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(54) Titre : ISOLATION, EXPRESSION GENIQUE ET RESISTANCE CHIMIOTHERAPEUTIQUE DE CELLULES CANCEREUSES MOTILES

(54) Title: ISOLATION, GENE EXPRESSION, AND CHEMOTHERAPEUTIC RESISTANCE OF MOTILE CANCER CELLS

(57) Abrégé/Abstract:
Methods of isolating motile cells of interest from an animal tissue is provided. Also provided are methods of determining mRNA or protein expression of a gene in motile cells of interest from an animal tissue. Additionally, methods of determining whether a cancer in a tissue of a mammal is likely to metastasize are provided. Methods are also provided for inhibiting metastasis of a cancer in a tissue of a mammal. Further provided are methods of determining resistance of a motile cancer cell population in an animal tissue to a chemotherapeutic agent.

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ISOLATION, GENE EXPRESSION, AND CHEMOTHERAPEUTIC RESISTANCE OF MOTILE CANCER CELLS

CROSS-REFERENCE TO RELATED APPLICATION

This application claims the benefit of U.S. Provisional Application No. 60/600,697, filed August 11, 2004.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

The U.S. Government has a paid-up license in this invention and the right in limited circumstances to require the patent owner to license others on reasonable terms as provided for by the terms of Grants No. CA089829 and CA100324 awarded by the National Institutes of Health.

BACKGROUND

(1) Field of the Invention

The present invention generally relates to the characterization of motile cells and invasive cells of tumors. More specifically, the invention is directed to methods of isolating motile cells, in particular invasive cells, and the characterization of gene expression in those cells.

(2) Description of the Related Art

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Understanding how cancer cells spread from the primary tumor is important for improving diagnostic, prognostic and therapeutic approaches that allow control of cancer metastasis. Alterations in gene expression along with protein activation by cancer cells leads to transformation, proliferation, invasion, intravasation, dissemination in blood or lymphatic vessels and eventually growth of distant metastases. In order for a tumor cell to become metastatic, it must be able to survive in the circulation and respond appropriately to new environments. This includes being able to migrate both within and beyond the primary tumor, in and out of blood and lymph vessels, and to utilize growth factors available at the site of metastasis for attachment and growth (Lin and Van Golen, 2004).

We have studied the motility-associated behavior of metastatic and non-metastatic mammary tumor cell lines by intravital imaging within primary tumors (Farina et al., 1998a; Wang et al., 2002; Wyckoff et al., 2000a). These studies have shown that the metastatic cells migrate to blood vessels and intravasate in a series of steps that involve active cell motility and may involve chemotaxis (Wang et al., 2002; Wyckoff et al., 2000a; Condeelis and Segall, 2003).

Many of the formative steps that determine the invasive and metastatic potential of carcinoma cells occur within the primary tumor. Much evidence suggests that the progress of cells from normal to invasive and then to metastatic involves progressive transformation through multiple genetic alterations selected by the tumor microenvironment (Hanahan and Weinberg, 2000). To identify the steps in progression and the genes involved in metastasis, recent emphasis has been on the use of molecular arrays to identify expression signatures in whole tumors with differing metastatic potential (Liotta and Kohn, 2001). A well recognized problem here is that primary tumors show extensive variation in properties with different regions of the tumor having

different growth, histology, and metastatic potential and where only a small subset of cells within the parental tumor population may be capable of metastasizing (Fidler and Kripke, 1977). The array data derived from whole tumors results inevitably in averaging of the expression of different cell types from all of these diverse regions. The expression signature of invasive tumor cells, arguably the population essential for metastasis, may be masked or even lost because of the contribution of surrounding cells which represent the bulk of the tumor mass. Even so, recent studies of expression profiling of primary tumors suggest that the metastatic potential of tumors is encoded in the bulk of a primary tumor, thus challenging the notion that metastases arise from rare cells within a primary tumor acquired late during tumor progression (Ramaswamy et al., 2003).

This leaves us with a conundrum concerning the contribution of rare cells to the metastatic phenotype. The relative contribution of subpopulations of cells to the invasive and metastatic phenotype of primary tumors has not been assessed due to the difficulty in isolating phenotypically distinct cell populations from whole tumors. In addition, the metastatic cascade has been studied most heavily at the level of extravasation and beyond using experimental metastasis models removing the primary tumor from scrutiny. Thus, the microenvironment of the primary tumor that contributes to invasion and intravasation, and the process of selection of metastatic cells, has not been studied directly (Chambers et al., 2002).

In this context it has become important to develop technologies to separate pure populations of invasive cancer cells for gene expression studies. To this end, the development of Laser Capture Microdissection (LCM) has been an important advance (Bonner et al., 1997). However, the identification of cells within the tumor relies on morphology within fixed tissue making uncertain the identity of the collected cells and their behavior within the tumor before fixation. Alternative approaches involve the collection of cells from metastatic tumors and their expansion in culture (Clark et al., 2000; Kang et al., 2003; Ree et al., 2002). The pitfall of these approaches is that during culturing, the gene expression patterns may change to represent the *in vitro* culture conditions which are likely to be irrelevant to invasion *in vivo*.

SUMMARY OF THE INVENTION

Accordingly, the inventor has developed methods of isolating motile cells from animal tissues, and the use of those methods to isolate metastatic cells from cancerous tissue and quantify expression of various genes in those cells.

Thus, in some embodiments, the invention is directed to methods of isolating motile cells of interest from an animal tissue, where the animal tissue comprises the motile cells of interest and other motile cells. The methods comprise obtaining a microneedle or capillary filled with a

porous matrix comprising a chemotactic factor; inserting the microneedle or capillary into the tissue for a time sufficient for the motile cells of interest to migrate into the porous matrix; expelling the porous matrix with motile cells from the microneedle or capillary; combining the porous matrix with microbeads, where the microbeads comprise a binding partner to a surface marker present on the other motile cells but not the motile cells of interest; and removing the microbeads.

In other embodiments, the invention is directed to methods of determining mRNA or protein expression of a gene in motile cells of interest from an animal tissue. The methods comprise isolating the motile cells of interest by the method described above, then extracting the mRNA or protein from the cells of interest, then determining mRNA or protein expression in the extraction of the cells of interest.

The invention is also directed to methods of determining whether a cancer in a tissue of a mammal is likely to metastasize. The methods comprise obtaining a microneedle or capillary filled with a porous matrix comprising a chemotactic factor; inserting the microneedle into the cancer for a time sufficient for motile cells to migrate into the porous matrix; expelling the porous matrix with motile cells from the microneedle; combining the porous matrix with microbeads, where the microbeads comprise a binding partner to a surface marker present on macrophages from the tissue; removing the microbeads; and quantifying the motile cells, where the presence of more motile cells than from the tissue when noncancerous or when comprising a non-metastatic cancer indicates that the cancer in the tissue of the mammal is likely to metastasize.

