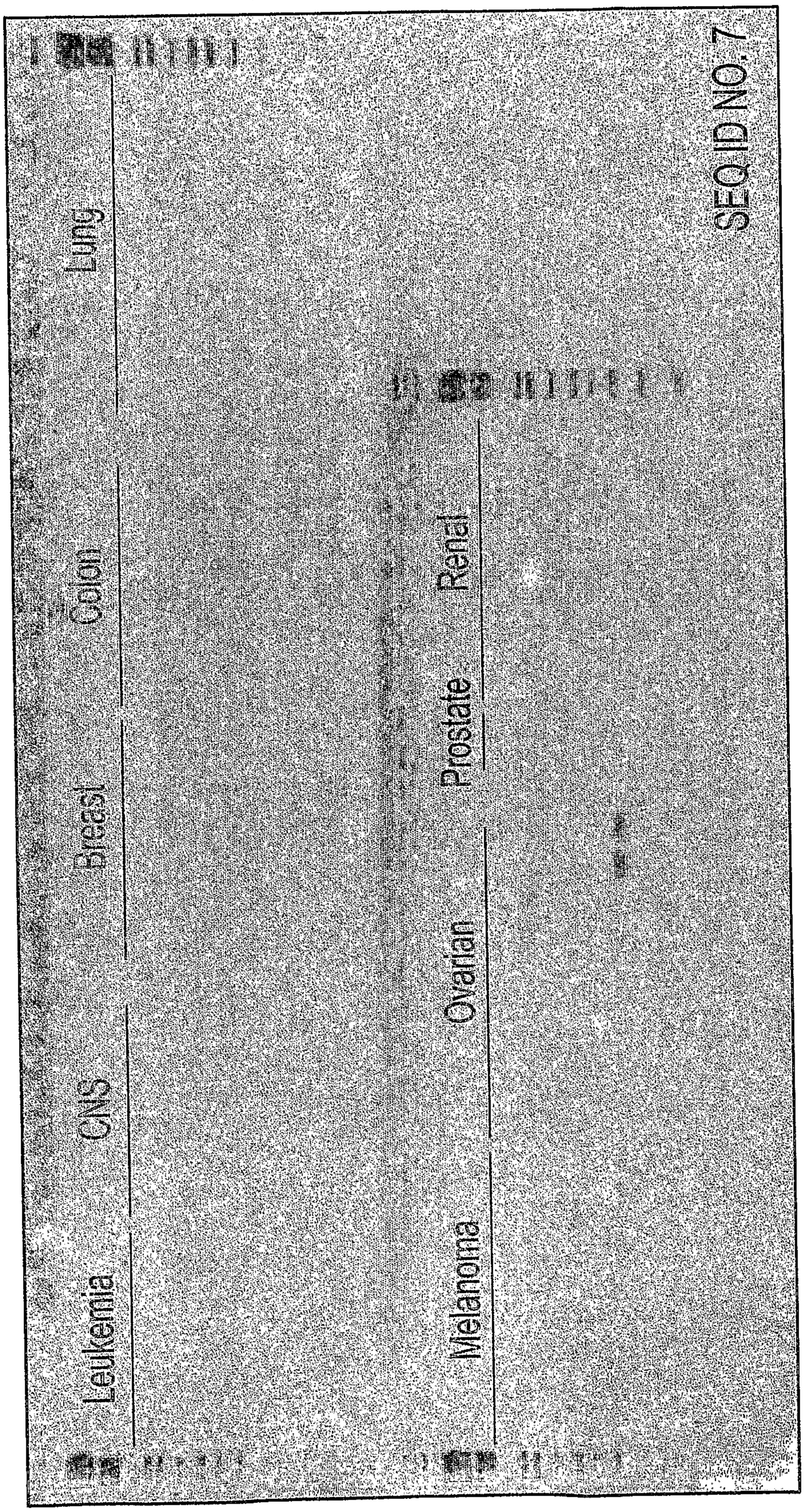

SEQ ID NO 7/1096-SL126
Lung
Colon
Renal
Breast
Prostate
CNS
Ovarian
Pancreatic
Melanoma
Leukemia

Fig. 63

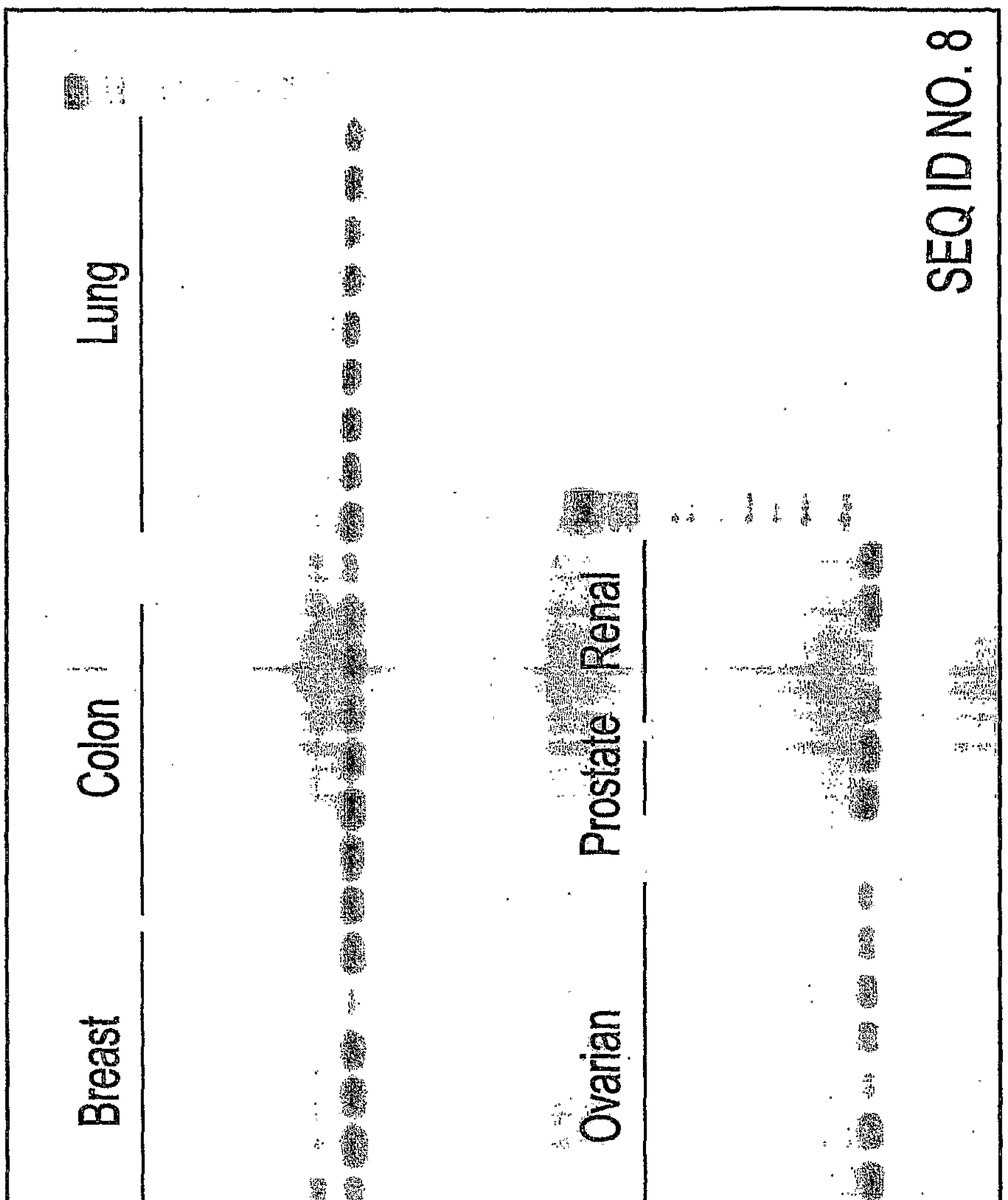

SEQ ID NO. 8
SEQ ID NO 8/065-SL126
Lung
Colon
Breast
CNS
Prostate
Renal
Ovarian
Melanoma
Renal
Leukemia

FIG. 64

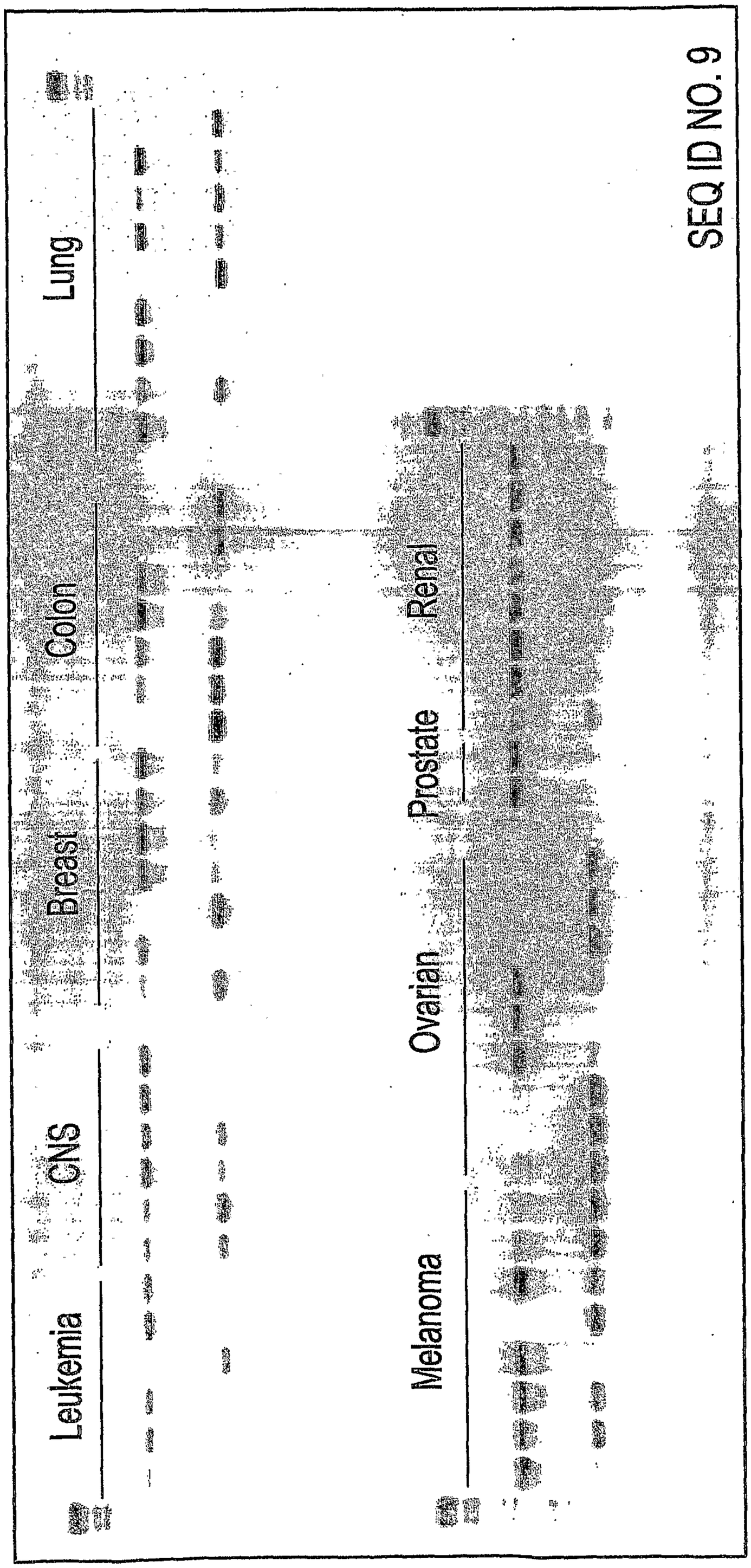

SEQ ID NO 9/131-SL123
SEQ ID NO. 9
Lung
Colon
Breast
Renal
Prostate
CNS
Ovarian
Leukemia
Melanoma

FIG. 65

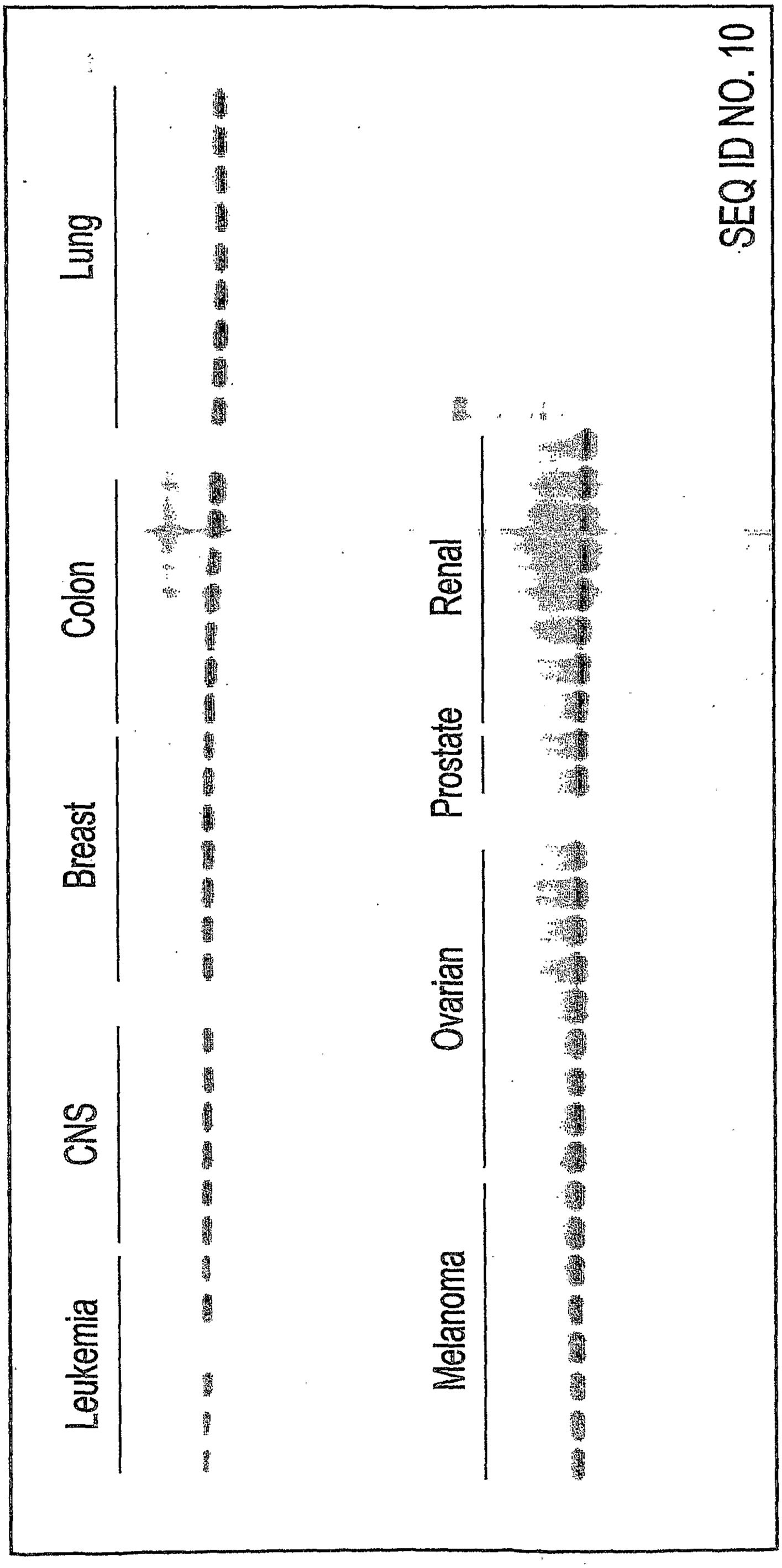

SEQ ID NO 10/0059-SL125
SEQ ID NO. 10
Colon
Lung
Breast
CNS
Prostate
Renal
Ovarian
Leukemia
Melanoma

FIG. 68

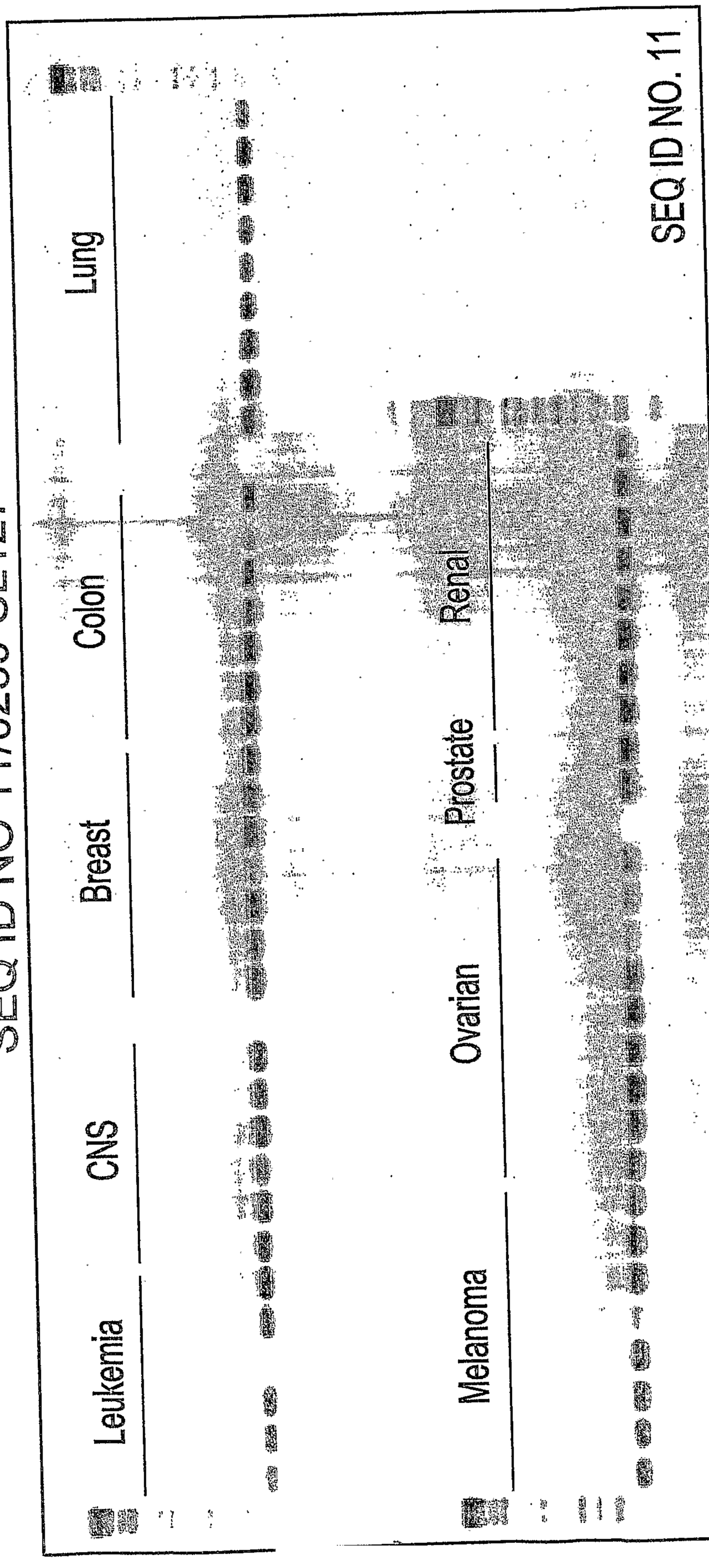

SEQ ID NO 11/0239-SL127
SEQ ID NO. 11
Colon
Lung
Breast
CNS
Renal
Prostate
Ovarian
Leukemia
Melanoma

FIG - 67

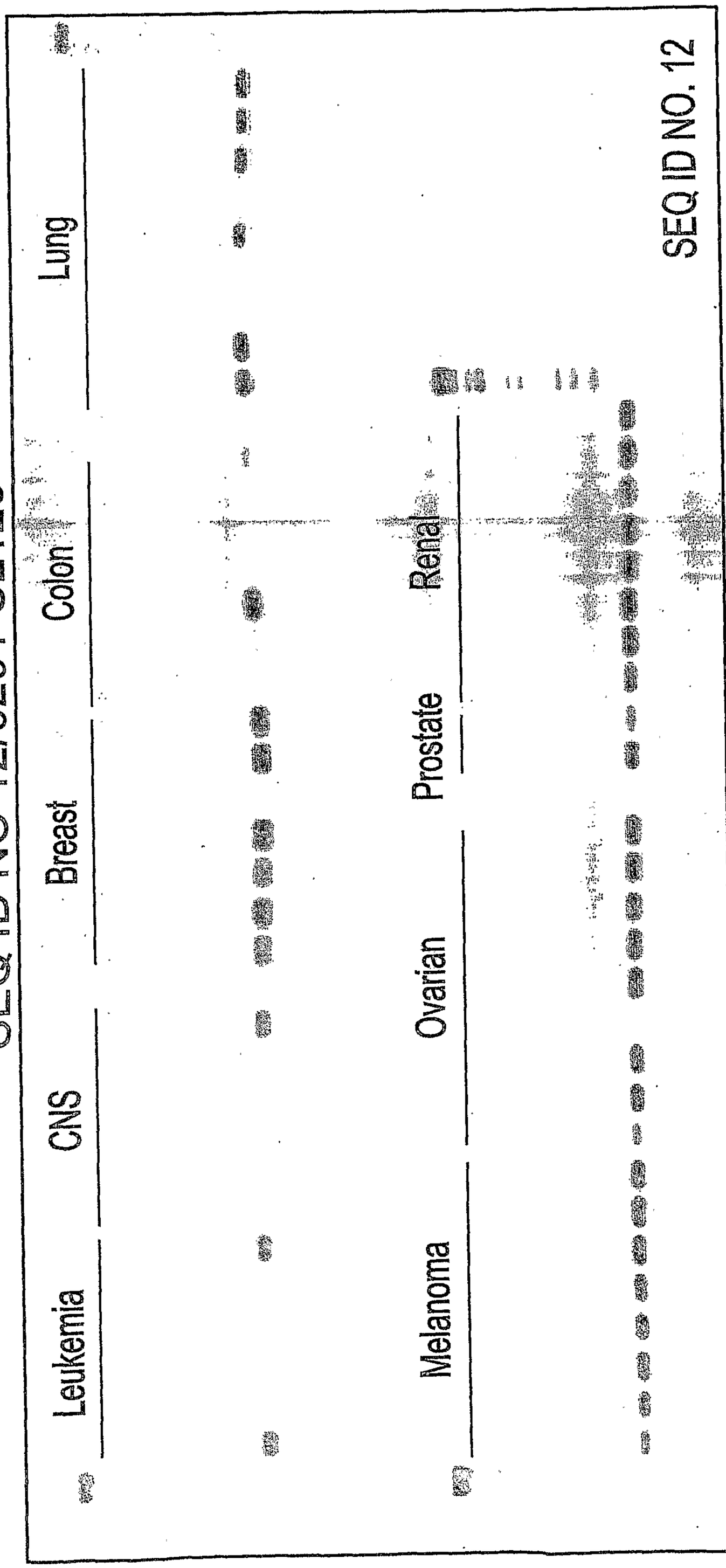

SEQ ID NO 12/02911-SL126
SEQ ID NO. 12
Colon
Lung
CNS
Breast
Renal
Prostate
Ovarian
Leukemia
Melanoma

FIG. 68

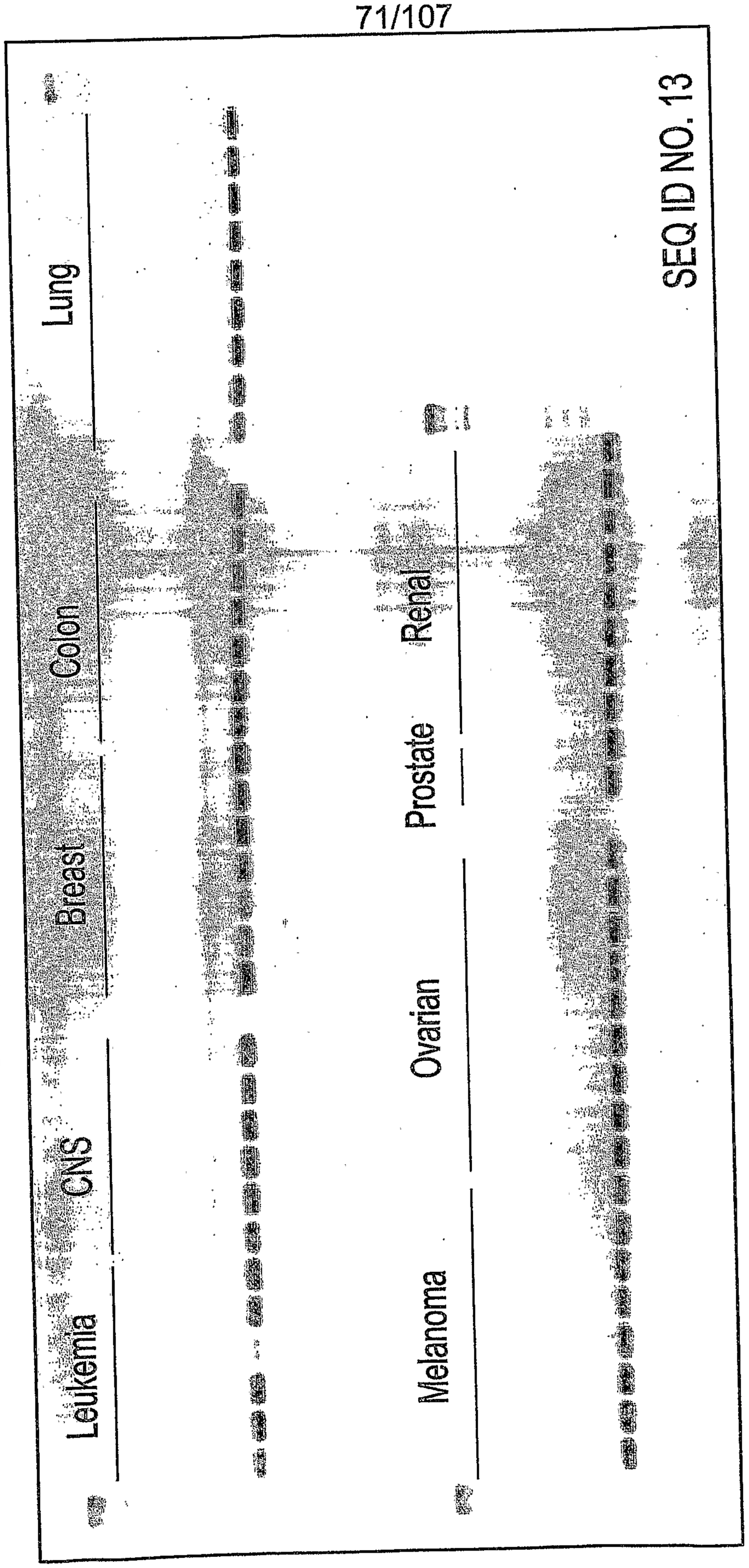

SEQ ID NO. 13
Lung
Colon
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia
SEQ ID NO 13/097972-SL123

Fig. 97

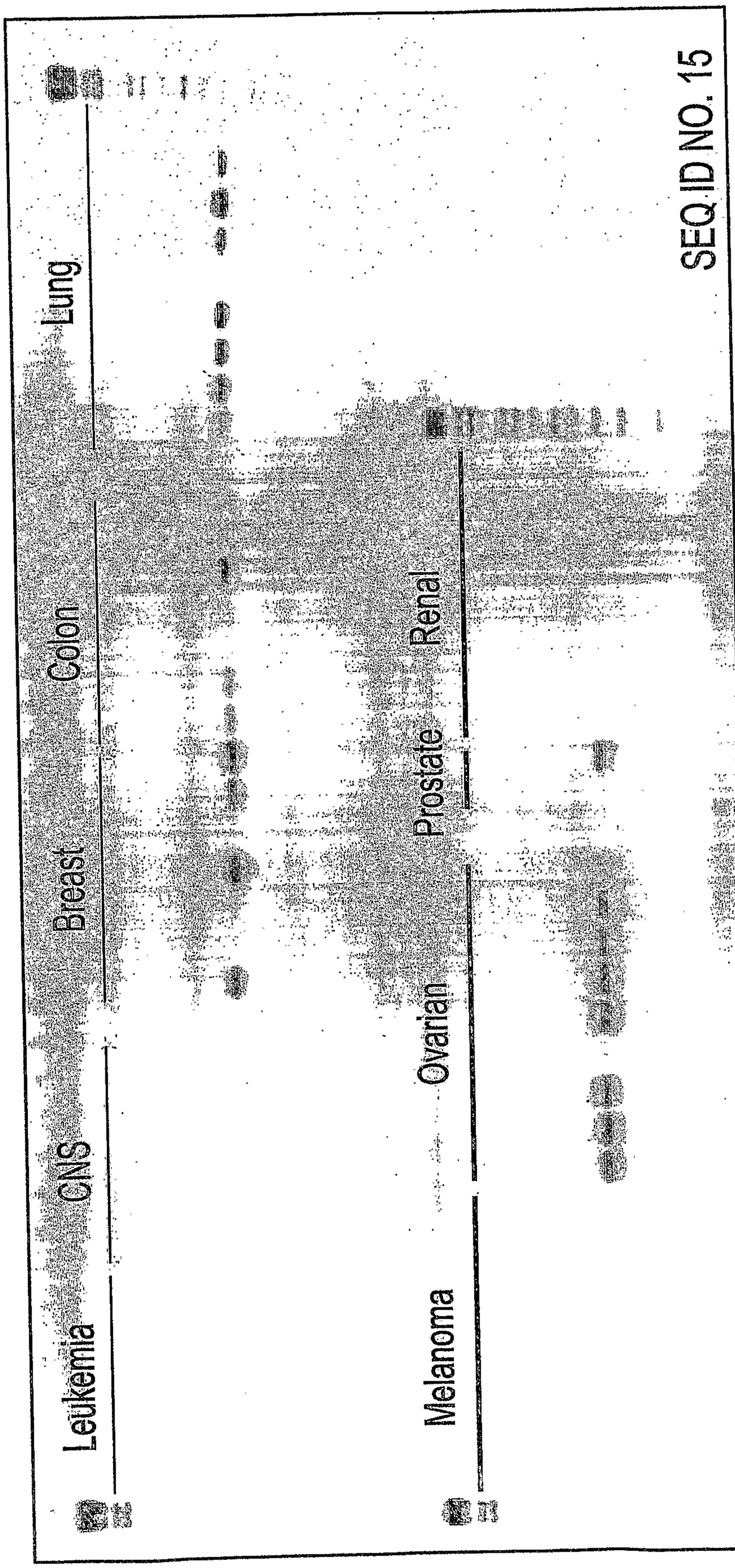

SEQ ID NO 15/420-SL123
Lung
Colon
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia

FIG - 70

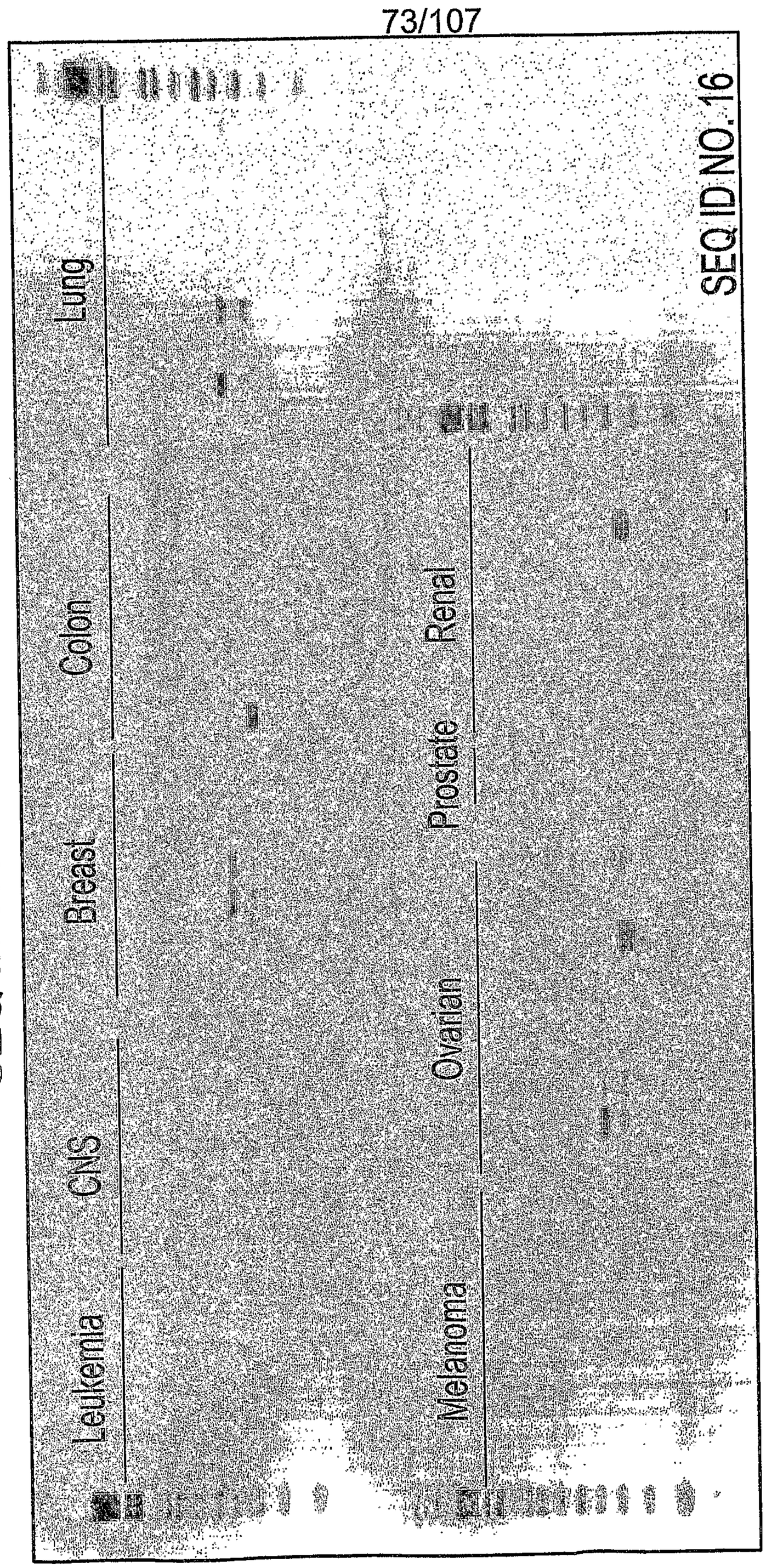

SEQ ID NO 16/012125-SL125
SEQ ID NO.16
Lung
Colon
Breast
CNS
Renal
Ovarian
Prostate
Melanoma
Leukemia

FIG. 71

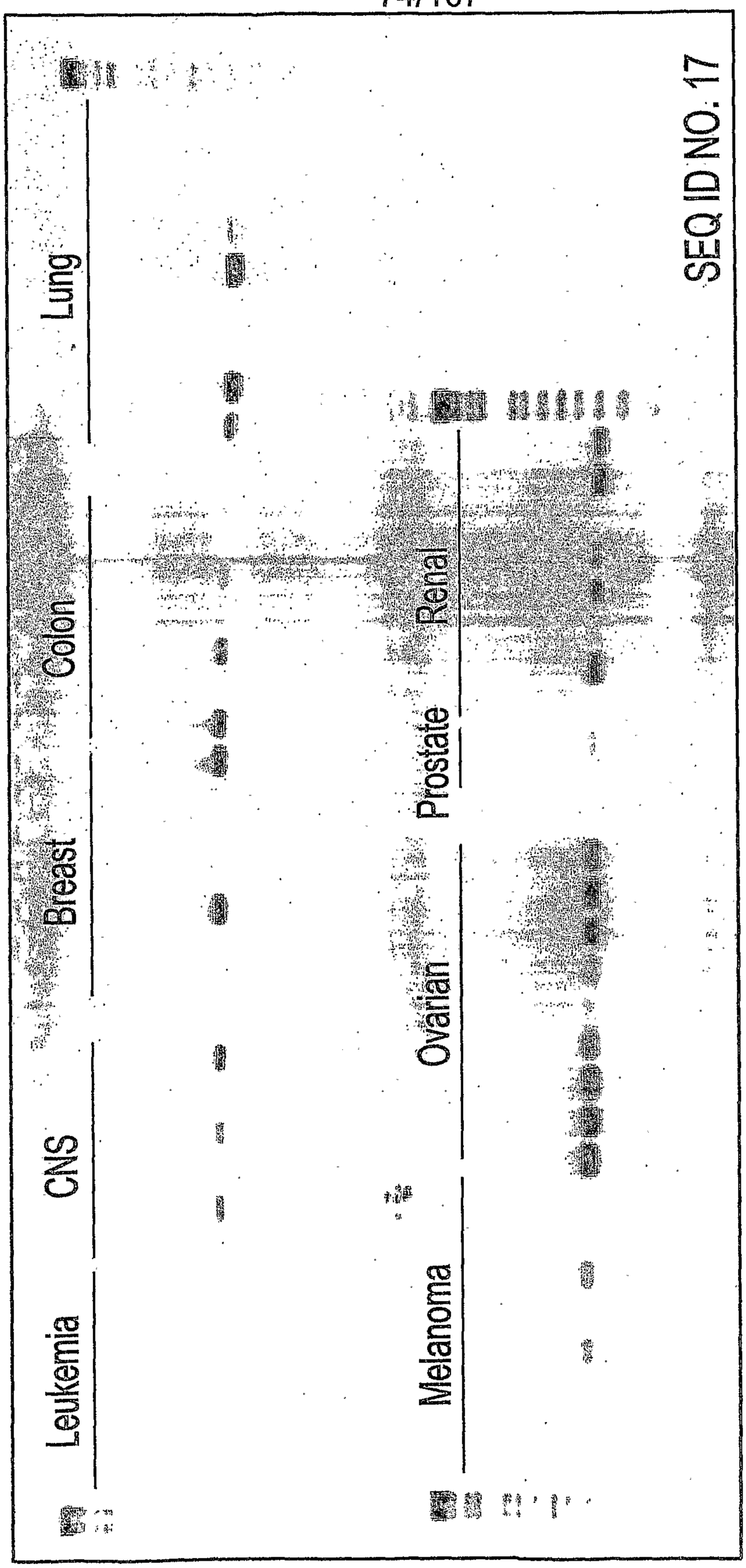

SEQ ID NO 17/0531-SL124
SEQ ID NO:17
Colon
Lung
Breast
Prostate
Renal
CNS
Ovarian
Pancreatic
Leukemia
Melanoma

FIG. 74

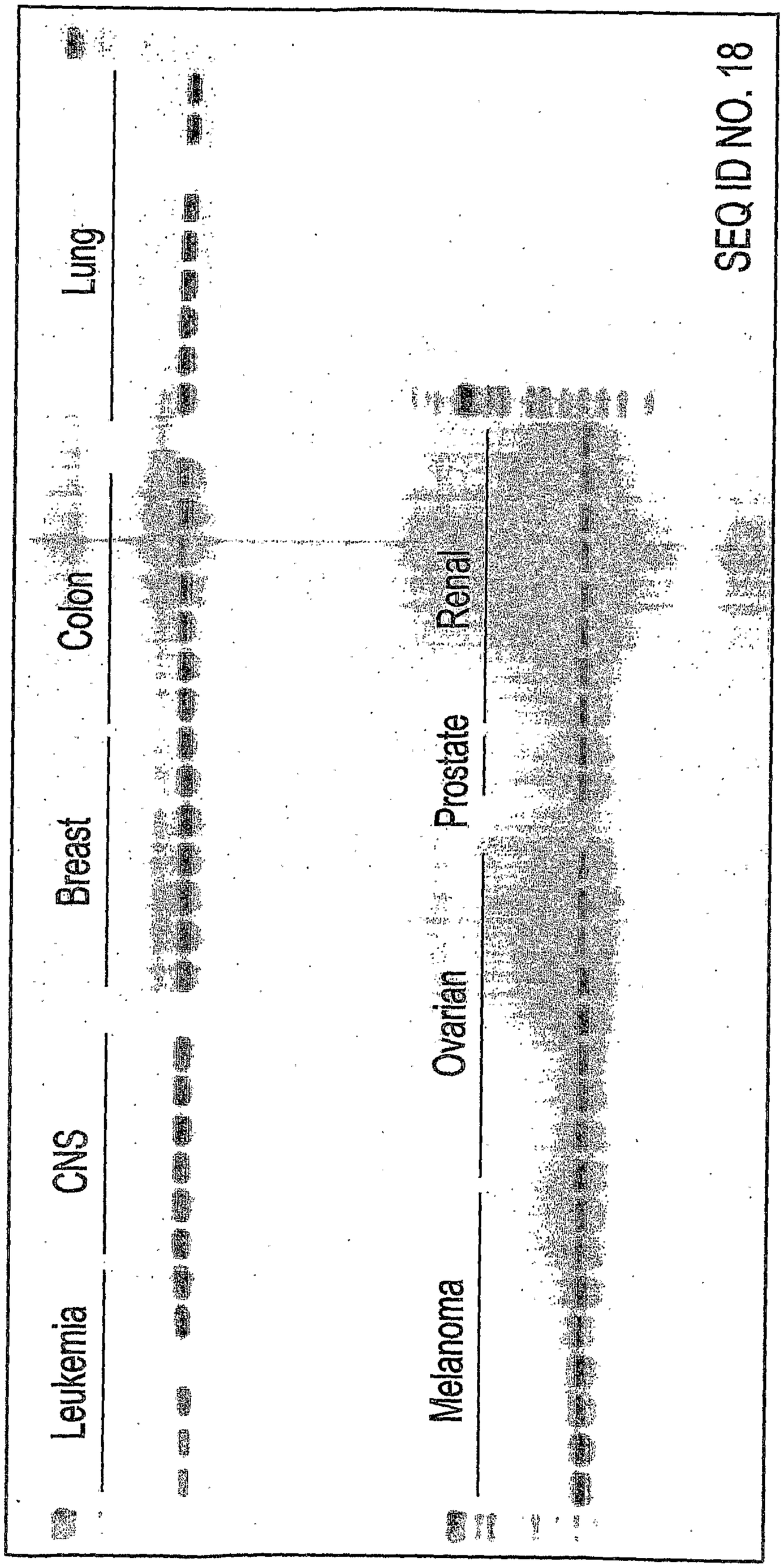

SEQ ID NO 18/0967-SL123
SEQ ID NO. 18
Leukemia
CNS
Breast
Melanoma
Ovarian
Prostate
Renal
Colon
Lung