In further embodiments, the invention is directed to methods of inhibiting metastasis of a cancer in a tissue of a mammal. The methods comprise enhancing ZBP-1 activity in the tissue.

The invention is additionally directed to methods of inhibiting metastasis of a cancer in a tissue of a mammal. The methods comprise reducing the presence or activity of a protein in the tissue, where the protein is selected from the group consisting of Arp2/3 p16 subunit, Arp2/3 p21 subunit, alpha subunit of capping protein, beta subunit of capping protein, cofilin, WAVE3, ROCK1, ROCK2, LIMK 1, PKCζ, LIM-kinase, PAK, type II alpha isoform of PI4, 5 kinase, mena, tropomyosin, calpain, gelsolin-like protein (CAPG), zyxin, vinculin, and integrin β1.

The invention is further directed to methods of determining resistance of a motile cancer cell population in an animal tissue to a chemotherapeutic agent. The methods comprise obtaining the motile cancer cell population by the method described above; contacting the motile cancer cell population with the chemotherapeutic agent at a concentration and for a time sufficient to cause apoptosis in cancer cells susceptible to the chemotherapeutic agent; and determining apoptosis in the motile cancer cell population. In these embodiments, less apoptosis in the motile cancer cell

population indicates that the motile cancer cell population is resistant to the chemotherapeutic agent.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1, top, is an illustration of a strategy for identification of gene expression patterns in invasive cells and their functional categories. MTLn3-derived mammary tumors in rats and the microneedle collection method were used to study the gene expression pattern of invasive subpopulation of carcinoma cells within live primary tumors. FACS sorting based on GFP expression in tumor cells was performed to isolate the general population of carcinoma cells from primary tumor, RNA extraction, probe labeling and microarray analysis were carried out as described in the Example 1 Materials and Methods. The resulting genelist from the SAM analysis is presented in Supplementary Table 1. The diagram at the bottom is a summary showing functional categories of the genes regulated in the invasive cells. The pie charts represent the relative proportion of genes (selected by SAM) in 6 categories based on their function using Gene-ontology Consortium classification.

FIG. 2, Panel A is a chart indicating the relative overexpression and underexpression of pro-apoptotic and anti-apoptotic genes respectively. N/F shows the relative ratios of the gene expression of invasive cells over the general population. Panel B is a graph showing validation of microarray results for selected genes by quantitative real time PCR (QRT-PCR). Real time PCR was performed by using the ABI 7700 and SYBR Green PCR Core Reagents system (Applied Biosystems Foster City, CA) along with sequence-specific primer pairs for all genes tested. Results were evaluated with the ABI Prism SDS 2.0 software. Comparison of expression analyses in needle collected invasive tumor cells gives similar results for cDNA microarrays and QRT-PCR.

FIG. 3 is micrographs and a graph showing drug resistance in invasive cells compared to the general population of the primary tumor measured by an apoptosis assay. The cells collected by the needle collection procedure were subjected to drug challenge using doxorobucin (17 μM), cisplatin (50 μM) or etoposide (50 μM). The apoptotic status and viability of these cells was assessed by staining with propedium iodide (PI) and Annexin V-Cy5. Micrograph A shows the GFP channel with all the carcinoma cells. Micrograph B shows the dead cells with PI staining, and micrograph C is the Cy5 channel showing the apoptotic cells. The graph represents viability status and apoptotic index of the cells after being challenged by the anticancer drugs.

FIG. 4 is a schematic diagram of an apoptotic pathway indicating the pathways in which the anti- and pro-apoptotic genes are co-coordinately up- or downregulated respectively. The numbers in parenthesis indicate fold change in gene expression in the invasive cells compared to the general population.

FIG. 5 is micrographs and a diagram showing *in vivo* selection and gene expression analysis of the highly invasive subpopulation of breast cancer cells collected by chemotaxis. Panel A shows multi-photon images of a live cell collection from an MTLn3 derived tumor. GFP-expressing carcinoma cells are seen moving toward the bevel (dashed line delineates edge) of a microneedle filled with matrigel and 25 nM EGF. Arrows indicate the final location of invading cells in both frames over the time lapse interval. Scale bar = 25 μm. Panel B shows a schematic representation of the chemotaxis based selection process. *MTLn3*-derived mammary tumors in rats and the microneedle collection method were used to study the gene expression pattern of invasive subpopulation of carcinoma cells within live primary tumors. FACS sorting based on GFP expression in tumor cells was performed to isolate the general population of carcinoma cells from primary tumor, RNA extraction, probe labeling and microarray analysis were carried out. Carcinoma cells from primary tumor were FACS sorted as described above. The resulting cells were split and plated on Mettek dish covered with matrigel (1:5) in the presence (iv) or absence of 1 nM EGF (iii) for 4 hr at 37°C. The cells were then lysed directly on the dish for total RNA extraction, probe labeling and microarray analysis. Genes that were up- or downregulated on control experiments (comparison: iii vs. ii and iv vs. ii) were removed from the list of differentially expressed genes obtained when comparing i and ii. The resulting final list of 1366 genes is shown in Supplementary Table 4.

FIG. 6 is summary diagrams showing functional categories of the genes regulated in the invasive cells. The pie charts represent the relative proportion of genes in 11 categories based on their function using Gene-ontology Consortium classification. Chart A represents the relative proportion of annotated spots compared to ESTs on the array. Chart B shows the proportional representation of the functional groups into which the genes annotated in A fall. Panel C shows the proportional representation of the functional groups into which the genes regulated in the invasive cells fall.

FIG. 7, Panel A is a graph showing validation of microarray results for selected genes by quantitative real time PCR (QRT-PCR). Comparison of expression analyses in needle collected tumor cells gives similar results for cDNA microarrays and QRT-PCR. Panel B is a diagram summarizing results showing that the minimum motility machine pathways in the invasive cells are upregulated. Genes involved in these pathways are upregulated in the invasive cells as shown by microarray and QRT-PCR. The extent of upregulated expression is indicated next to each component of the pathway as Nx.

FIG. 8 is a diagram and photographs of ZBP-1 construct and overexpression in MTLn3. Panel A is a diagram of the full length ZBP-1 gene was subcloned in a pMCSVneo vector and transfected into parental MTLn3 cells. The control plasmid used in the experiments was the

pGreenLantern-1. Panel B is western blots showing stable MTLn3-ZBP-1 clones 1 and 11B selected in the presence of neomycin. The western blots on the left show the increased ZBP-1 protein expression in these 2 separate clones. The western blot on the right shows a longer exposure time so that the endogenous ZBP-1 expression in wild type MTLn3 cells can be seen relative to the overexpression.