FIG. 74

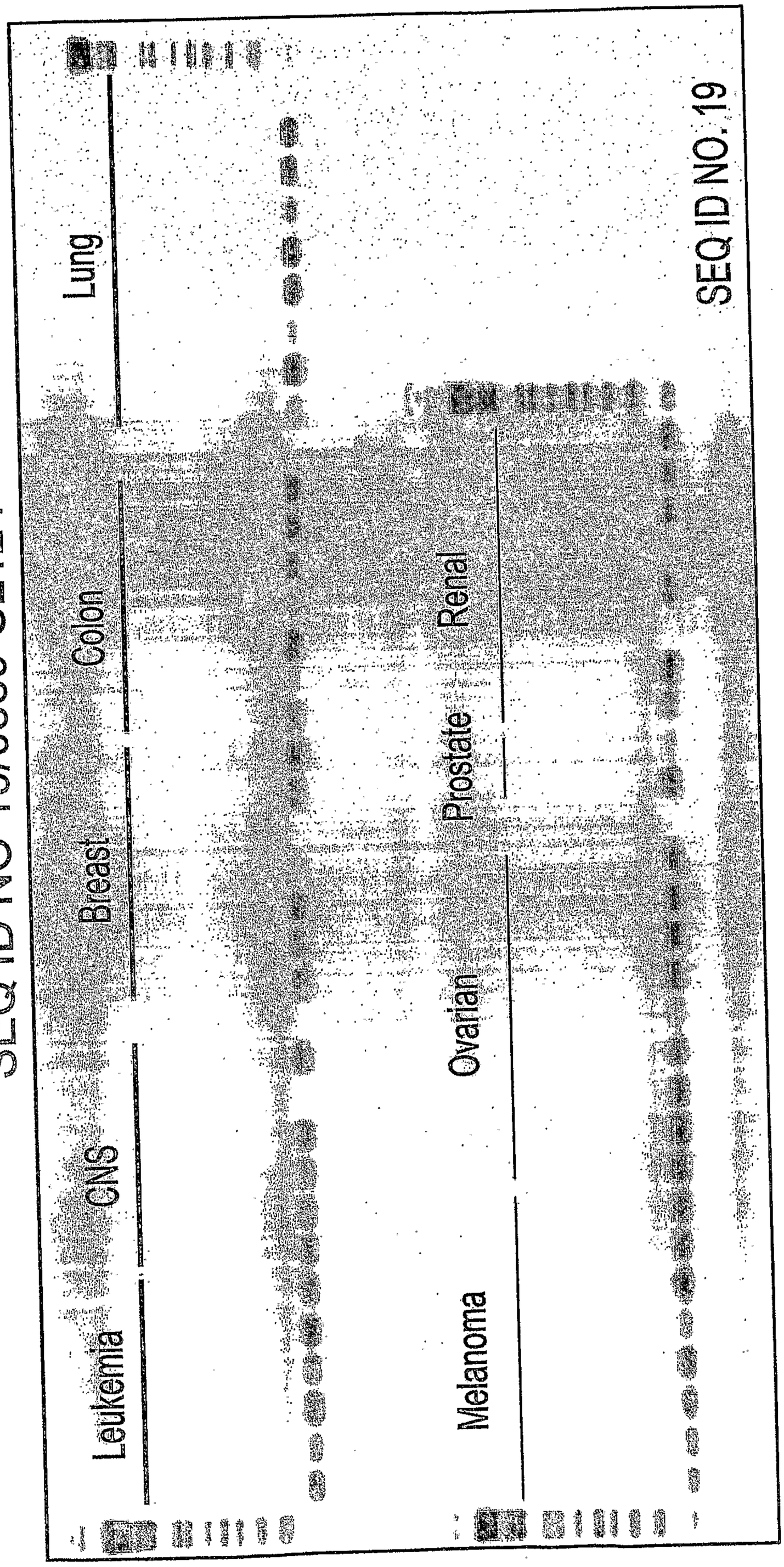

SEQ ID NO 19/0889-SL124
SEQ ID NO:19
Lung
Colon
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia

FIG. 74

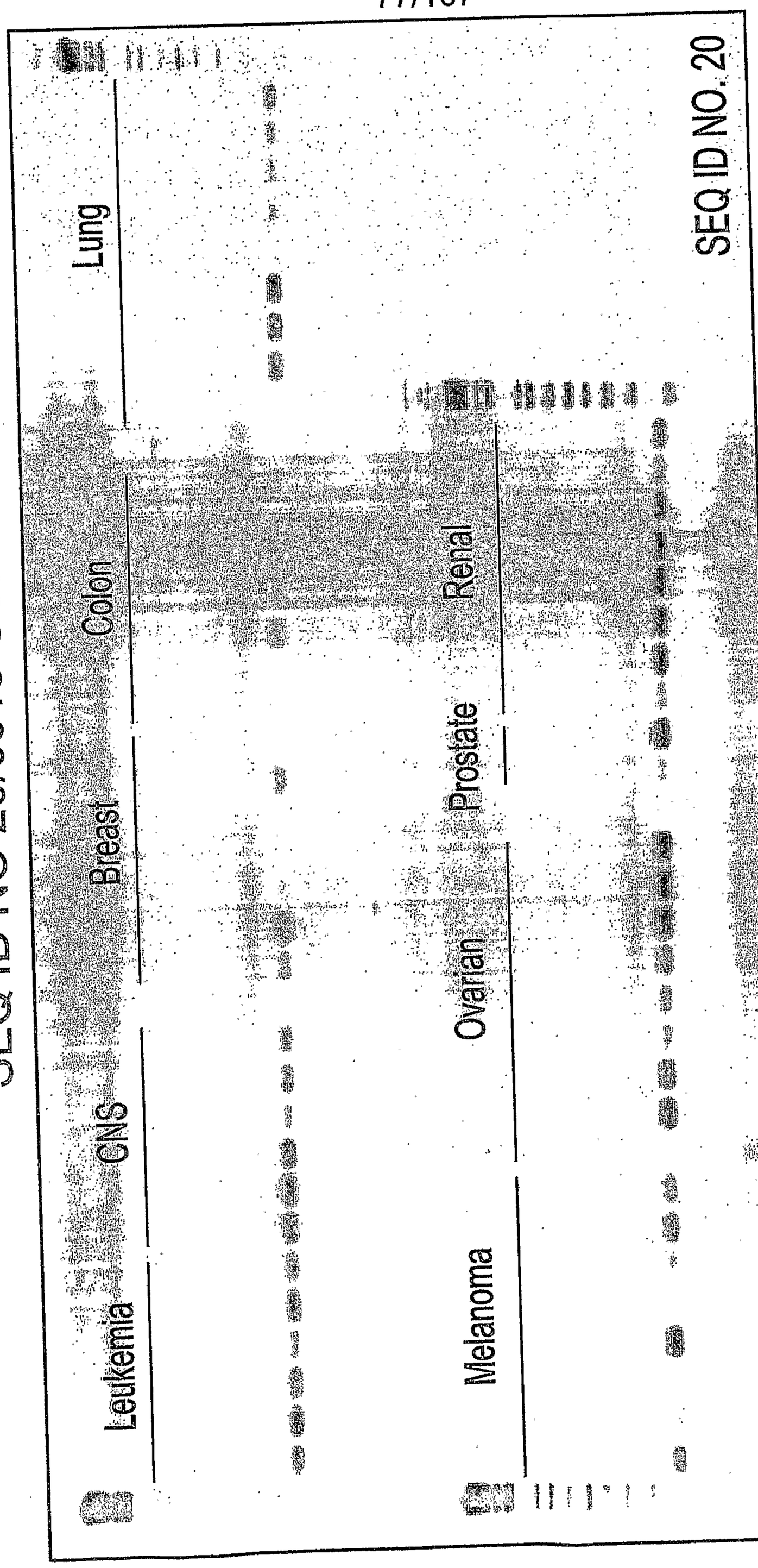

SEQ ID NO 20/313-SL123
Lung
Colon
Renal
Breast
Prostate
CNS
Ovarian
Leukemia
Melanoma

FIG - 77

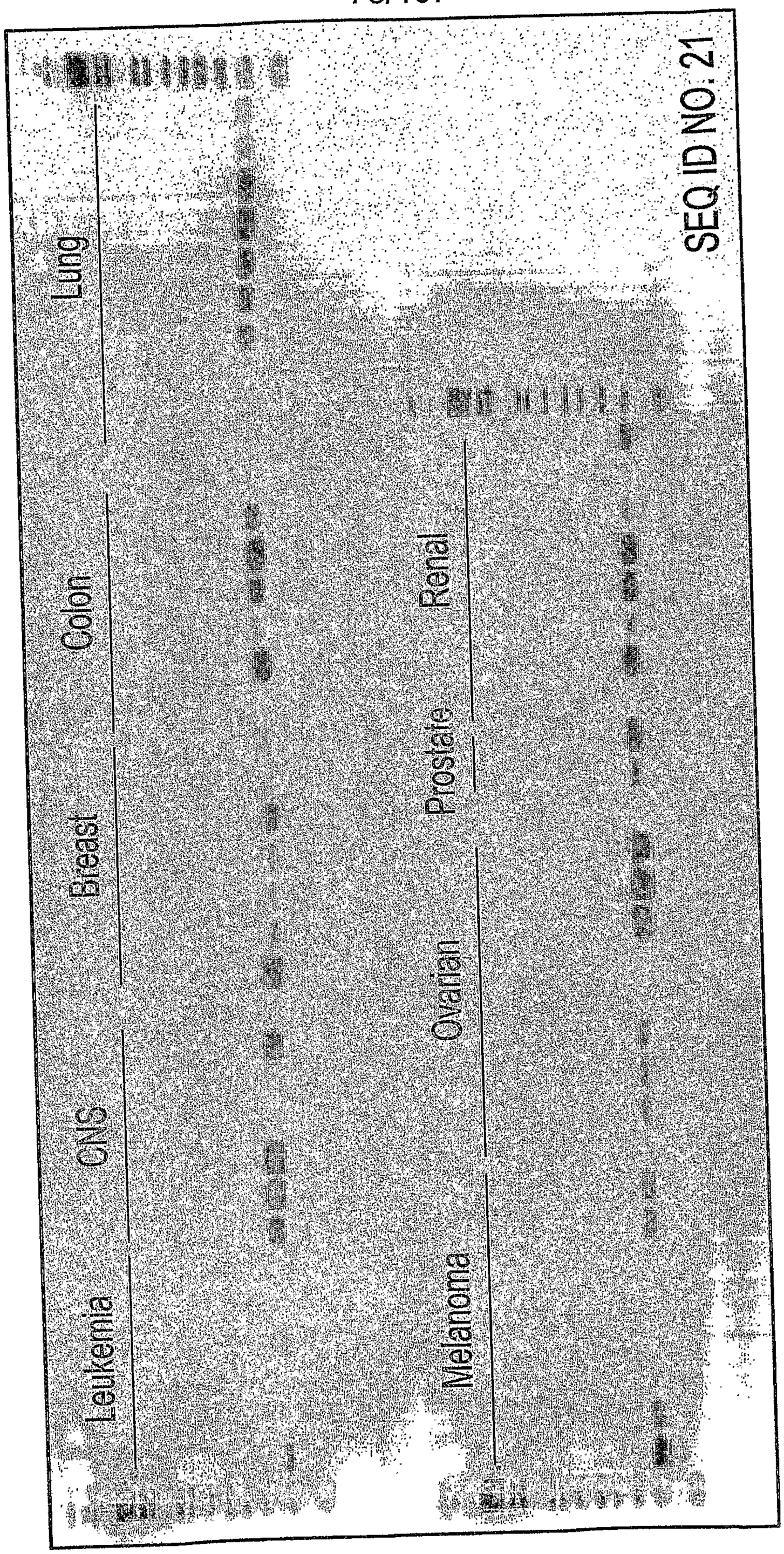

SEQ ID NO 21/1134-SL126
SEQ ID NO. 21
Colon
Lung
Breast
Renal
Prostate
CNS
Ovarian
Leukemia
Melanoma

FIG. 78

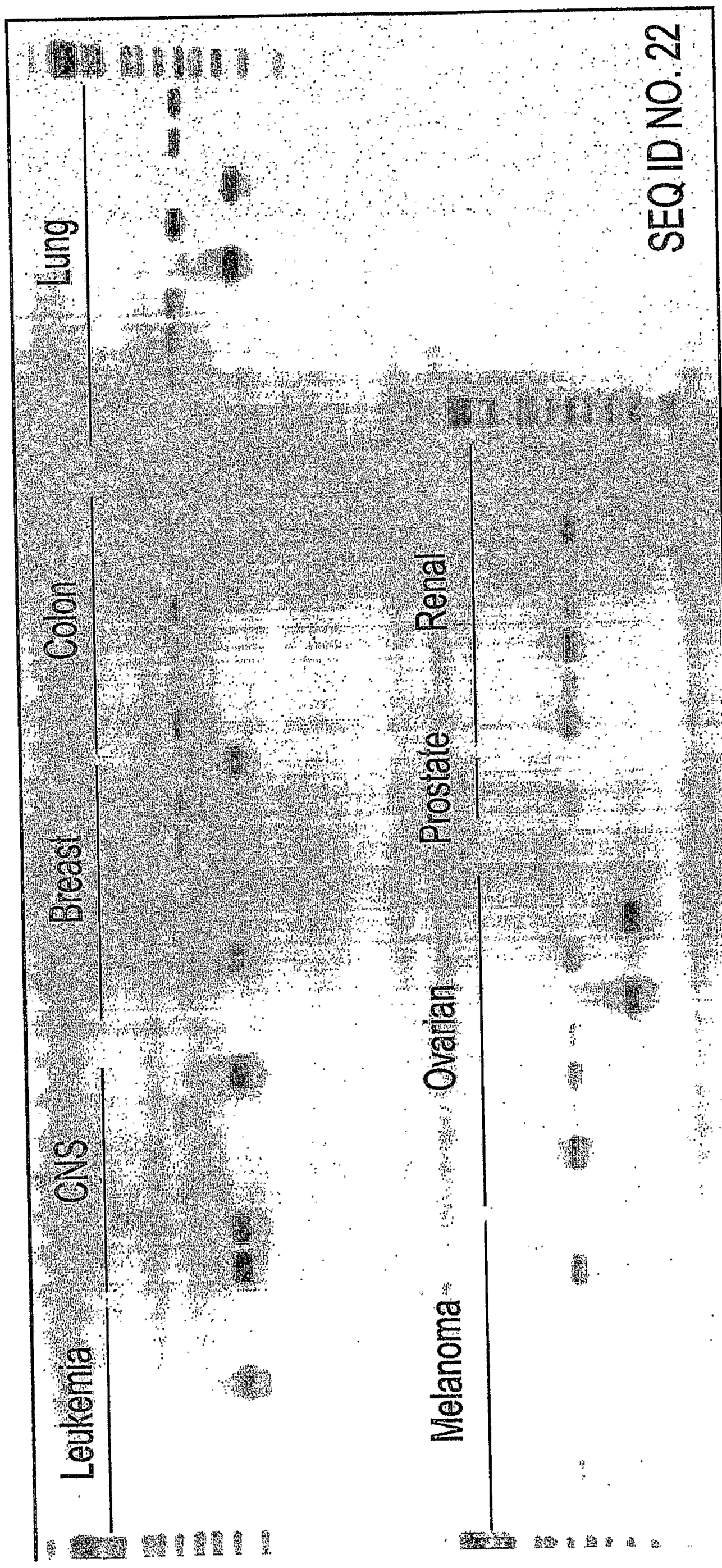

SEQ ID NO 22/0488-SL123
SEQ ID NO. 22
Lung
Colon
Renal
Breast
Prostate
Ovarian
CNS
Leukemia
Melanoma

FIG. 77

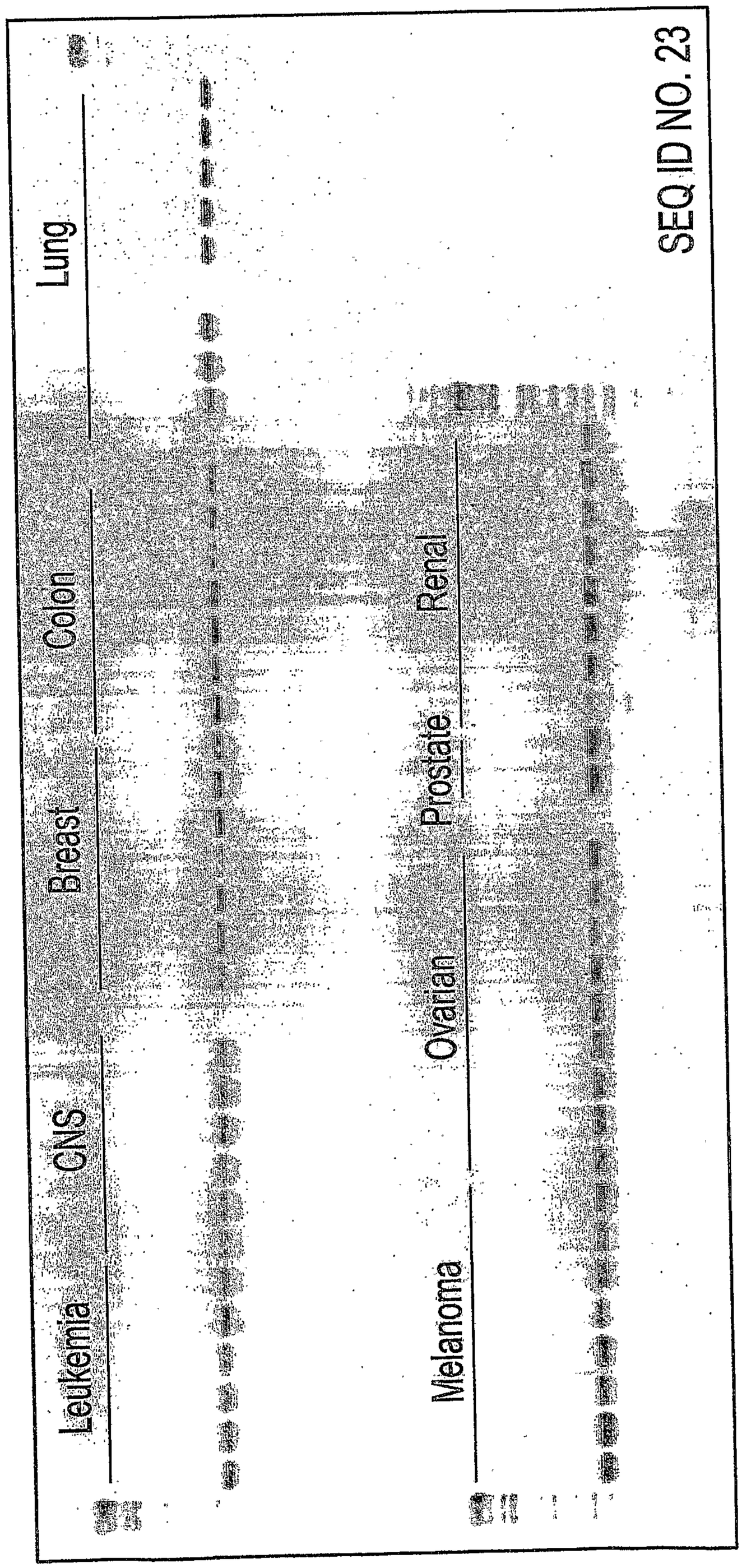

SEQ ID NO 23/0216-SL126
SEQ ID NO. 23
Lung
Colon
Renal
Breast
CNS
Prostate
Ovarian
Melanoma
Leukemia

Fig. 7B

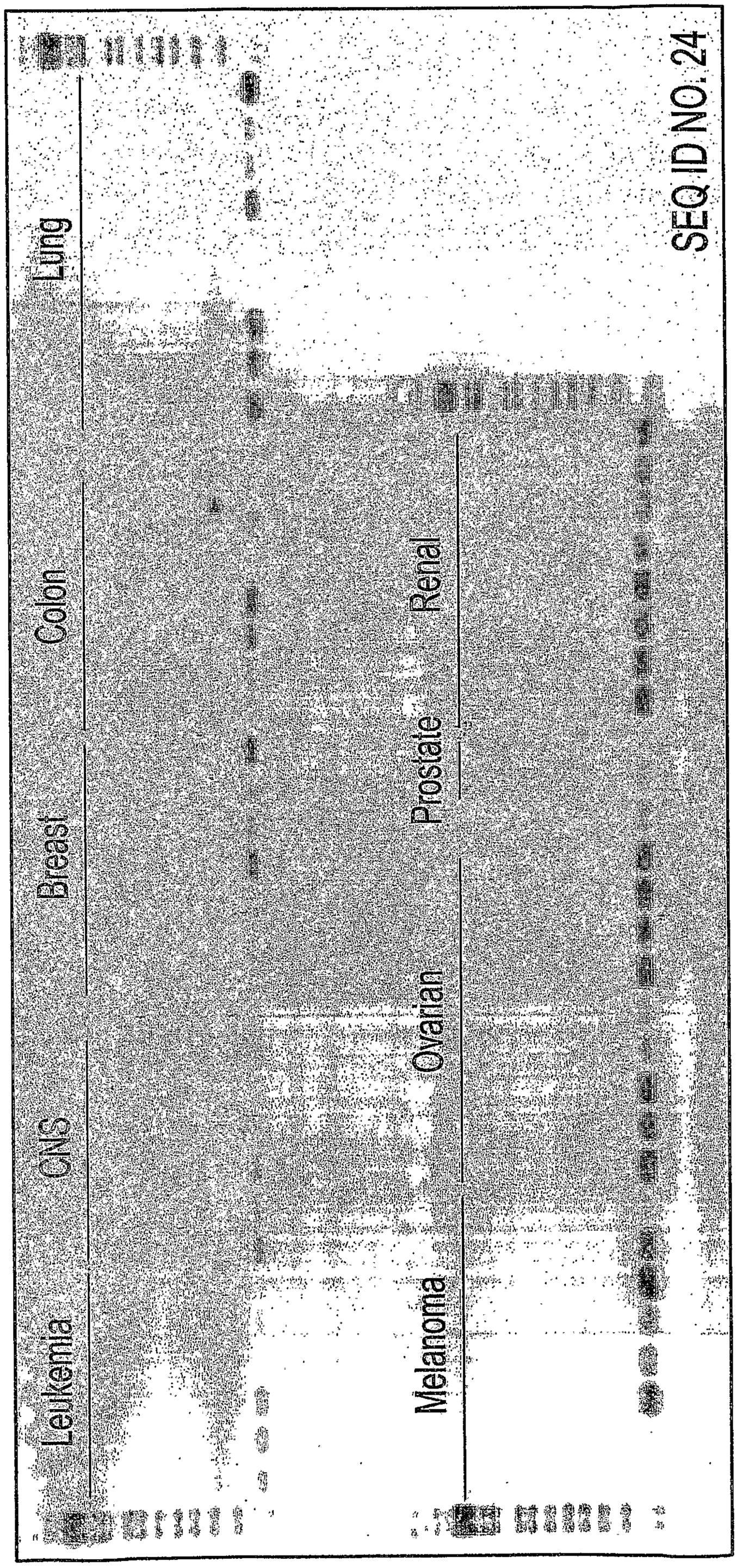

SEQ ID NO 24/44747-SL124
SEQ ID NO:24
Lung
Colon
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia

FIG. 78

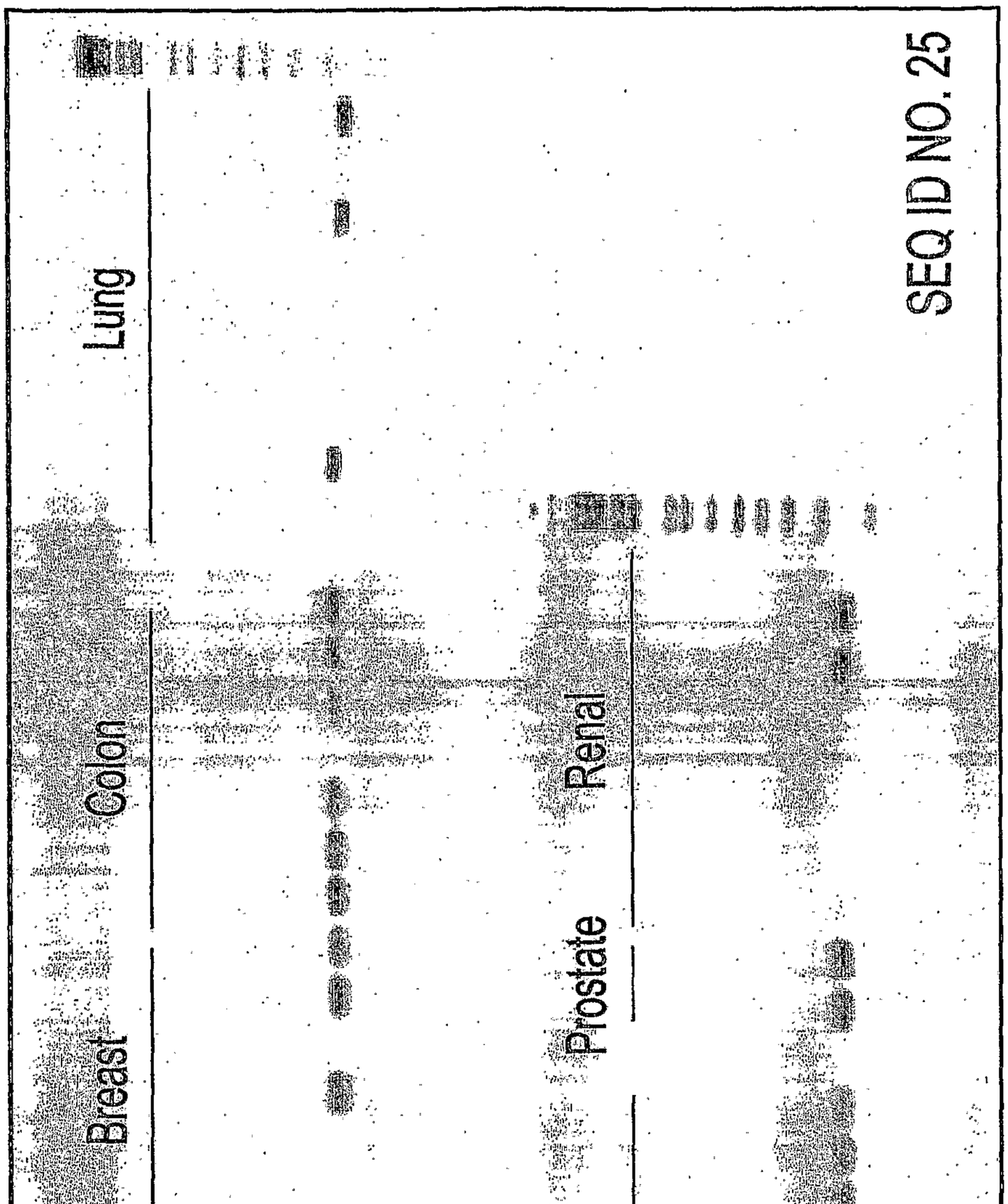

SEQ ID NO 25-SL126
SEQ ID NO. 25
CNS
Breast
Colon
Renal
Ovarian
Prostate
Lung
Melanoma
Leukemia

FIG. 80

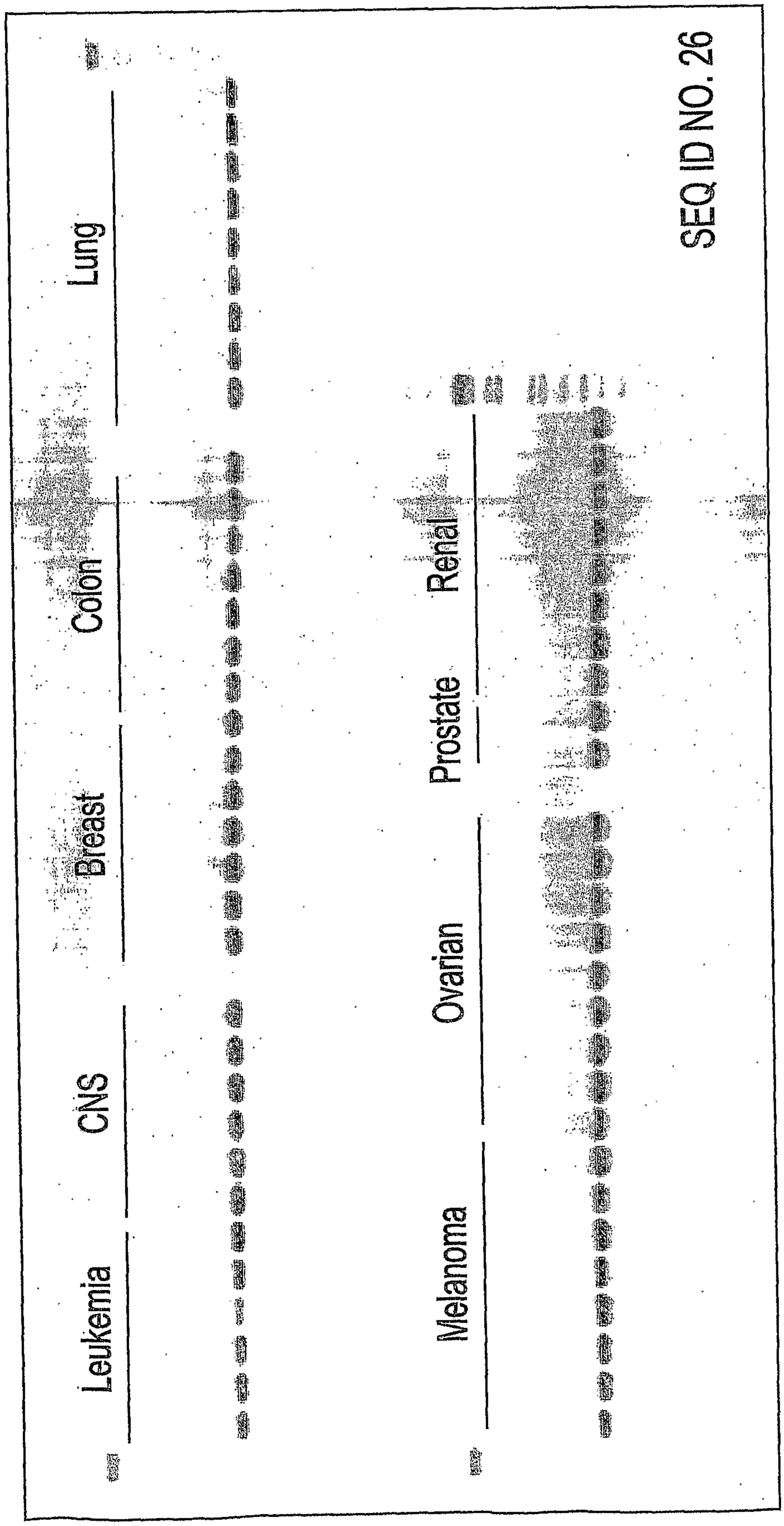

SEQ ID NO. 26
SEQ ID NO 26/0698-SL127
CNS
Breast
Colon
Lung
Leukemia
Ovarian
Prostate
Renal
Melanoma

FIG. 81

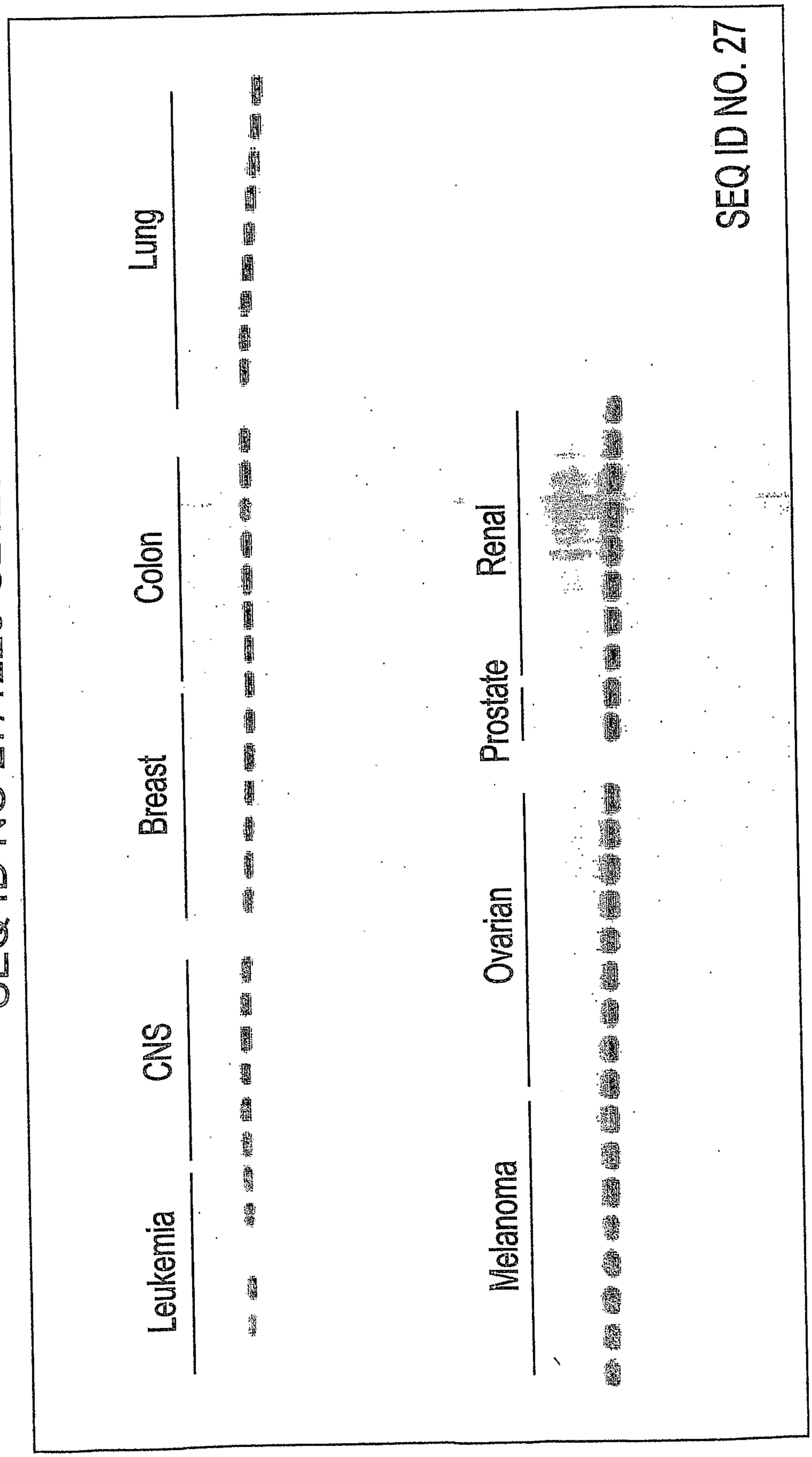

SEQ ID NO 27/1223-SL123
SEQ ID NO. 27
Colon
Lung
Breast
CNS
Renal
Prostate
Ovarian
Leukemia
Melanoma

FIG. 82

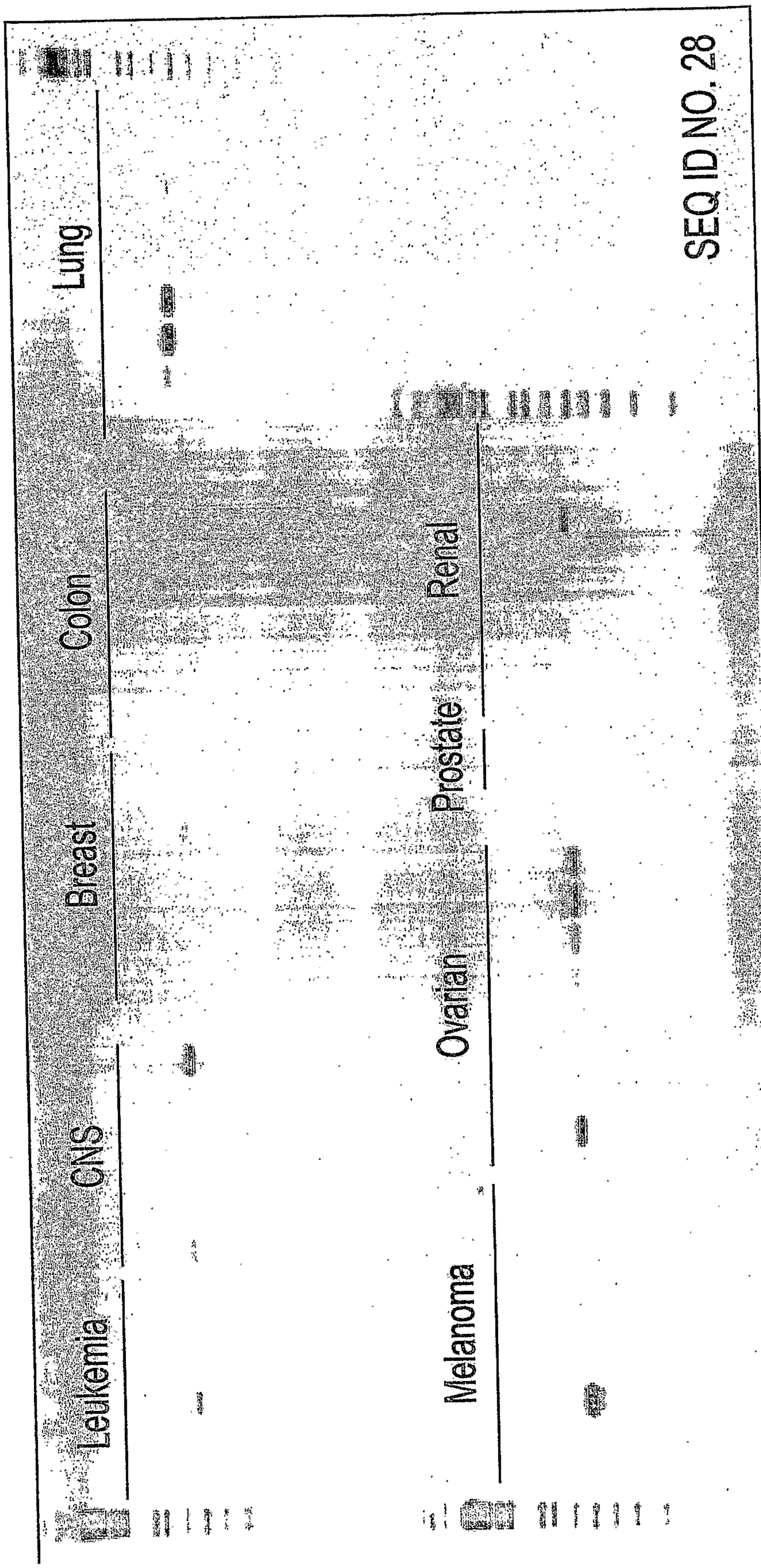

SEQ ID NO 28/1448-SL123
SEQ ID NO. 28
Lung
Colon
Breast
Renal
Ovarian
Prostate
CNS
Leukemia
Melanoma

Fig. 87

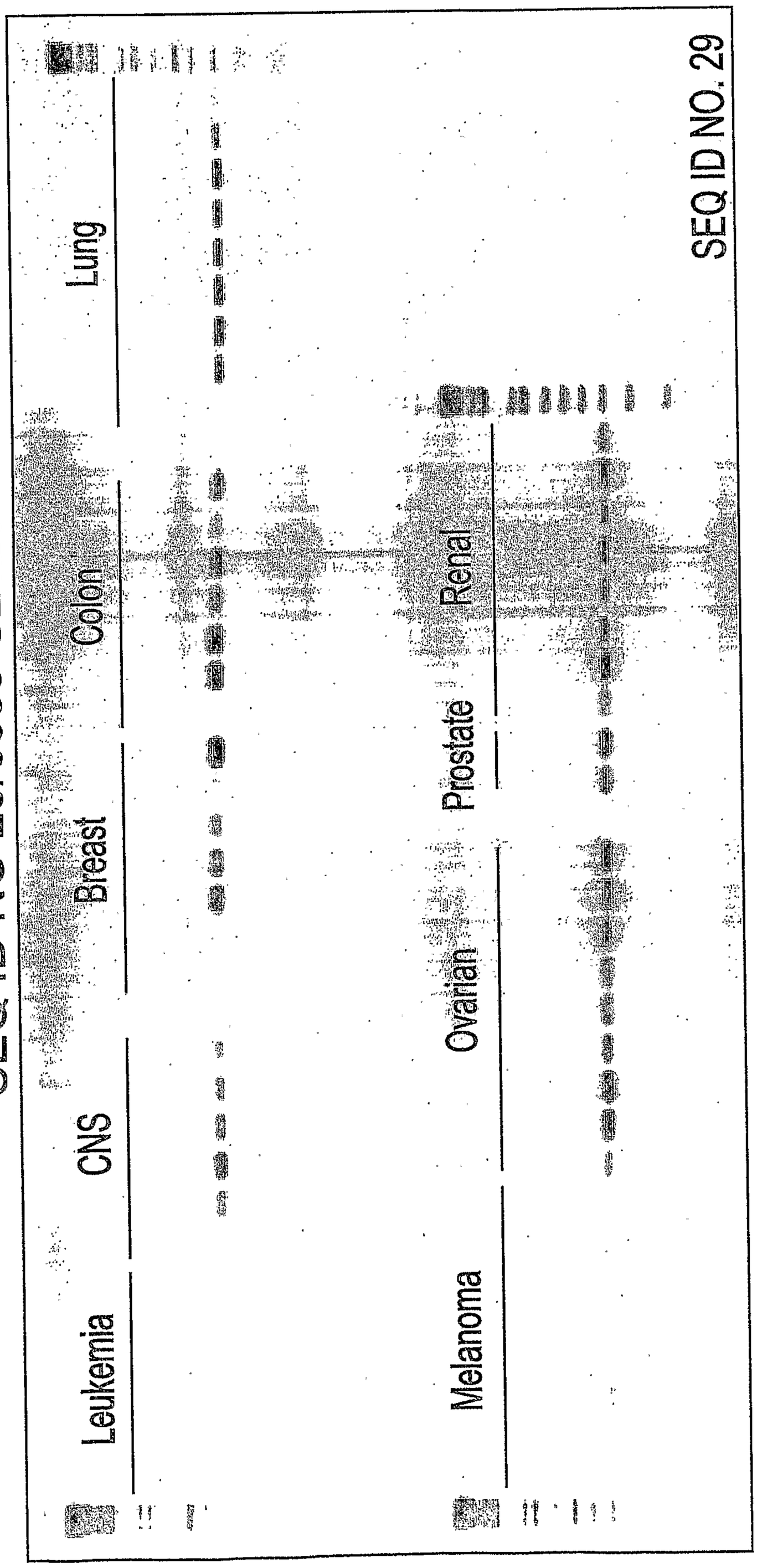

SEQ ID NO. 29
SEQ ID NO 29/0635-SL126
Lung
Colon
Breast
Prostate
Renal
CNS
Ovarian
Leukemia
Melanoma