FIG. 9 is graphs showing the effect of ZBP-1 overexpression. Panel A shows that ZBP-1 over expression inhibits cell motility. Chemotaxis was measured in a Boyden chamber. ZBP-1 over expressing cells migrated through the filter in response to EGF poorly compared to the parental MTLn3 cells. Panel B shows that ZBP-1 over expression inhibits invasion as confirmed by the needle collection assay. The ability of carcinoma cells to invade microneedles placed into primary tumors derived from MTLn3 cells over expressing ZBP-1 was greatly reduced in ZBP-1 over expressing cells.

FIG. 10 is graphs showing ZBP-1 over expression inhibits tumor invasion and metastasis. ZBP-1 over expressing cells show lower metastatic potential. The number of tumor cells present in circulating blood (Panel A), and the number of lung metastatic tumors (Panel B) were greatly reduced in animals with tumors prepared with cells over expressing ZBP-1 ($p<0.05$, by Mann-Whitney Test). However, as shown in Panel C, tumor growth was not affected by increasing the expression of ZBP-1.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is based on the development of methods of isolating motile cells, especially motile (metastatic) cancer cells from animal tissues, and the use of those methods to quantify expression of various genes in those motile cells.

Thus, in some embodiments, the invention is directed to methods of isolating motile cells of interest from an animal tissue, where the animal tissue comprises the motile cells of interest and other motile cells. The methods comprise obtaining a microneedle or capillary filled with a porous matrix comprising a chemotactic factor; inserting the microneedle or capillary into the tissue for a time sufficient for the motile cells of interest to migrate into the porous matrix; expelling the porous matrix with motile cells from the microneedle or capillary; combining the porous matrix with microbeads, where the microbeads comprise a binding partner to a surface marker present on the other motile cells but not the motile cells of interest; and removing the microbeads. Some preferred embodiments of these methods are described in Wang et al., 2003.

These methods can be used with tissue from any animal. Preferably, the animal is a vertebrate, more preferably a mammal, for example a rodent or a human.

Any tissue in the animal can be utilized in these methods, where the tissue has motile cells that are directed toward a chemotactic factor. Preferably, the issue is cancerous, since the isolation of motile cells from cancerous tissue is particularly useful, e.g., for determining the metastatic potential of the cancer. A non-limiting example of a tissue useful for these methods is mammary tissue. See examples.

The methods can be used with tissue in culture, tissue taken from a biopsy, or directly on tissue in a living mammal.

These methods are not narrowly limited to the use of any particular porous matrix. The matrix must only allow motile cells in the tissue to move through the matrix in response to the chemotactic factor. In preferred embodiments, the matrix is matrigel, since that matrix is similar chemically to vertebrate extracellular matrix.

The methods are also not limited to any particular microneedle or capillary; the microneedle or capillary must only be of sufficient bore to be capable of being filled with the porous matrix and to allow the motile cells to move into the matrix in response to the chemotactic factor. In some preferred embodiments, a microneedle is used; a preferred bore is 33-gauge.

Any binding partner capable of binding to the other motile cells but not the motile cells of interest, and capable of being bound (either covalently or noncovalently) to a microbead can be used. Nonlimiting examples include aptamers or, preferably, antibodies or antibody fragments, where the binding site is preferably specific for a cell surface marker present on the surface of the other motile cells but not the motile cells of interest. For example, where the motile cells of interest are carcinoma cells and the other motile cells are macrophages, a preferred microbead has antibodies specific for CD11b, which is present on the surface of macrophages but not carcinoma cells. See Wang et al., 2003. The skilled artisan could formulate a binding partner for any particular motile cell of interest/other motile cell combination without undue experimentation.

As used herein, "antibody" includes the well-known naturally occurring immunoglobulin molecules as well as fragments thereof that comprise a typical immunoglobulin antigen binding site (e.g., Fab or Fab2). The antibodies can be from a polyclonal, monoclonal, or recombinant source, and can be of any vertebrate (e.g., mouse, chicken, rabbit, goat or human), or of a mixture of vertebrates (e.g., humanized mouse).

These methods are also not narrowly limited to any particular microbeads for binding the other motile cells. For example, the microbeads can be heavy particles that are pelleted under centrifugal conditions that do not pellet the motile cells of interest. Alternatively, the microbeads can be buoyant particles that are not pelleted under centrifugal conditions that pellet the motile cells of interest. In preferred embodiments, the microbeads are colloidal super-paramagnetic beads as described in Wang et al., 2003.

The chemotactic factor can be any factor capable of attracting the motile cells of interest. Where the motile cells of interest are cancer cells, a preferred chemotactic factor is an epidermal growth factor.

Although the other motile cells in the examples herein and in Wang et al., 2003 are substantially macrophages, it is anticipated that other normal stromal cells such as fibroblasts or eosinophils may be predominant in other applications, e.g., where the cancer is in tissues other than mammary tissue. It is believed that the skilled artisan could easily identify binding partners that are effective for removal of any other motile cells without undue experimentation.

The motile cells of interest for these methods are not limited to cancer cells, and can be normal stromal cells such as macrophages. Additionally, the other motile cells (such as macrophages where the motile cells of interest are cancer cells) can be retained and further analyzed, since they are generally isolated in essentially pure form on the microbeads. The further analysis can include, e.g., quantitation of the cells, or analysis of mRNA or protein expression.

These methods are generally useful for isolating live motile cells of interest in highly enriched form, such that culture of the cells, and/or further analysis, can be performed. For example, the cells can be quantified, in order to approximate the number of motile cells of interest present in a given amount of tissue, or to compare the amount of motile cells of interest to the amount of the other motile cells.

In some preferred embodiments, mRNA or protein expression of at least one gene is determined in the motile cells of interest. See Example 2, where mRNA expression of various genes is quantified in the motile cells of interest (carcinoma cells) and compared with expression of the same genes in other carcinoma cells in the same tissue.