FIG. 84

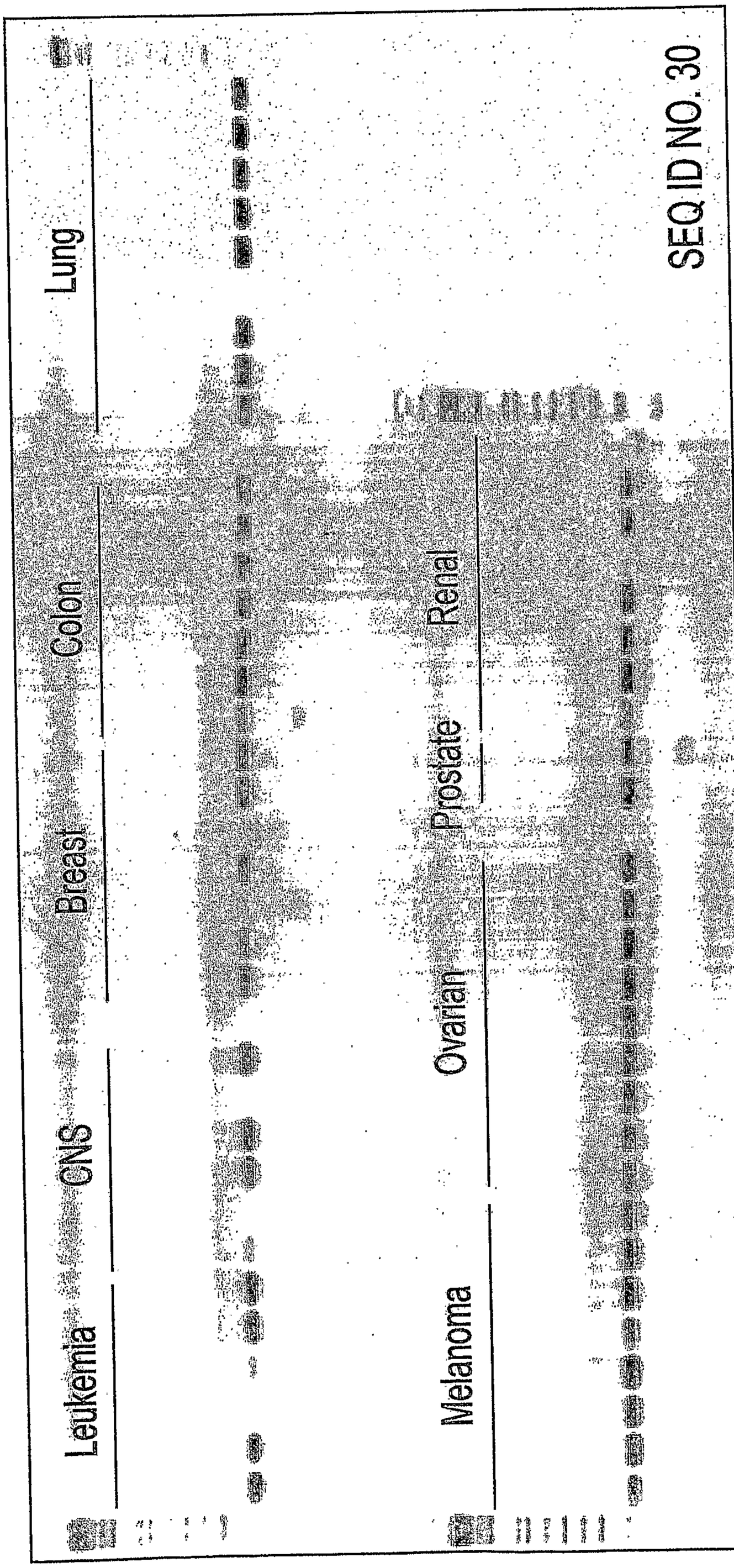
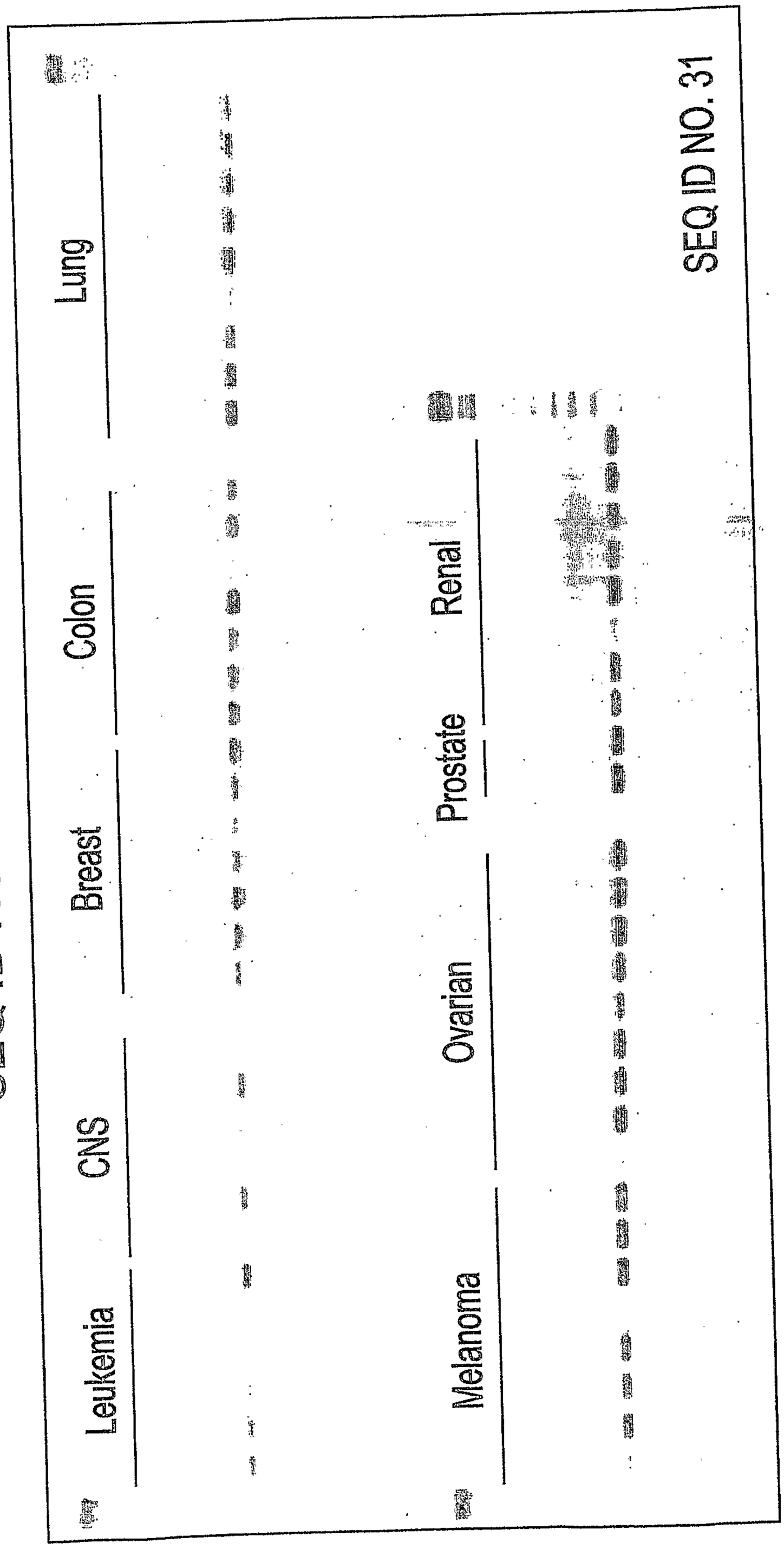

SEQ ID NO 30/037575-SL126
SEQ ID NO. 30
Lung
Colon
Renal
Breast
Ovarian
Prostate
CNS
Leukemia
Melanoma

FIG. 87


SEQ ID NO 31/0979-SL124
SEQ ID NO. 31
CNS
Colon
Lung
Breast
Ovarian
Renal
Prostate
Leukemia
Melanoma
FIG. 88

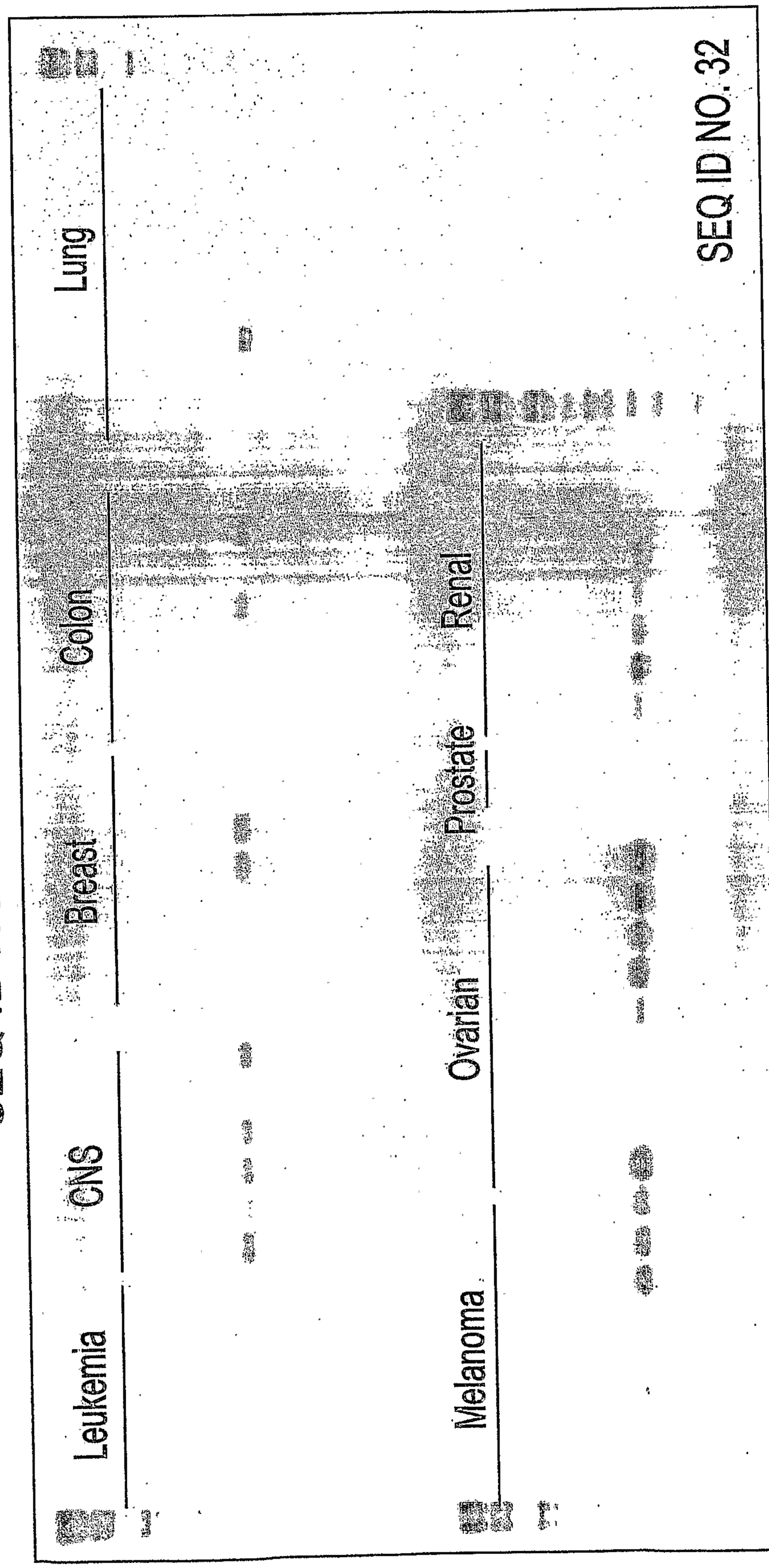

SEQ ID NO 32/1133-SL127
SEQ ID NO. 32
Lung
Colon
Renal
Breast
Prostate
CNS
Ovarian
Leukemia
Melanoma

Fig - 87

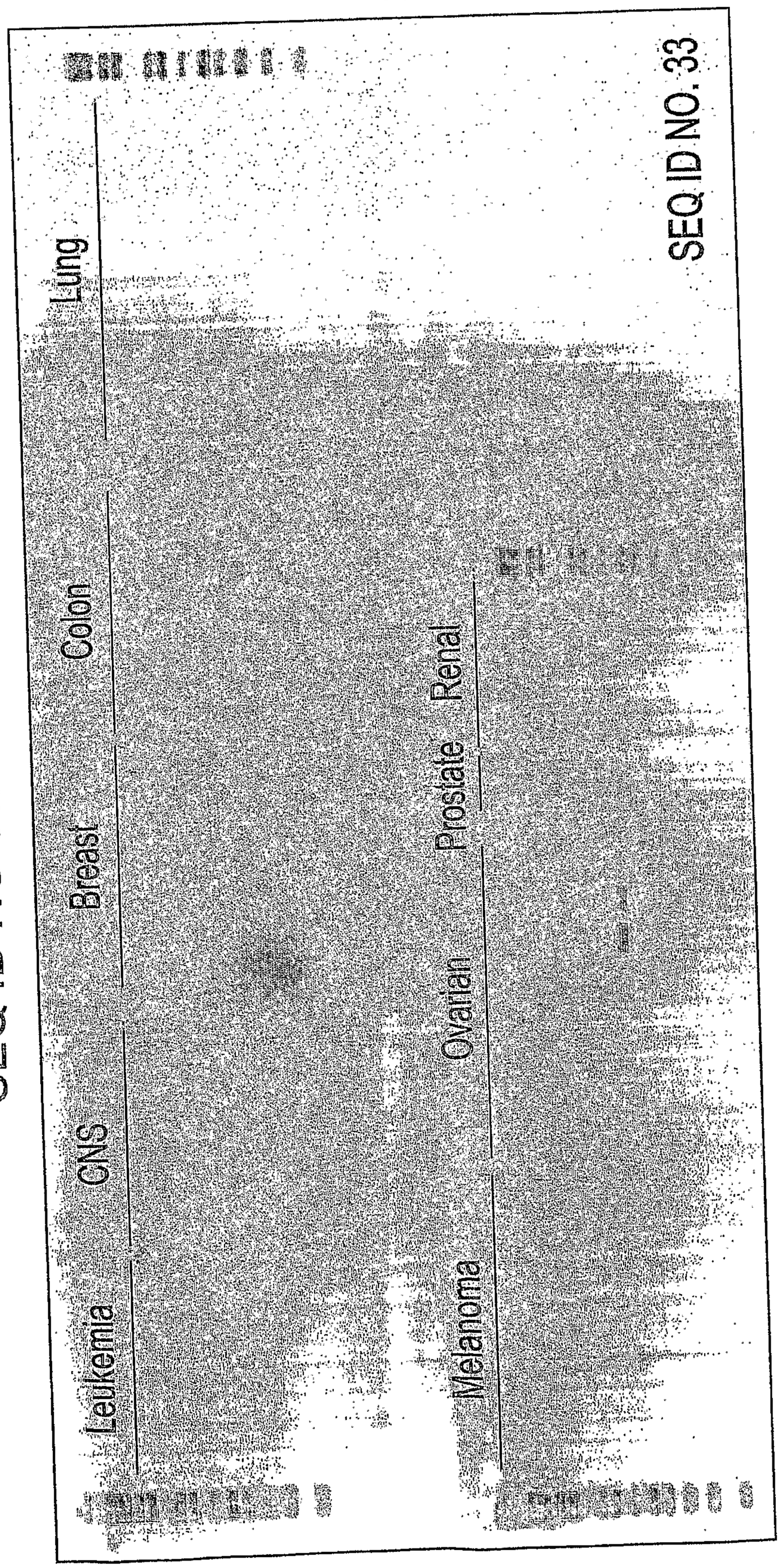
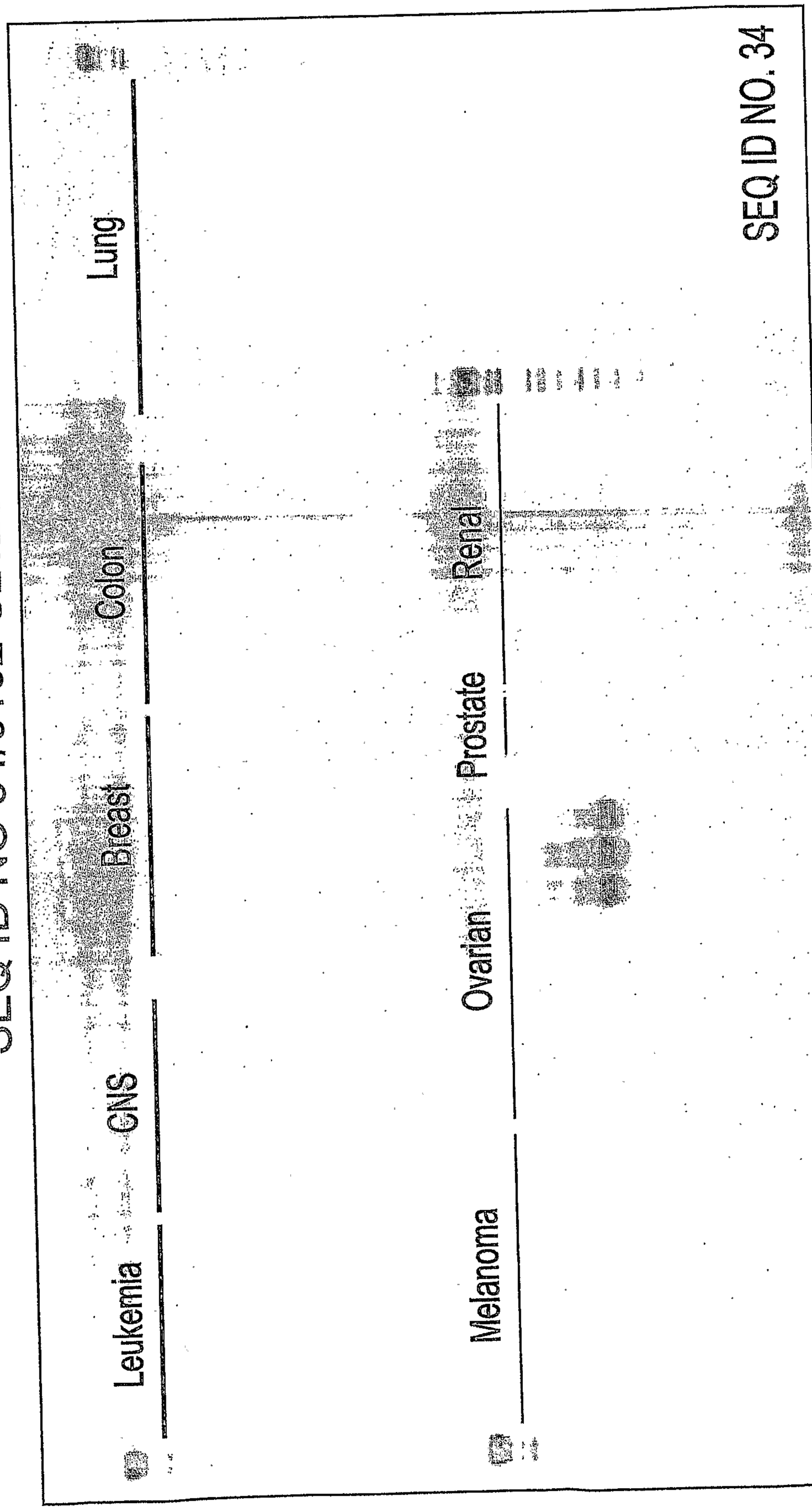

SEQ ID NO 33/0120-SL126
SEQ ID NO. 33
Lung
Colon
Breast
CNS
Prostate
Renal
Ovarian
Melanoma
Leukemia

Fig. 88

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SEQ ID NO. 34
Lung
SEQ ID NO 34/0192-SL126
Colon
Renal
CNS
Breast
Ovarian
Prostate
Leukemia
Melanoma
TE-80