As shown in Example 2, motile breast carcinoma cells have significantly higher mRNA expression of Arp2/3 p16 subunit, Arp2/3 p21 subunit, alpha subunit of capping protein, beta subunit of capping protein, cofilin, WAVE3, ROCK1, ROCK2, LIMK 1, PKCζ,, LIM-kinase, PAK, type II alpha isoform of PI4, 5 kinase, mena, tropomyosin, calpain, gelsolin-like protein (CAPG), zyxin, vinculin, integrin β1, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor than nonmotile carcinoma cells from the same tissue, indicating involvement of these genes in the metastatic phenotype. Additionally, mRNA expression of ZBP-1, collagen type III α1, G-protein coupled receptor 26, and fibroblast growth factor receptor 1 is significantly reduced in motile breast carcinoma cells when compared to the nonmotile carcinoma cells, indicating a role of these proteins in regulation of metastasis. Additionally, when ZBP-1 is overexpressed in a carcinoma cell line, motility of the cells is greatly reduced (Example 2), further

establishing the role of ZBP-1 in metastasis regulation. Thus, determination of protein, or, preferably, mRNA expression of any of those genes, especially ZBP-1 is particularly desirable.

As shown in Table 2 and the accompanying discussion in Example 2, motile cancer cells have a characteristic pattern of downregulation of collagen type III α1, G-protein coupled receptor 26, ZBP-1, and fibroblast growth factor receptor 1, and upregulation of Arp2/3 p16 subunit, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor. Thus, it is also preferred that protein or, especially, mRNA expression is determined in at least two, and preferably all, of those genes.

When analysis of mRNA or protein expression of more than one gene is desired, microarray technology can be employed. This well-established technology can analyze mRNA or protein expression of many thousands of genes at once, allowing comparison of expression of, e.g., an entire genome between motile and non-motile cells.

These methods are capable of isolating a few hundred motile cells from a tissue. This typically provides 20-50 ng of total RNA, which is insufficient for array analysis. Therefore, the mRNA from these cells is preferably amplified prior to the determination of expression of the genes. Preferably, the amplification is by reverse transcription and cDNA amplification. A preferred method is the SMART PCR cDNA amplification method (ClonTech Laboratories). See Wang et al., 2003.

The motile cells of interest can also be tested for resistance to chemotherapeutic agents. See Example 1.

In other embodiments, the invention is directed to methods of determining mRNA or protein expression of a gene in motile cells of interest from an animal tissue. The methods comprise isolating the motile cells of interest by the method described above, then extracting the mRNA or protein from the cells of interest, then determining mRNA or protein expression in the extraction of the cells of interest. Preferably, mRNA or protein expression of more than one gene is determined, for example using a microarray by known methods.

When mRNA expression is determined using these methods, the mRNA is preferably extracted and amplified in the motile cells of interest, then mRNA expression of the gene(s) are determined from the amplified mRNA. As described above, the mRNA in these methods is preferably amplified by reverse transcription and cDNA amplification.

In these methods, the animal is preferably a vertebrate; more preferably the animal is a mammal, such as a rodent or a human.

These methods are particularly useful for analysis of motile cells of interest in cancerous tissue, for example carcinoma tissue, such as breast cancer in mammary tissue. See Example 2.

As with the methods described above, these methods can be used with tissue in culture, tissue taken from a biopsy, or directly on tissue in a living mammal.

As discussed above, preferred genes for determination of protein or mRNA expression are Arp2/3 p16 subunit, Arp2/3 p21 subunit, alpha subunit of capping protein, beta subunit of capping protein, cofilin, WAVE3, ROCK1, ROCK2, LIMK 1, PKCζ,, LIM-kinase PAK, type II alpha isoform of PI4, 5 kinase, mena, tropomyosin, calpain, gelsolin-like protein (CAPG), zyxin, vinculin, integrin β1, collagen type III α1, G-protein coupled receptor 26, ZBP-1, fibroblast growth factor receptor 1, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor. In particular, mRNA expression of the group collagen type III α1, G-protein coupled receptor 26, ZBP-1, fibroblast growth factor receptor 1, Arp2/3 p16 subunit, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor is desirable to identify a characteristic signature of metastasis.

The present invention is also directed to methods of determining whether a cancer in a tissue of a mammal is likely to metastasize. The method comprises obtaining a microneedle or capillary filled with a porous matrix comprising a chemotactic factor; inserting the microneedle into the cancer for a time sufficient for motile cells to migrate into the porous matrix; expelling the porous matrix with motile cells from the microneedle or capillary; combining the porous matrix with microbeads, where the microbeads comprise a binding partner to a surface marker present on macrophages from the tissue; removing the microbeads; and quantifying the motile cells, where the presence of more motile cells than from the tissue when noncancerous or when comprising a non-metastatic cancer indicates that the cancer in the tissue of the mammal is likely to metastasize. Since the motile cell isolation method isolates metastatic cells from cancerous tissue, the presence of more motile cells from a cancerous tissue than from a normal tissue establishes that the cancerous tissue as metastatic potential.

These methods are useful for analyzing potentially metastatic cancer in any tissue. In some preferred embodiments, the tissue is mammary tissue, since breast carcinoma is often metastatic.

These methods can be used with any animal. Preferably, the animal is a mammal, such as a rodent or a human.

As established in Wang et al., 2003, and Example 2, where the cancer is a carcinoma, and in particular a breast cancer, common other motile cells in these methods are macrophages. In those cases, a preferred binding partner is an antibody is specific for CD11b. Additionally, where the cancer is a carcinoma, a preferred chemotactic factor is an epidermal growth factor.

The motile cells resulting from these methods can be quantified by any known method. Preferred methods include the use of a fluorescence-activated cell sorter, after labeling the cells

with a fluorescent marker by known methods. Alternatively, the motile cells may be quantified by simple microscopic observation, e.g., with a hemocytometer.

As described above, the microneedle or capillary is a preferably a microneedle, and the porous matrix preferably comprises matrigel.

As established in Example 2, enhancing ZBP-1 activity in a cancerous tissue decreases the metastatic potential in that tissue. Also, since collagen type III α1, G-protein coupled receptor 26, and fibroblast growth factor receptor 1 are characteristically decreased in metastatic cells, decreasing the expression or activity of those proteins would also be expected to decrease the metastatic potential of cancer cells. Thus, the present invention is further directed to methods of inhibiting metastasis of a cancer in a tissue of a mammal. The methods comprise enhancing collagen type III α1, G-protein coupled receptor 26, fibroblast growth factor receptor 1, or especially ZBP-1 activity in the tissue. It is anticipated that these methods are particularly useful for treatment of breast cancer.

In some embodiments of these methods, the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 activity is enhanced by transfecting the tissue with a vector comprising a collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 transgene, where the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 transgene is translated from the vector in the tissue. Such methods, and vectors for executing those methods, are well known in the art, and can be established by a skilled artisan without undue experimentation.