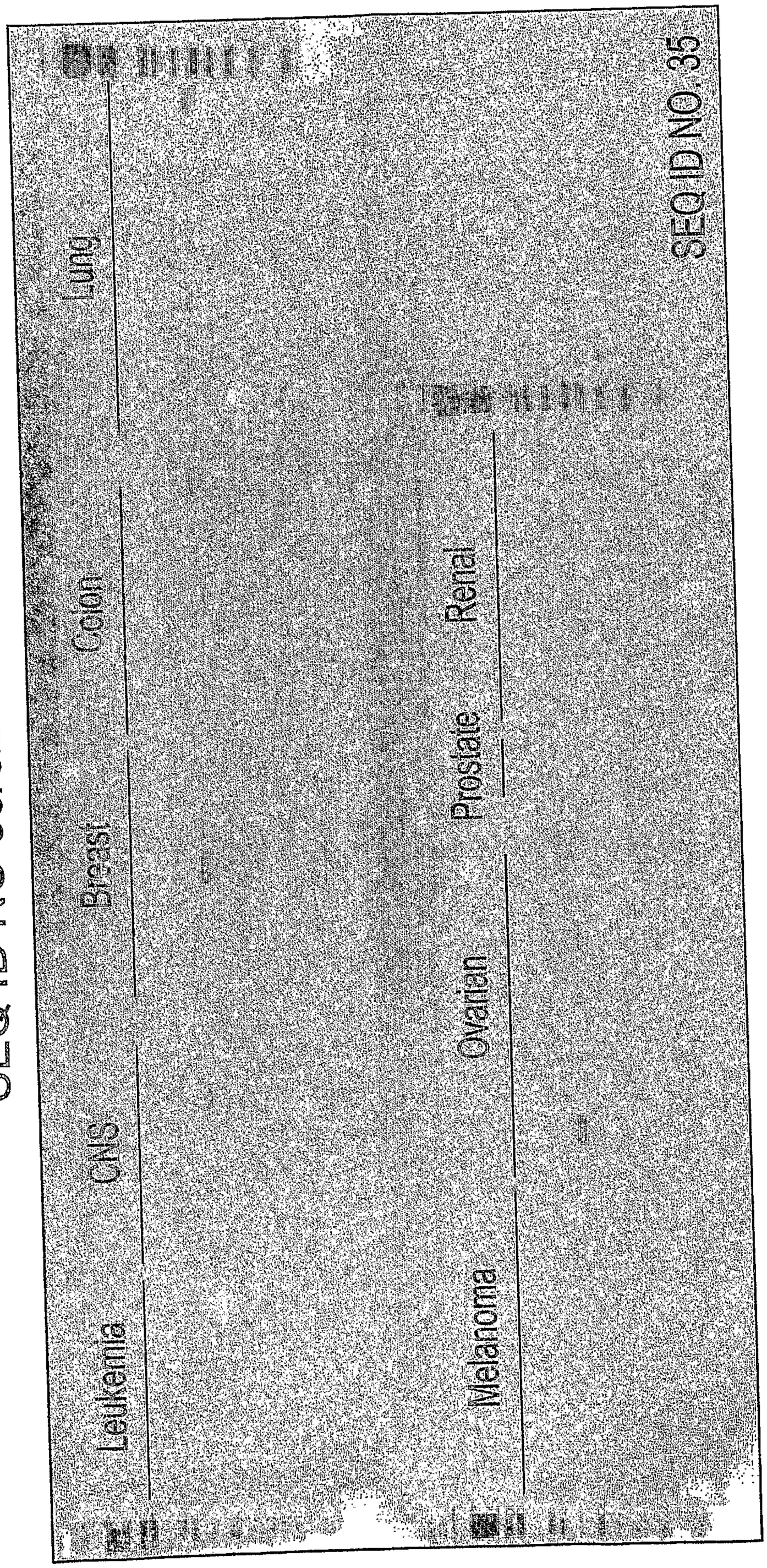
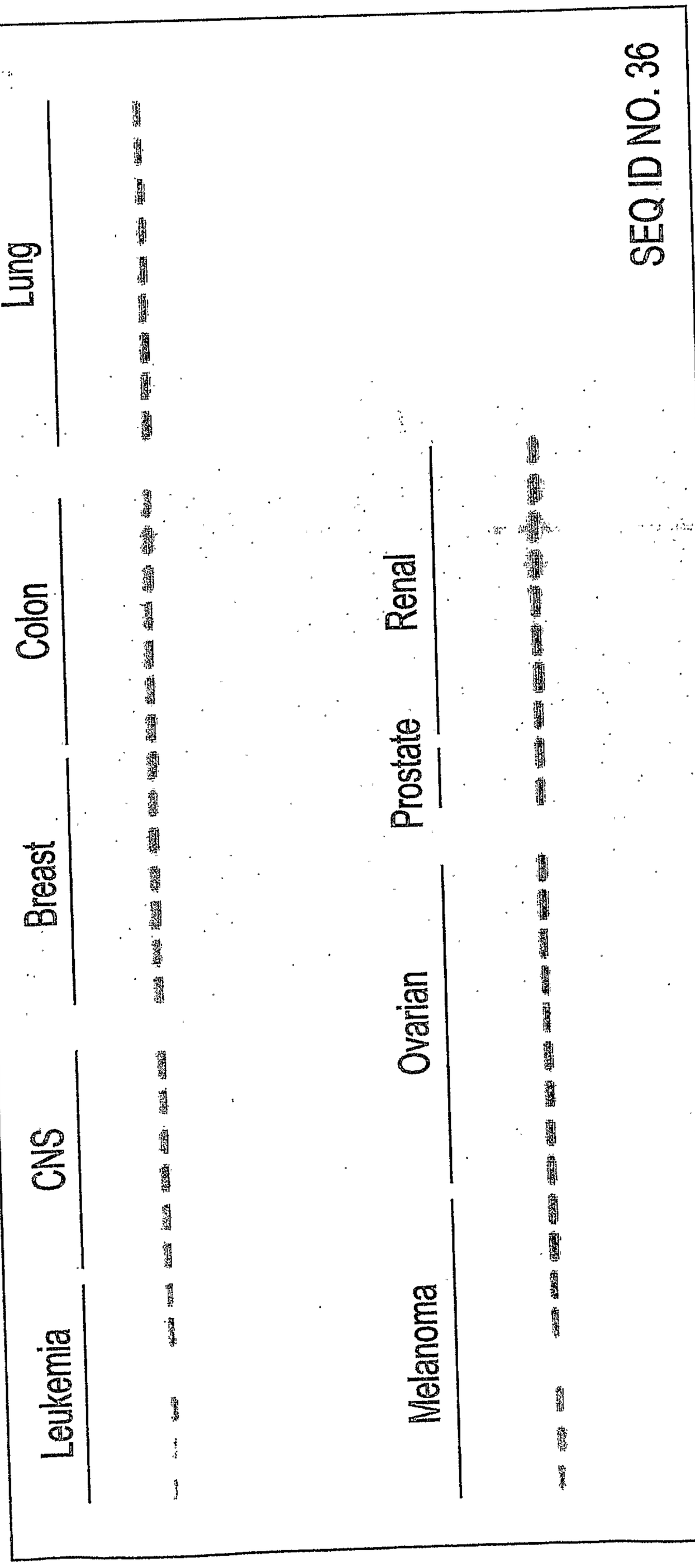
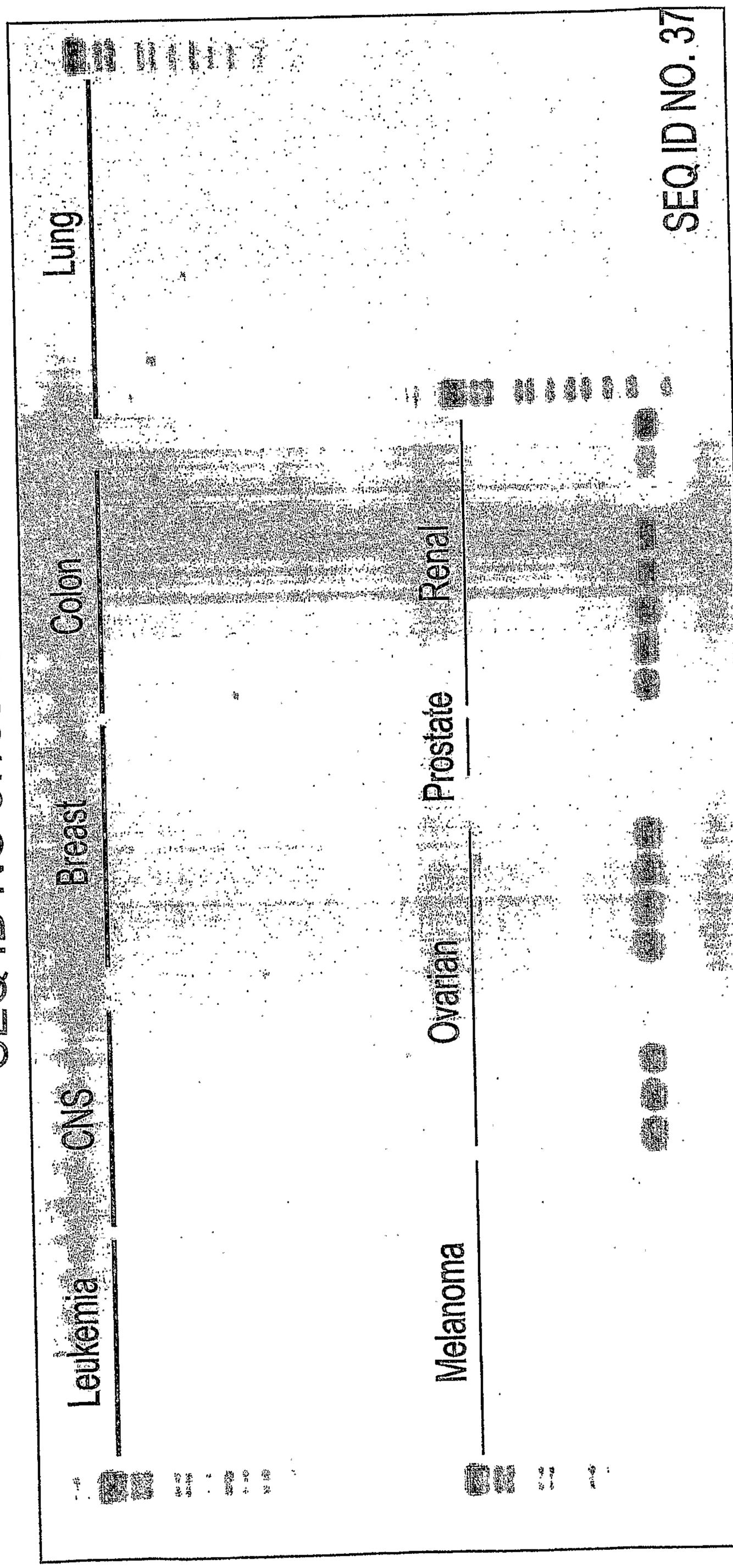
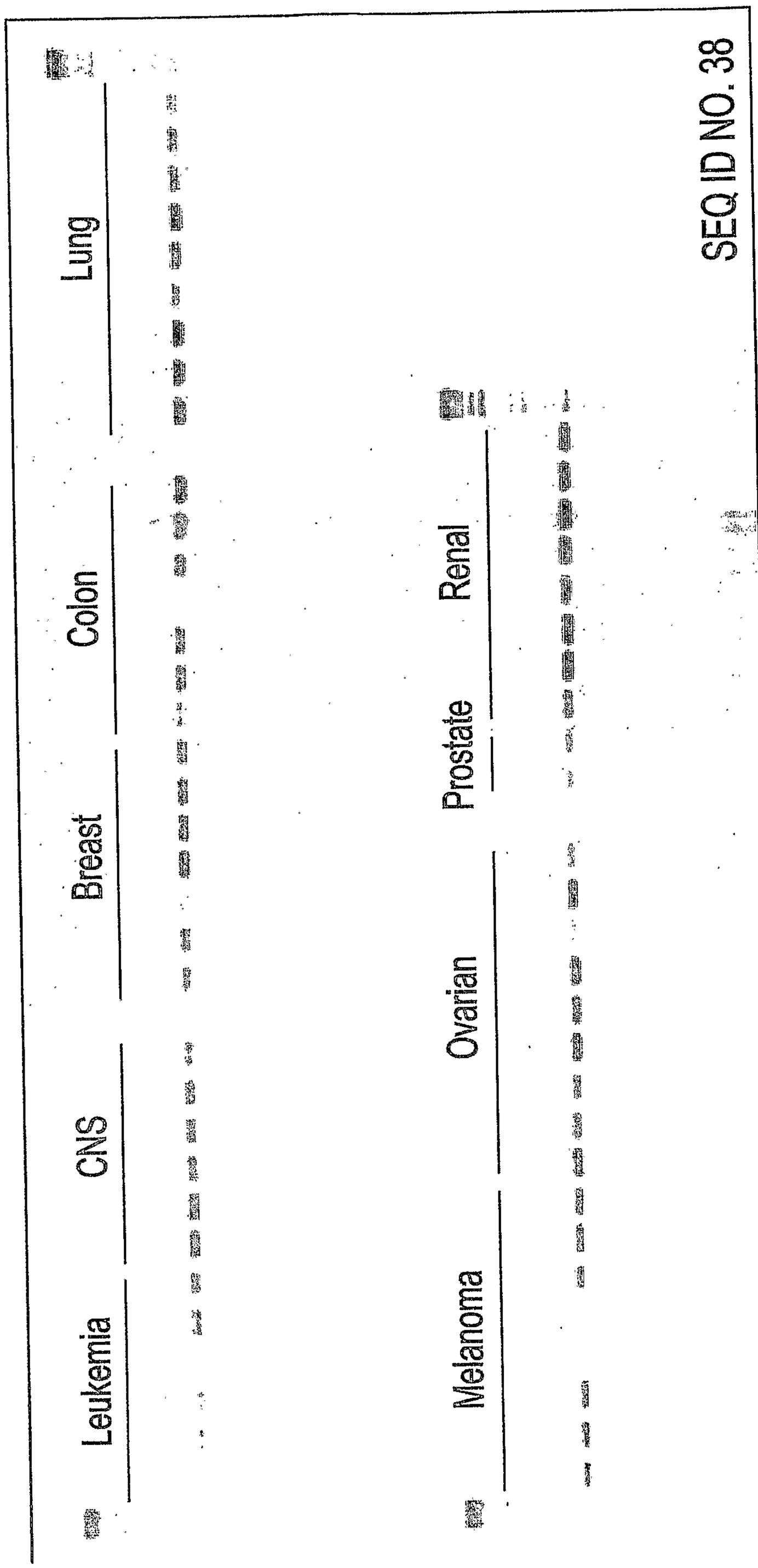

SEQ ID NO 35/0201-SL125
SEQ ID NO:35
Lung
Colon
Breast
Renal
Prostate
Ovarian
CNS
Melanoma
Leukemia

FIG - 89


SEQ ID NO. 36
SEQ ID NO 36/0205-SL127
CNS
Breast
Lung
Colon
Ovarian
Prostate
Renal
Melanoma
Leukemia


SEQ ID NO 37/03197-SL124
SEQ ID NO. 37
Lung
Colon
Renal
Leukemia
CNS
Breast
Ovarian
Prostate
Melanoma


SEQ ID NO 38/0332-SL126
SEQ ID NO. 38
CNS
Breast
Lung
Colon
Leukemia
Ovarian
Prostate
Renal
Melanoma

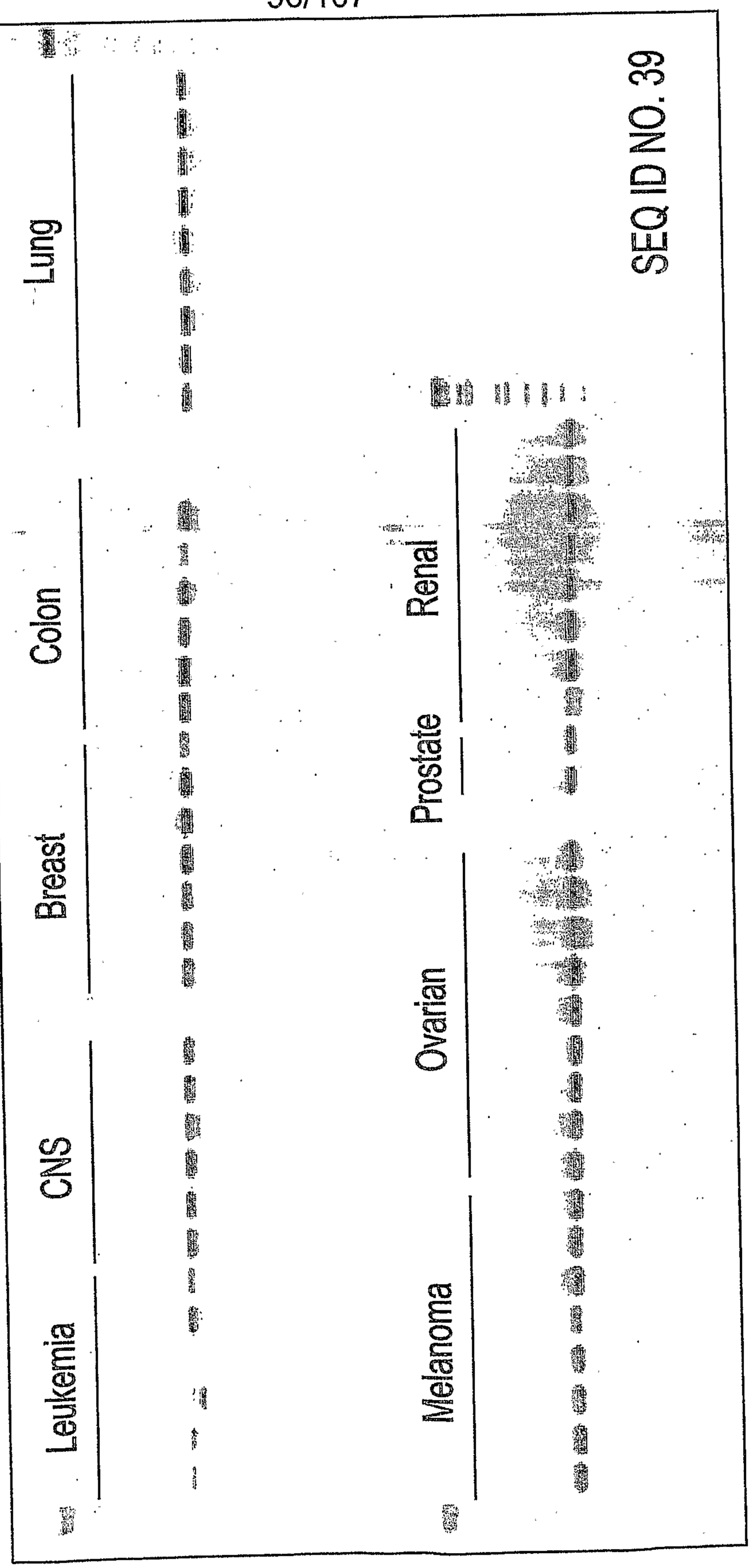

SEQ ID NO 39/0344-SL127
Lung
Colon
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia

FIG - 94

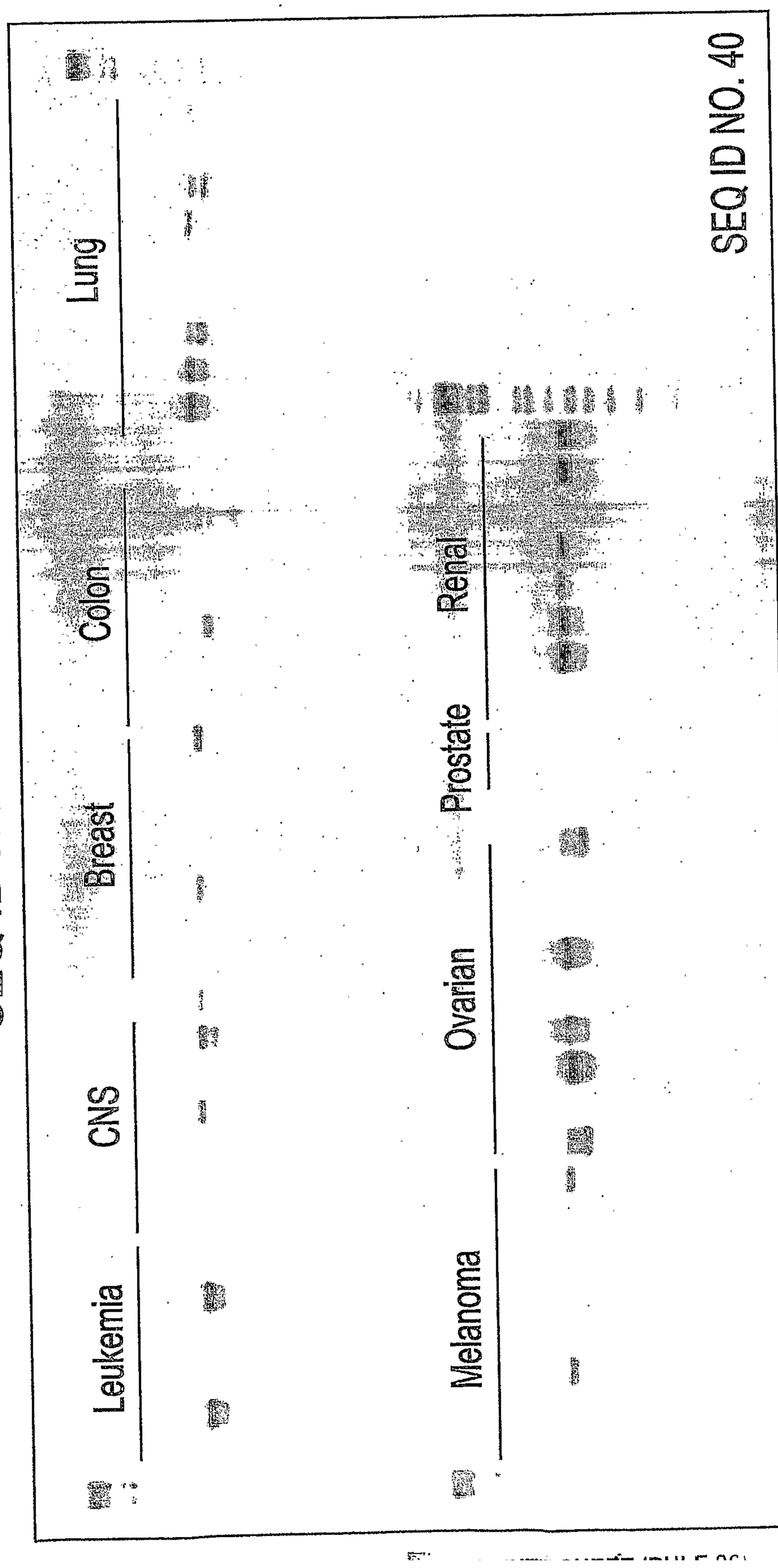

SEQ ID NO. 40
Lung
SEQ ID NO 40/0405-SL123
Colon
Renal
CNS
Breast
Prostate
Ovarian
Leukemia
Melanoma