In other embodiments, the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 activity is enhanced by adding a pharmaceutical composition of collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 protein to the tissue. Preferably, the pharmaceutical composition comprises an agent to enhance penetration of the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 protein into the cell, such as liposomes, etc., the use of which are well known in the art.

Example 2 also establishes that several genes are upregulated in metastatic tissue. It is therefore anticipated that metastasis can be inhibited by reducing the activity of these genes in a cancer having metastatic potential. Thus, the invention is additionally directed to methods of inhibiting metastasis of a cancer in a tissue of a mammal. The methods comprise reducing the presence or activity of a protein in the tissue, where the protein is a protein whose expression is upregulated in metastatic cells. Examples of such proteins are Arp2/3 p16 subunit, Arp2/3 p21 subunit, alpha subunit of capping protein, beta subunit of capping protein, cofilin, WAVE3, ROCK1, ROCK2, LIMK 1, PKCζ, LIM-kinase, PAK, type II alpha isoform of PI4, 5 kinase,

mena, tropomyosin, calpain, gelsolin-like protein (CAPG), zyxin, vinculin, integrin β1, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor.

The presence of any of these proteins can be reduced without undue experimentation by addition of an antisense molecule, a ribozyme, or an RNAi molecule to the tissue, where the antisense molecule, ribozyme or RNAi molecule specifically inhibits expression of the protein. In these embodiments, the antisense molecule, ribozyme, or RNAi molecule can be comprised of nucleic acid (e.g., DNA or RNA) or nucleic acid mimetics (e.g., phosphorothionate mimetics) as are known in the art. Methods for treating tissue with these compositions are also known in the art. In some embodiments, the antisense molecule, ribozyme or RNAi molecule can be added directly to the cancerous tissue in a pharmaceutical composition that preferably comprises an excipient that enhances penetration of the antisense molecule, ribozyme or RNAi molecule into the cells of the tissue. In other embodiments, the antisense molecule, ribozyme or RNAi is expressed from a vector that is transfected into the cancerous tissue. Such vectors are known in the art, and these embodiments can be developed for any of the subject proteins without undue experimentation.

In other embodiments, the presence or activity of the protein is reduced by addition of an antibody or aptamer to the tissue, wherein the antibody or aptamer specifically binds and reduces the activity of the protein in the tissue. The antibody or aptamer can be added directly to the tissue, preferably in a pharmaceutical composition comprising an agent that enhances penetration of the antibody or aptamer into the tissue. Alternatively, the antibody or aptamer can be encoded on a vector that is used to transfect the cancerous tissue.

Aptamers are single stranded oligonucleotides or oligonucleotide analogs that bind to a particular target molecule, such as a protein or a small molecule (e.g., a steroid or a drug, etc.). Thus, aptamers are the oligonucleotide analogy to antibodies. However, aptamers are smaller than antibodies, generally in the range of 50-100 nt. Their binding is highly dependent on the secondary structure formed by the aptamer oligonucleotide. Both RNA and single stranded DNA (or analog), aptamers are known.

Aptamers that bind to virtually any particular target can be selected by using an iterative process called SELEX, which stands for Systematic Evolution of Ligands by EXponential enrichment. Several variations of SELEX have been developed which improve the process and allow its use under particular circumstances. See the references cited in PCT/US04/15752, all of which are incorporated by reference.

The invention is further directed to methods of determining resistance of a motile cancer cell population in an animal tissue to a chemotherapeutic agent. The methods comprise obtaining the motile cancer cell population by the methods described above; contacting the motile cancer

cell population with the chemotherapeutic agent at a concentration and for a time sufficient to cause apoptosis in cancer cells susceptible to the chemotherapeutic agent; and determining apoptosis in the motile cancer cell population. In these embodiments, less apoptosis in the motile cancer cell population indicates that the motile cancer cell population is resistant to the chemotherapeutic agent. See Example 1 for some preferred embodiments of these methods.

Examples of chemotherapeutic agents that can be utilized in these embodiments are doxorobucin, cisplatin, or etoposide.

Preferred embodiments of the invention are described in the following examples. Other embodiments within the scope of the claims herein will be apparent to one skilled in the art from consideration of the specification or practice of the invention as disclosed herein. It is intended that the specification, together with the examples, be considered exemplary only, with the scope and spirit of the invention being indicated by the claims, which follow the examples.

Example 1. Breast cancer cells isolated by chemotaxis from primary tumors show increased survival and resistance to chemotherapy

Example Summary

A novel observation resulting from intravital imaging of these tumors is the dramatic fragmentation of carcinoma cells when in contact with blood vessels in non-metastatic tumors (Wyckoff et al., 2000a) compared with the ability of carcinoma cells in metastatic tumors to enter blood vessels as intact whole cells. This suggests a survival advantage for metastatic cells during migration and intravasation.

In the current study we have collected a migratory population of carcinoma cells by chemotaxis to EGF containing microneedles held in the primary tumor. The collected cells were subjected to microarray analysis for differential gene expression. The results show that anti-apoptotic genes are up regulated and pro-apoptotic genes are down regulated coordinately in the migratory subpopulation. Induction of apoptosis by doxorubicin, cisplatin and etoposide in these cells demonstrates that they exhibit a lower drug induced apoptotic index and lower cell death as compared to carcinoma cells of the whole tumor. Our study indicates, for the first time, the capability of using a rat allograft model for evaluating the apoptotic status of a migratory subpopulation of tumor cells and the ability to study their resistance to chemotherapeutic agents directly. In addition, these results indicate that tumor cells that are chemotactic and migratory in response to EGF in the primary tumor have a survival advantage over stationary tumor cells.

Introduction

Recently we have shown that microarray based gene expression studies can be successfully performed on cells collected by chemotaxis into microneedles held in the primary tumor (Wang et al., 2003). In the current example we have combined this method with the analysis of pro- and anti-apoptosis gene expression to determine if migratory cells in the primary tumor have a survival advantage over that of sedentary carcinoma cells within the same tumor. In addition, anticancer drugs designed against the proliferative property of cancer cells were used to investigate if the migratory cells respond equally to the antiproliferative drugs compared to their non-migratory counterparts.

Materials and Methods

Needle collection and FACS sorting of primary tumor cells. We used MTLn3-derived mammary tumors in rats (Farina et al., 1998a), and the microneedle collection method described previously (Wyckoff et al., 2000b; Wang et al., 2003), to study the gene expression pattern of invasive subpopulation of carcinoma cells within live primary tumors. Briefly, the invasive cells were collected from MTLn3 tumor using microneedles containing EGF. Macrophages were removed from this population by using MACS CD11b Microbeads (Miltenyi Biotec) as described before (Wang et al., 2003). The residual carcinoma cells were lysed for RNA extraction. To isolate the general population of carcinoma cells from primary tumor, a small piece tumor was minced, and filtered twice through a nylon-filter to obtain a single cell suspension. FACS sorting was performed on the resulting single cell suspensions based on their GFP expression in tumor cells using a Becton Dickinson (San Jose, CA) FACSVantage cell sorter. GFP-positive tumor cells were collected and lysed directly for RNA extraction. All the procedures were done on ice or 4°C.

RNA extraction and amplification. RNA extraction was performed using the RNeasy kit (QIAGEN), as per manufacturer's protocol and eluted with 30 µl RNase-free water. The total RNA was reverse-transcribed and amplified directly using the SMART PCR cDNA synthesis kit (Clontech, Palo Alto, CA) as described previously (Wang et al., 2003).

Use of pooled reference RNA as control. An equal quantity of reference RNA (pooled RNA from rat liver, spleen, brain and kidney, 4:2:1:1, Ambion TX) was used as a control in all our microarray experiments, which allowed us to use one of the channels as a hybridization control for all the spots on the microarray. The use of pooled reference RNA from the same species as the MTLn3 cells allowed the same interspecies cross hybridization as the background, allowing us to use Mouse cDNA microarrays for our experiments. The pooled reference RNA covers a very broad range of gene expression and is routinely used as controls in cDNA microarray studies (Zhao et al., 2002).

Probe labeling and microarray hybridization. After amplification, cDNAs were purified using the QIAquick PCR Purification Kit (Qiagen) and eluted with TE buffer. Labeling was performed using Label IT® (Mirus) following the manufacturer's instructions. Briefly, labeling reactions were prepared by mixing 10X Mirus Labeling Buffer A, purified cDNA and Cy5 (or Cy3) dye. After incubating the reaction mix at 37°C for 1 hour, the two resulting probes were purified by passing through gel filteration columns. The purified probes were then combined and concentrated using Microcon columns. The concentrated cDNA probes were denatured at 94°C, and hybridized to an arrayed slide overnight at 50°C. Details of slide washing and image collection were described in previous studies (Wang et al., 2002; Wang et al., 2003).

Quality control and data analysis for microarrays. The scanned images were analyzed using the software Genepix (Axon Instruments, Inc. CA) and an absolute intensity value was obtained for both the channels. The entire raw data set was filtered to accommodate a requirement of at least 2 good quality measurements for each triplicate experiment. Values from only the good quality measurements (where the signal strength was more than twice the standard deviation of the background plus the background) were considered for further analysis. Two types of normalization were performed routinely in tandem on all the experiments using the GeneSpring software package (Silicon Genetics, Redwood City, CA). First, intensity-based-normalization was performed to take into consideration the overall signal strength of both channels and normalize the signal strength between all the different chips, reducing the chance of chip-to-chip variability. Second, a reference channel-based normalization was performed which takes into consideration the reference channel (which in this case is pooled reference RNA) and normalizes the values in all the spots. This reduces the chance of spot to spot variability. The final data was a result of both these types of normalization.

Significance analysis of microarrays. In order to determine the significance of up-regulated and down-regulated genes, we performed significance analysis using the software Significance Analysis of Microarrays (SAM)(8). Briefly after normalizing the data as mentioned above the data was log transformed to Log2 and subjected to SAM analysis. The algorithm performs a significance analysis by comparing the relative variance of the replicates between the samples. The result were determined at 5% False Discovery Rate (FDR).

Real time PCR confirmation. To verify the data obtained from microarrays, QRT-PCR analysis of selected over expressed and under expressed genes was performed by using the ABI 7900 (Applied Biosystems, Foster City, CA) with sequence-specific primer pairs for all genes tested (see Supplement Table 2 for primer sequences, amplicon size and annealing temperature) as described previously (Wang et al., 2002). SYBR Green was used for real-time monitoring of

amplification. Results were evaluated with the ABI Prism SDS 2.0 software. All the genes tested for regulation were compared to at least two housekeeping genes (Beta actin and GAPDH).

Cell culture and apoptosis assay. The cells extruded from the needles and tumor cells FACS sorted were cultured in DMEM 20% FCS along with streptomycin and penicillin, for 16 hrs. Subsequently, the cells were challenged with either doxorobucin (17μM) or cisplatin (50 μM) or etoposide (50 μM) for 1 hr, washed and allowed to recover for 24 hrs. The cells were then subjected to an apoptosis assay kit containing Annexin V Cy5 for staining the apoptotic cells and Propedium Iodide (PI) for staining the dead cells (BD Biosciences San Jose, CA). After staining the cells using the manufacturer's protocol, the cells were observed under a fluorescent microscope in the green, red and high red channel for GFP, PI and Cy5 respectively. The total number of GFP cells counted was compared to the number of PI positive and Annexin V-Cy5 positive cells.

Results and Discussion

GFP-labeled tumor cells were injected into rat mammary fat pads, and primary tumors were allowed to grow for 2– 2.5 weeks. To provide insight into the pattern of gene expression associated with chemotactic and migratory carcinoma cells *in vivo*, we compared the gene expression profile of a subpopulation of tumor cells collected from the primary tumor by chemotaxis into a microneedle, called the invasive cells, with that of the general population of GFP-expressing tumor cells sorted from the whole primary tumor by FACS sorting (FIG. 1). Differential gene expression analysis comparing the invasive and general populations of tumor cells was performed using SAM analysis at 5% FDR level revealing 679 genes that were differentially expressed significantly relative to all genes on the array (Supplementary Table 1). The genes that are previously known to be associated with the EGF response (28 genes) were removed from this population. As shown in FIG. 1, genes with known functions whose regulation was changed in the chemotactic and migratory population of cells in the primary tumor were divided into six different functional categories based on the definitions provided by the gene-ontology consortium (http://www.geneontology.org/). It was evident that amongst the functional categories mentioned here the largest change in the number of regulated genes was observed in the genes associated with the cell cycle indicating a large change in the cell proliferation pattern of migratory cells. A detailed scrutiny of these cells showed that the genes associated with increasing cell proliferation were down regulated and those genes associated with a reduction in cell proliferation were upregulated.

Another category of genes found to be significantly regulated in the chemotactic and migratory population of cells in the primary tumor is that of cell motility. These genes have been explained in detail in an accompanying paper. Since there are 5 steps of the motility cycle which

are coordinated to assure efficient cell motility, the up regulation of genes for major effectors in the pathways of each step predicts that the invasive cells will have a heightened migratory activity compared to carcinoma cells of the general tumor population and this is consistent with the high velocities of migration seen in tumors (Condeelis and Segall, 2003).