FIG. 95

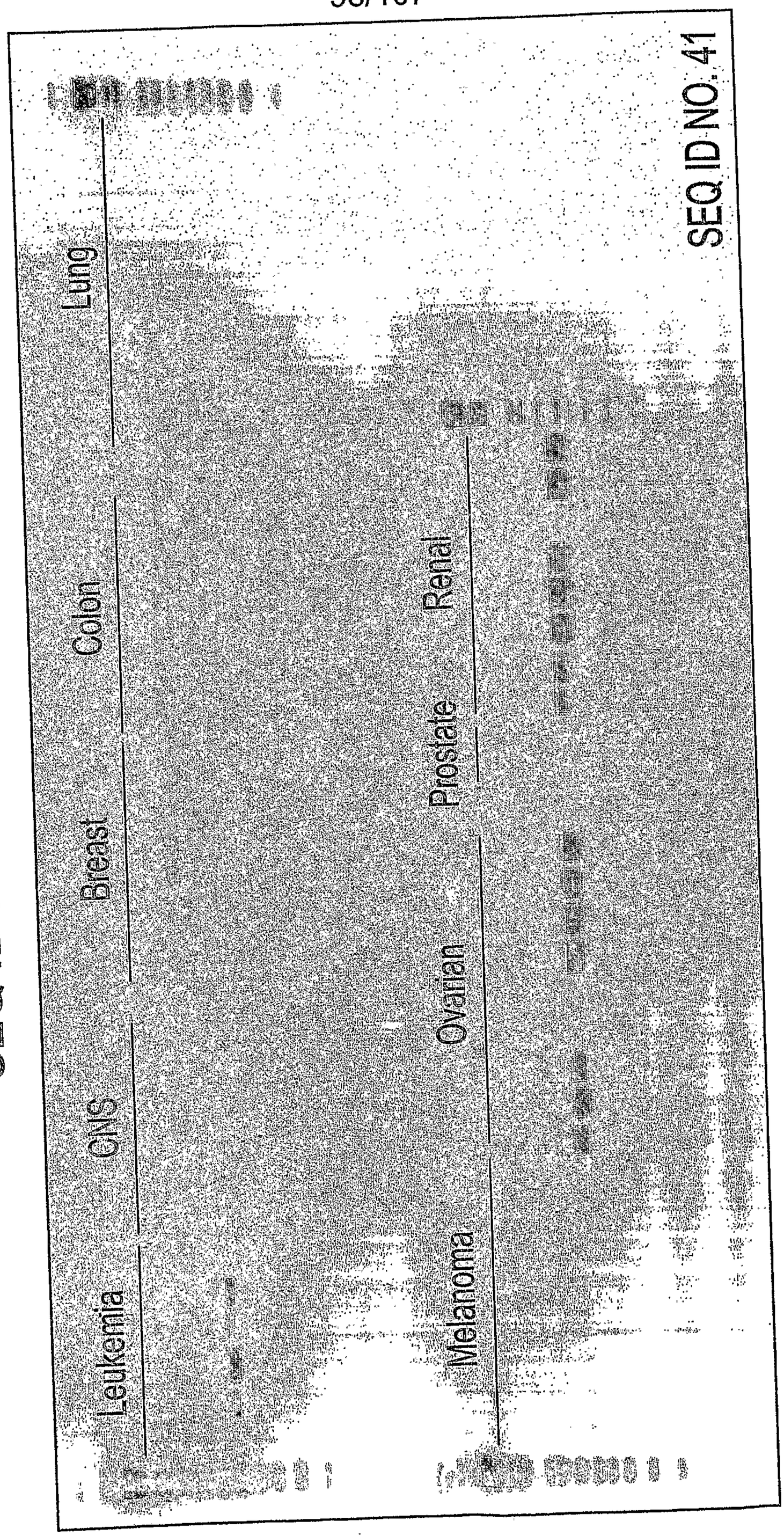

SEQ ID NO 41/0532-SL124
SEQ ID NO. 41
Lung
Colon
Breast
Renal
Prostate
CNS
Ovarian
Melanoma
Leukemia

FIG. 98

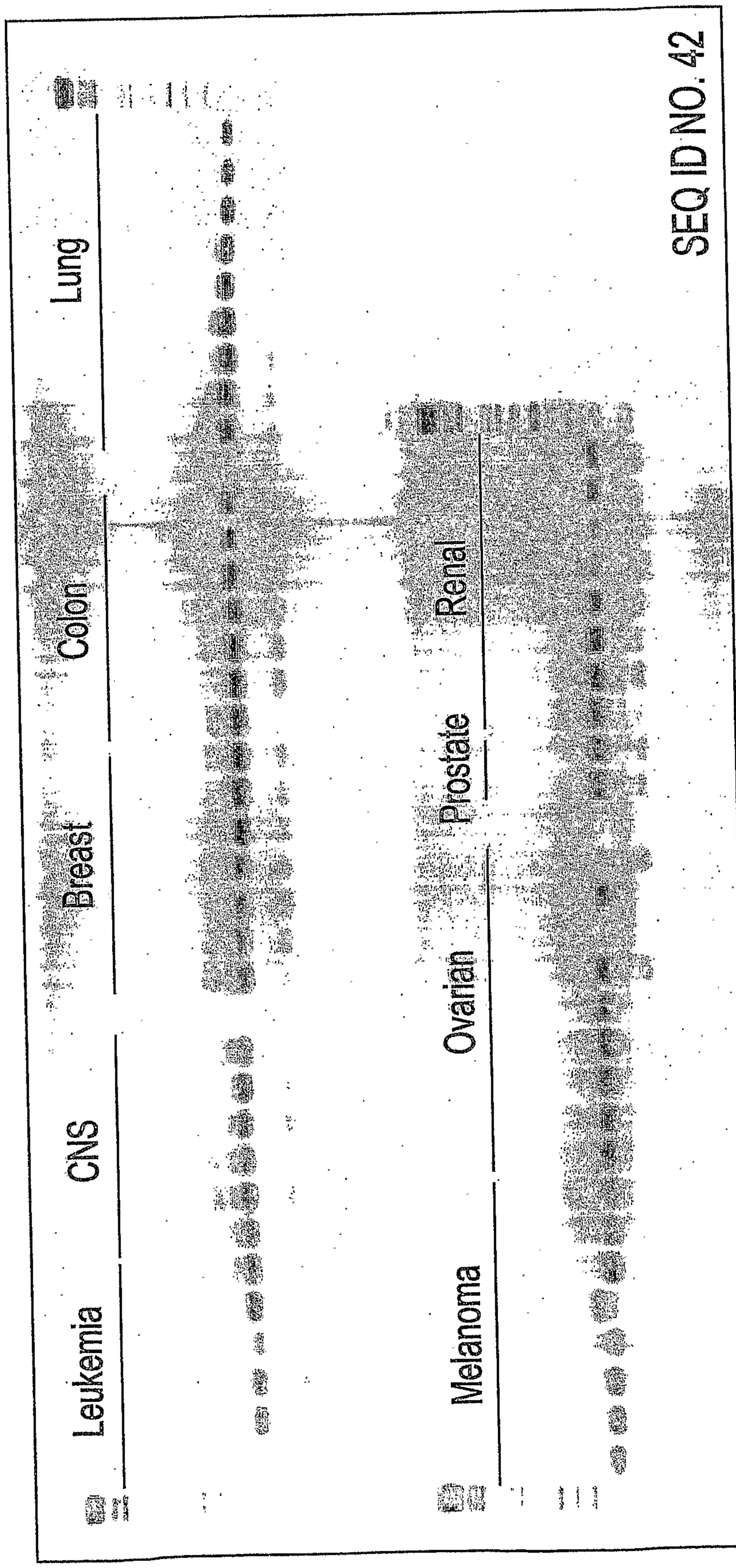

SEQ ID NO 42/0567-SL123
SEQ ID NO. 42
Lung
Colon
Breast
Renal
CNS
Ovarian
Prostate
Leukemia
Melanoma

FIG - 97

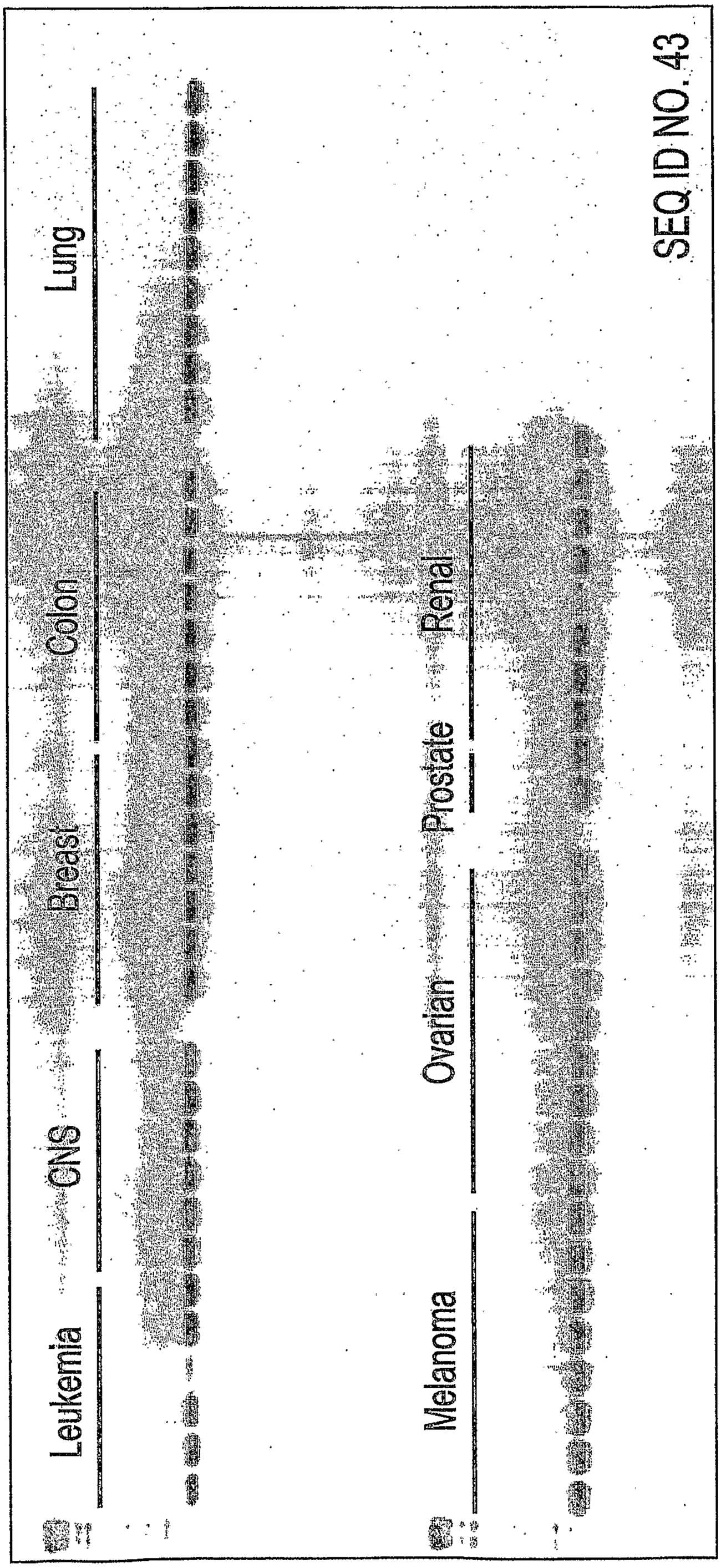
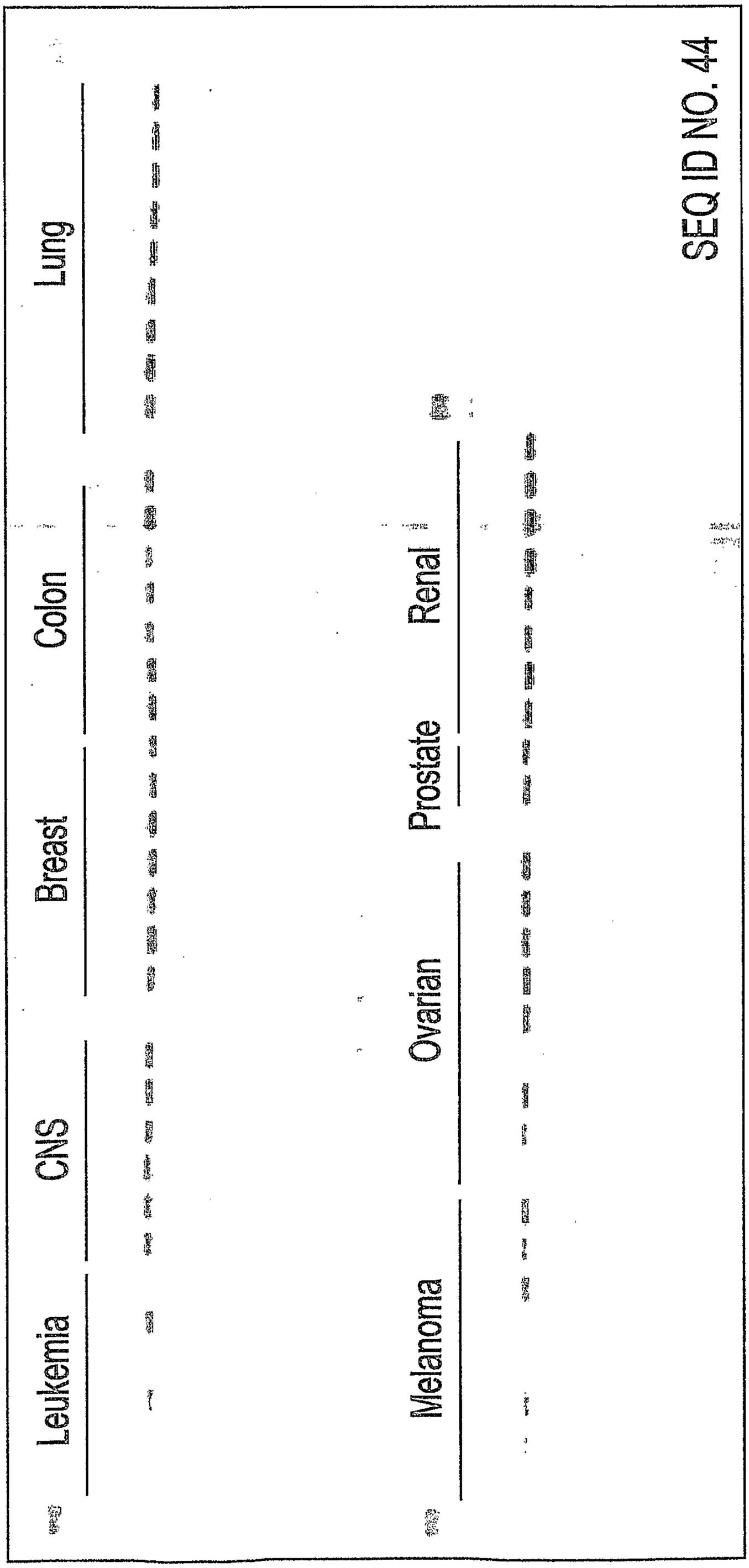

SEQ ID NO 43/721-SL124
SEQ ID NO. 43
Leukemia
CNS
Breast
Colon
Lung
Ovarian
Prostate
Renal
Melanoma

FIG. 88


SEQ ID NO 44/0795-SL125
Colon
Lung
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia
SEQ ID NO. 44
42/95

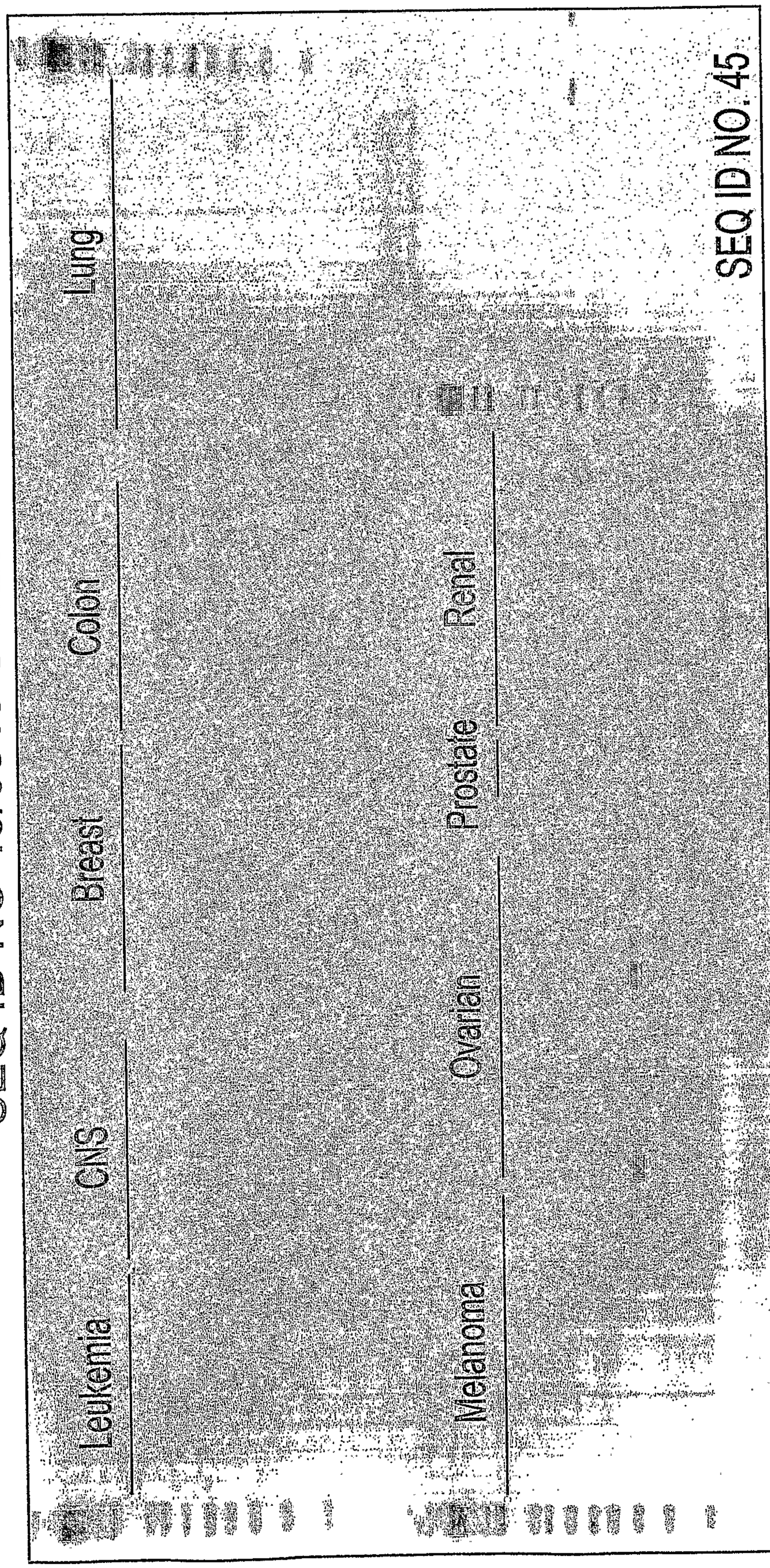
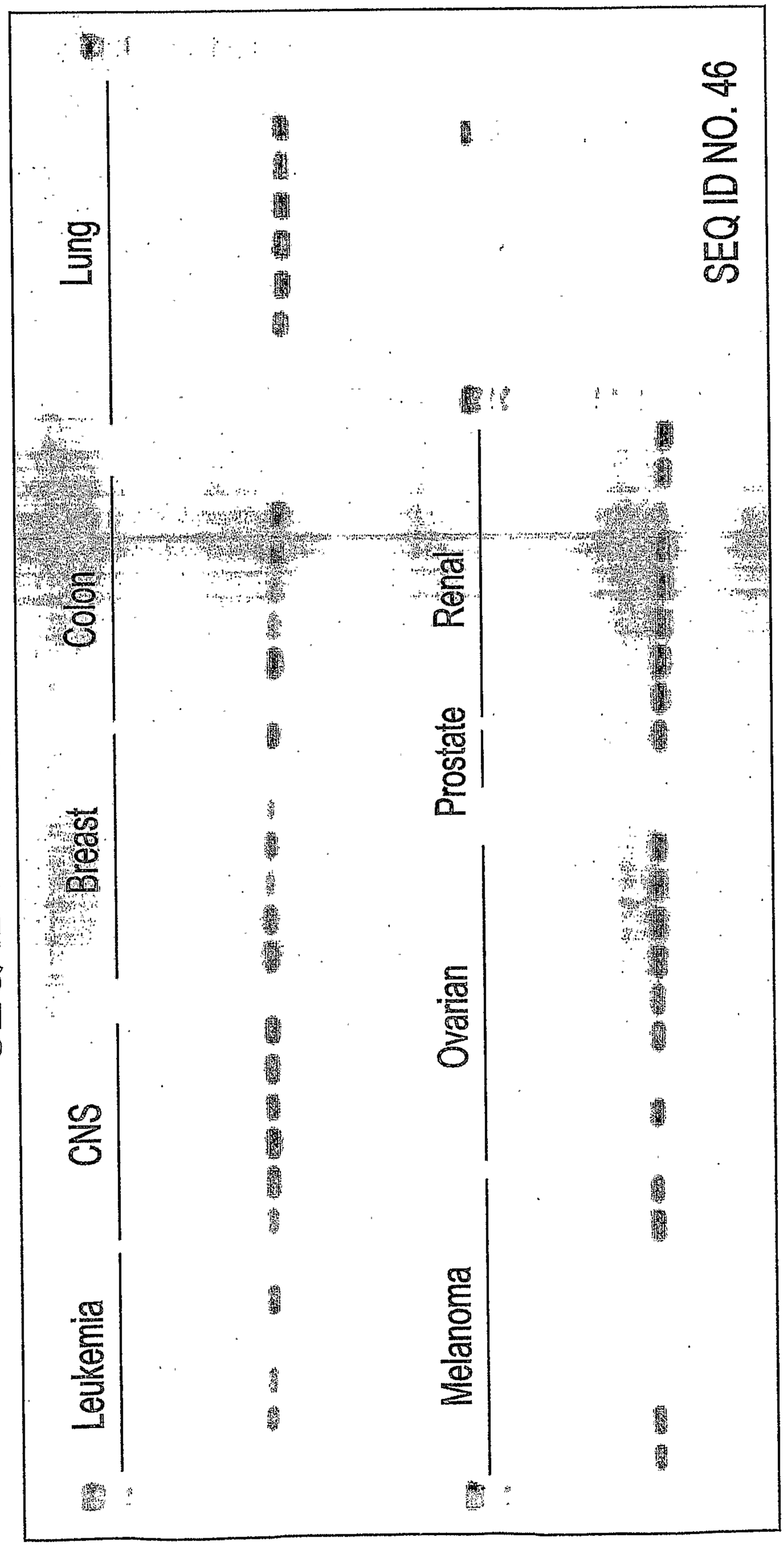