Regulation of pro and anti-apoptotic genes along with mechanical stability genes. Of particular relevance to survival, stress and apoptosis associated genes showed large changes in regulation (FIG. 2). The up regulation of the heat shock proteins indicates a survival phenotype (Jolly and Morimoto, 2000). This is particularly interesting here as the MTLn3 cells used to generate the primary tumors in this study have been shown to over express heat shock proteins as compared to non-metastatic cell lines (MTC) derived from the same tumor (10). This indicates that in the chemotactic and migratory population of cells in the primary tumor there is a further up regulation of the heat shock gene expression over that in the MTLn3 cells used to generate the primary tumor.

A potential explanation for mechanical stability and survival advantage observed in invasive cells (Jolly and Morimoto, 2000; Condeelis et al., 2003) is the large relative over expression of cytokeratins by carcinoma cells and the suppression of apoptosis gene expression in metastatic tumors and cell lines (Wang et al., 2002). Keratins form the largest subfamily of intermediate filament proteins that play critical roles in the mechanical stability of epithelial cells subjected to shear forces (Coulombe and Omary, 2002). In addition, it was found that carcinoma cells in metastatic tumors and in culture express laminins and cadherins and apoptosis suppressor genes at high levels, all of which might contribute to survival during intravasation and in the circulation (Wang et al., 2002). In contrast, carcinoma cells in non-metastatic tumors and in culture express genes involved in programmed cell death at higher levels. The combination of these factors may contribute to the increased numbers of viable carcinoma cells in the circulation of metastatic tumors and to fragmentation during intravasation and cell death seen in non metastatic tumors (Wyckoff et al., 2000a; Condeelis et al., 2003).

In addition, the anti-apoptotic and pro-apoptotic genes are inversely regulated in the chemotactic and migratory population of cells in the primary tumor (FIG. 2A). The ratio of expression of each gene in the invasive cells, when compared to the general population indicates that a significant number of the anti-apoptotic genes were up regulated while the pro-apoptotic genes were unregulated or down regulated. This is consistent with a previous study where the apoptosis suppressor genes were up regulated in a cell line (MTLn3), which causes metastasis *in vivo* when compared to another cell line from the same lineage (MTC), which does not (Wang et al., 2002). In the current study we show a similar difference between the invasive and general populations of the primary tumor even though the tumor is derived from the same parental cells

(MTLn3). This is important because it means that the microenvironment that induces the chemotactic and migratory behavior of tumor cells induces the survival expression pattern in cells with a previously identical genetic background. We verified the array results using real time PCR for selected genes belonging to the functional category of apoptosis. As shown in FIG. 2B, the same pattern of expression was observed in the invasive cells with both microarray and real time PCR analysis using gene specific primers (see Supplementary Table 2).

Drug resistance in invasive cells measured by apoptosis assay. The finding that the anti-apoptotic genes are up regulated in the invasive cells prompted us to study the functional importance of this finding and whether these cells indeed have a survival advantage over the resident population. We challenged the invasive cells with three most commonly used anticancer drugs, doxorobucin, cisplatin and etoposide. Previous studies have shown that these drugs to induce apoptosis in the MTLn3 cells (Huigsloot et al., 2002). We performed these studies on the invasive and general populations of cells from MTLn3-derived tumors. After treatment with the drugs the cells were allowed to recover for 24 hr. Subsequently, the apoptotic index and cell viability was measured as described in the Methods section. The results, shown in FIG. 3, demonstrate that as a percentage of all the carcinoma cells the invasive cells are able to tolerate all three drugs better than the general population of tumor cells. The process of FACS sorting by itself did not cause any change in the apoptotic index of the tumor cells (data not shown).

Most of the anticancer drugs like doxorobucin, cisplatin and etoposide are designed against the proliferative cells (Awada et al., 2003) making them cytotoxic. Recently, there is an increasing effort to make cytostatic drugs, which prevent the proliferation and invasion as opposed to killing the cells. There has been a demand in the field to have a method to isolate these invasive cells and look for the effect of cytostatic drugs specifically on invasive cells. We believe that in our studies we have demonstrated a method that makes possible this analysis on migratory cells of the primary tumor.

Coordinate regulation of survival genes in the invasive cells. Previous studies have shown that the anti-apoptotic pathways are overexpressed in the metastatic cell lines (Real et al., 2002), and these cells have a survival advantage via Stat3 dependent over expression of BCL-2. In our study we find that a number of anti-apoptotic genes are upregulated. These genes belong to all three pathways, rendering a survival advantage to the cells. On one hand upregulation of the defender against death 1 (DAD1) gene indicates that the extrinsic pathway is blocked in these invasive cells. On the other hand there are signs of down regulation of the intrinsic pathway as well by the over expression of ornithine decarboxylase 1 (ODC1). Upregulation of the expression of apoptosis inhibitor 1, 4 and 5 (Api1, Api4 and Api5) genes indicate an involvement of the convergence pathway as well. Finally there is the robust over expression of the genes like

immediate early response gene 3 (IER3) which is a multi-pathway regulator involving the NFκB family of transcription factors (Reed, 2003). Simultaneously a number of the pro-apoptotic were down regulated, significantly a key regulator of the intrinsic pathway APAF-1 was downregulated in the invasive cells. FIG. 4 summarizes these findings and indicates the extent of change that occurs in the transcriptome of invasive cells.

In the current study we have attempted to investigate the pathways leading to metastasis, which provides this survival advantage to these cells. In previous studies, authors have used cell lines derived from an established secondary tumor (Real et al., 2002). We on the other hand have performed a dynamic assessment of the process of metastasis and have captured the cells prior to the entry into the blood.

In our studies we have identified pathways, which get regulated in the invasive cells, which are not proliferative (FIG. 1). The majority of the genes indicated in the functional category of "cell cycle" are genes that cause a reduction in cell proliferation and prevent the progression of the cell cycle. Recent studies have shown that the overexpression of Bcl2 in MTLn3 cells causes the cells to become resistant to doxorobucin (Huigsloot et al., 2002) as observed by a reduction in drug-induced DNA fragmentation. Previous studies using cell lines derived from metastatic and resident cells from human breast adenocarcinoma have shown that the metastatic cell line was more resistant to anti-cancer drug treatment than the cell line from the primary tumor. However, it remains unknown at which stage of cancer progression (i.e. transformation, proliferation, invasion, intravasation, dissemination of metastases) the selection of the cells that have a survival advantage occurs. In this paper we show for the first time that this selection of cells with a survival advantage probably takes place at the very initial stage of invasion, as evident by the overexpression of anti-apoptotic genes and resistance to anticancer drugs by the invasive cells. The gene expression pattern observed here is associated with an invasive signature unique to these cells. Hence we have identified an expression pattern of survival genes that offer a survival advantage to non-proliferating invasive cells.