SEQ ID NO 45/0846-SL125
SEQ ID NO:45
Lung
Colon
Breast
Renal
Prostate
CNS
Ovarian
Leukemia
Melanoma

FIG - 100


SEQ ID NO 46/0960-SL125
Lung
Colon
Breast
Prostate
Renal
CNS
Ovarian
Melanoma
Leukemia
SEQ ID NO. 46
FIG. 101

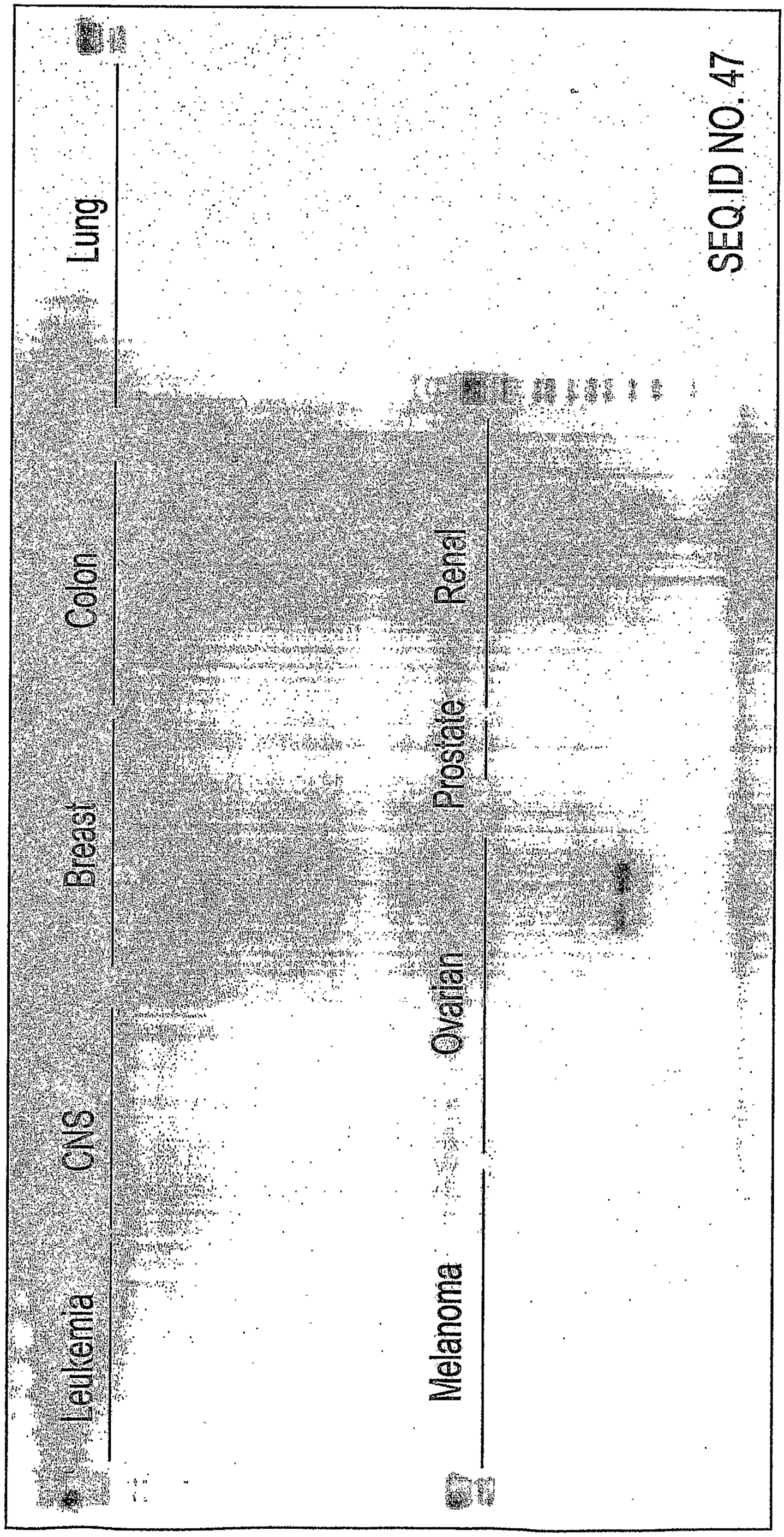
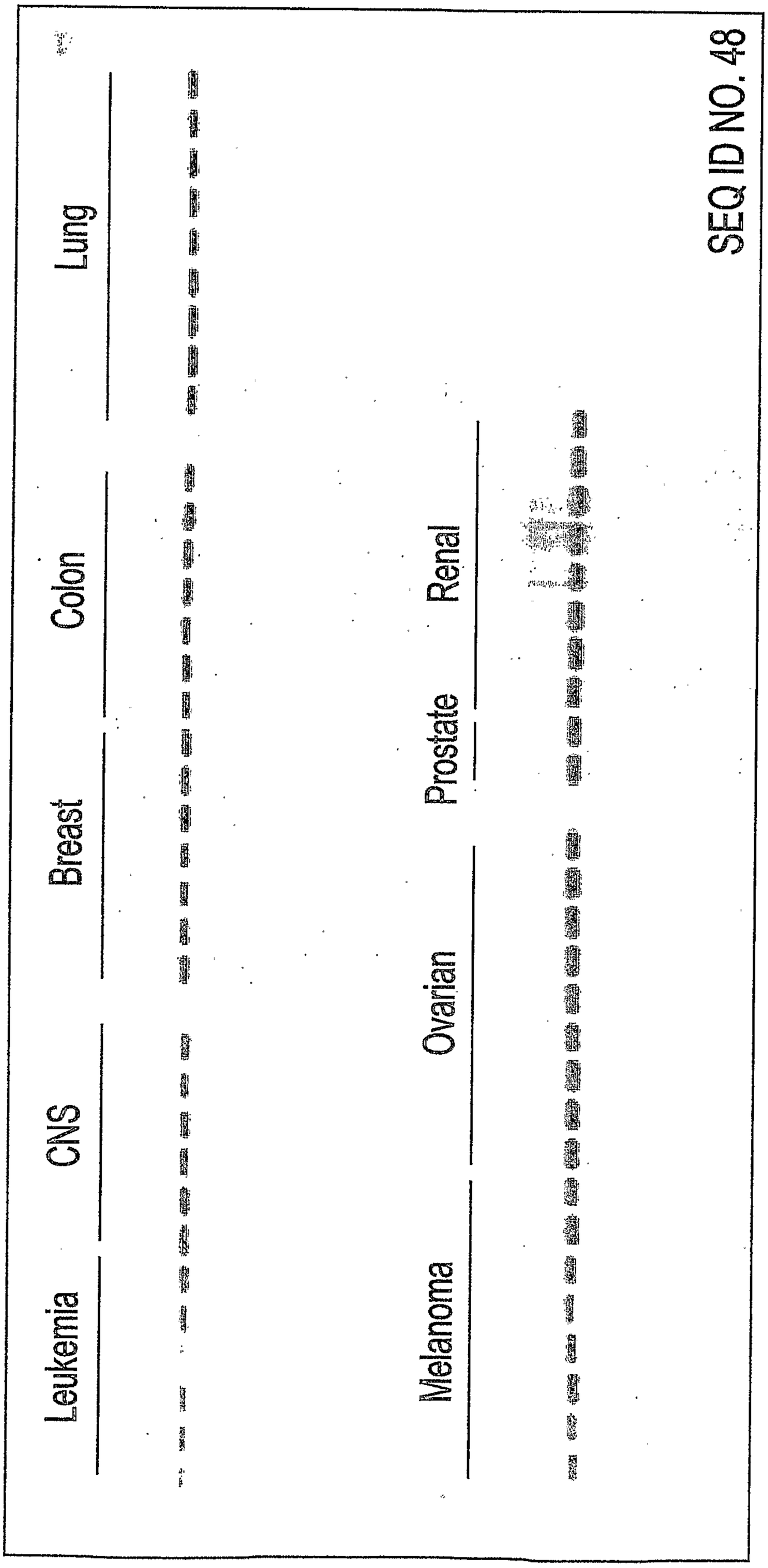

SEQ ID NO 47/1083-SL126
Lung
Colon
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia
SEQ ID NO. 47

FIG - 104


SEQ ID NO 48/1120-SL123
SEQ ID NO. 48
Colon
Lung
Breast
CNS
Renal
Prostate
Ovarian
Melanoma
Leukemia
FIG. 103

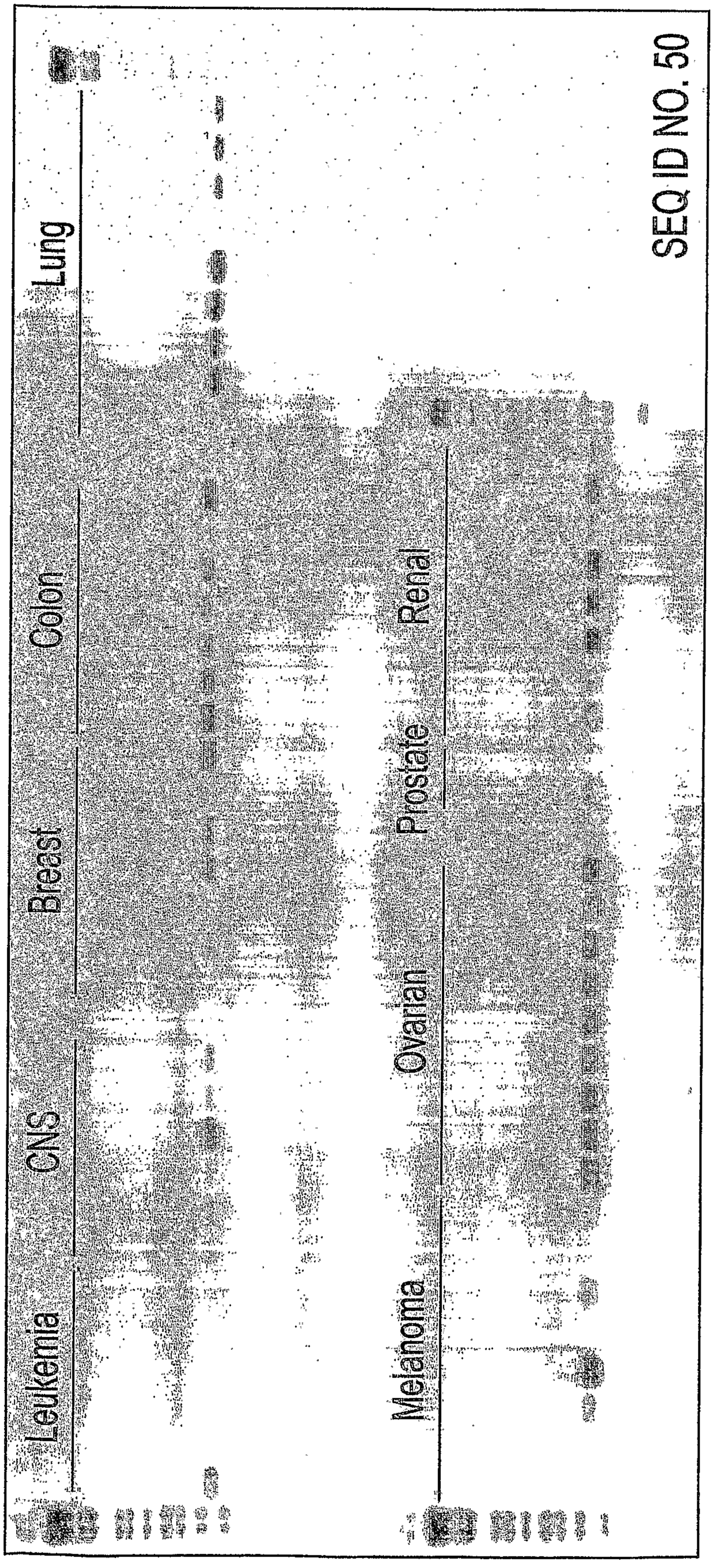

SEQ ID NO 50/0967-SL126
SEQ ID NO. 50
Lung
Colon
Breast
Renal
Prostate
Ovarian
CNS
Melanoma
Leukemia

Fig. 104

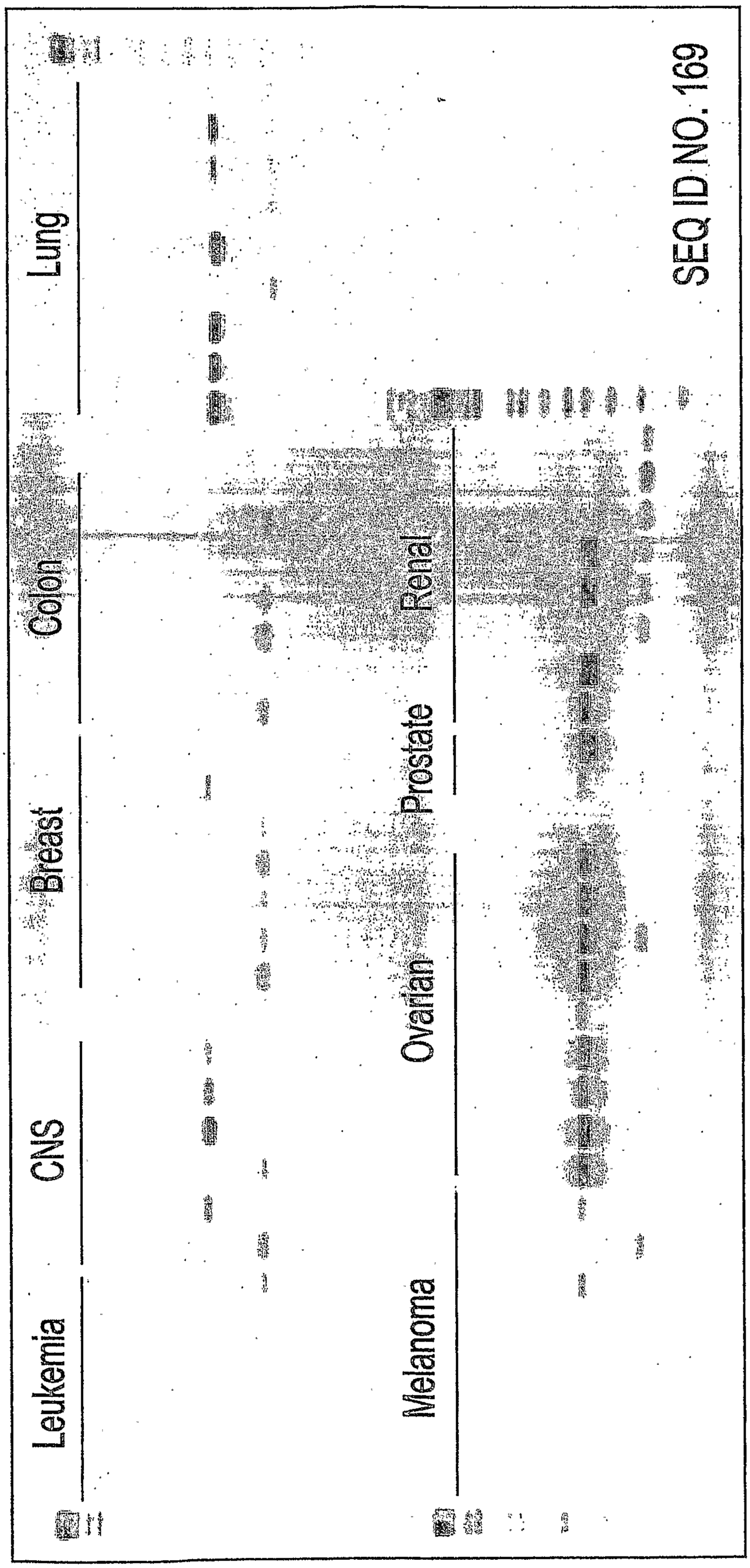
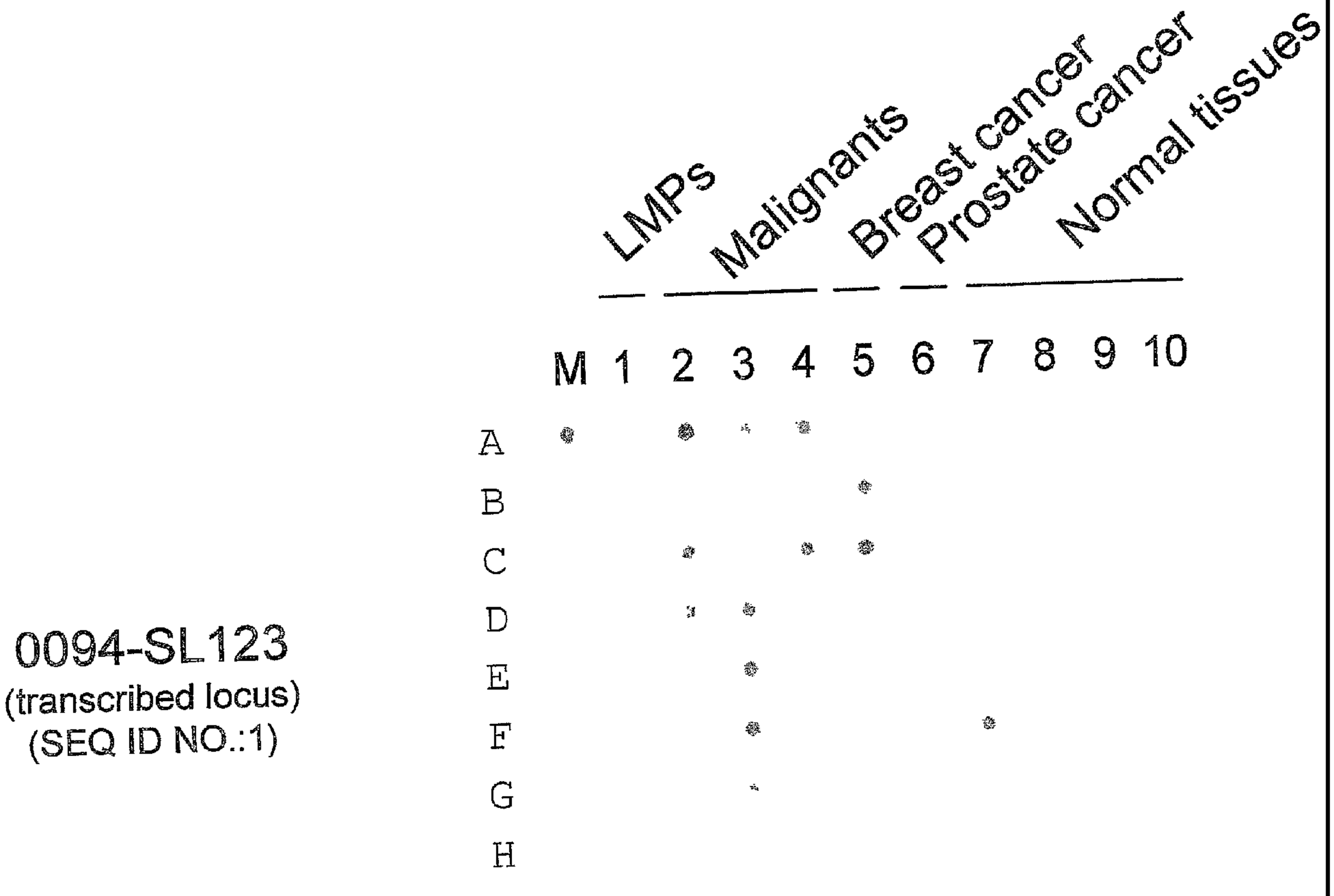

SEQ ID NO 169/0064-SL126
SEQ ID NO.169
Lung
Colon
Breast
Prostate
Renal
CNS
Ovarian
Melanoma
Leukemia

FIG - 105



0094-SL123
(transcribed locus)
(SEQ ID NO.:1)