Example 2. Identification and testing of a gene expression signature of invasive carcinoma cells within primary mammary tumors

Example Summary

We combined chemotaxis-based cell collection and cDNA microarray technology to identify the gene expression profile of invasive carcinoma cells from primary mammary tumors in experimental animals. Expression of genes involved in cell division and survival, metabolism, signal transduction at the membrane, and cell motility were most dramatically increased in invasive cells, indicating a population that is not dividing but intensely metabolically active and

motile. In particular, the genes coding for the minimum motility machine that regulates β-actin polymerization, and therefore the motility of carcinoma cells, were dramatically up regulated, while ZBP-1, which regulates the localization of β-actin, was downregulated. This pattern of expression suggested ZBP-1 is a suppressor of invasion. Overexpression of ZBP-1 suppressed chemotaxis and invasion in primary tumors and inhibited metastasis from tumors generated using intensely metastatic cell lines. We identified genes important for the invasion of tumor cells in this study. We demonstrate that the identification of these genes provides new insight for the invasion process and the regulation of invasion and demonstrate the importance of these pathways in invasion and metastasis by altering the expression of a master gene, ZBP-1.

Introduction

A potential approach to determine the cellular mechanisms that contribute to invasion is to collect live cells from the primary tumor based on their ability to invade, and profile their gene expression patterns. One of the properties correlated with metastasis is chemotaxis to blood vessels (Wyckoff et al., 2000a). This cell behavior allows cells to orient and move toward blood vessels facilitating their intravasation. Based on these observations, we have developed a complementary approach to directly select for live, invasive cells from live primary tumors in intact rats using a microneedle containing a chemoattractant to mimic chemotactic signals from blood vessels and/or surrounding tissue (Wyckoff et al., 2000b). Overexpression of the EGF receptor and other family members has been correlated with poor prognosis (Nicholson et al., 2001), and therefore we have developed methods for collecting invasive tumor cells that use gradients of EGF to direct tumor cell invasion into microneedles. Gradients of EGF receptor ligands can be generated by diffusion from the blood as well as stromal cells in the tumor microenvironment (O'Sullivan et al., 1993; LeBedis et al., 2002). Thus we are using a physiologically relevant stimulus to mimic tumor cell invasion induced at the borders of tumors near blood vessels and other elements of connective tissue. We have used this method to test the hypothesis that chemotaxis to blood vessels is an important form of egress of carcinoma cells from the primary tumor. Cells have been collected from live rats with tumors that have been generated by the injection of carcinoma cells with different metastatic potential (Wyckoff et al., 2000b), and from live mice with mammary tumors derived from the expression of the PyMT oncogene (Lin et al., 2002; Lin et al., 2001; Wang et al., 2003).

In order to perform gene expression profiling using high density arrays on the few hundred cells commonly collected in microneedles, it is necessary to amplify mRNA by about 1000 fold to the amounts required for arrays. It is also necessary to have a pure cell population. Both of these conditions have been met using recently developed methods (Wang et al., 2003). RNA obtained from as few as 400 cells collected in a single microneedle from the primary tumor,

when amplified as cDNA using the PCR based cDNA amplification technique (18), can be used for microarray expression analysis. We have validated this amplification method and demonstrated that it retains the original mRNA's copy abundance and complexity in the amplified product (Wang et al., 2003).

In the current study, the collection of invasive cells from the primary tumor using chemotaxis is combined with gene expression profiling using the above-described PCR based cDNA amplification techniques. This technology has allowed the characterization of gene expression patterns of invasive carcinoma cells from the primary tumor without potential artifacts that arise from the culturing of small populations of cells. We identified a group of genes that define motility pathways that are coordinately up regulated in invasive cells. These pathways may account for the enhanced migratory behavior of the collected cells. Furthermore, we tested the contribution of these pathways to invasion and metastasis by altering the expression of a master gene that regulates the expression of the common molecule on which these pathways converge.

Materials and Methods

Needle collection and FACS sorting of primary tumor cells. We used MTLn3-derived mammary tumors in rats (Farina et al., 1998b), and the microneedle collection method described previously (Wyckoff et al., 2000b; Wang et al., 2003), to study the gene expression pattern of invasive subpopulation of carcinoma cells within live primary tumors. Briefly, the invasive cells were collected from MTLn3 tumor using microneedles containing EGF. Cell collection was imaged using a multi-photon microscope as described previously (Wang et al., 2002) by inserting the bevel of a matrigel and EGF containing needle into the field of view. A 50 mm z-series consisting of 5 mm steps allows for the imaging of a large number of cells around the needle. 1/10th of the volume from each needle was used to determine the number of cells collected. From the remaining 9/10 volume from the microneedle, macrophages were removed by magnetic separation, and RNA extraction was done as previously described (Wang et al., 2003).

To isolate the general population of carcinoma cells from primary tumor, a small piece tumor was separated from the whole tumor, minced, and filtered twice through a nylon-filter to obtain a single cell suspension. FACS sorting was performed on the resulting single cell suspensions based on their GFP expression in tumor cells. GFP-positive tumor cells were collected into a tube and lysed directly for RNA extraction. All the procedures were done on ice or 4°C.

Because EGF and Matrigel are present in the needle, as a control experiment, we identified genes whose expression is altered by EGF or Matrigel application. Carcinoma cells from the primary tumor were FACS-sorted as described above. The resulting cells were split and

plated on Mattek dishes covered with Matrigel (1:5) in the presence or absence of EGF (1 nM) for 4 hr at 37°C. The cells were then lysed directly on the dish for total RNA extraction.

An equal quantity of reference RNA (pooled RNA from rat liver, spleen, brain and kidney, 4:2:1:1, Ambion TX.) was used to generate probes as a control in all our microarray experiments, which allowed us to use one of the channels as a hybridization control for all the spots on the microarray. The use of pooled reference RNA from the same species as the MTLn3 cells allowed the same interspecies cross hybridization as the background, allowing us to use mouse cDNA microarrays for our experiments. The pooled reference RNA covers a very broad range of gene expression and is routinely used as controls in cDNA microarray studies (Zhao et al., 2002).

RNA amplification, probe labeling and microarray hybridization. The RNA was then concentrated by ethanol precipitation and re-dissolved in 3.5 µl DEPC water. The total RNA was reverse-transcribed directly using the SMART PCR cDNA synthesis kit (Clontech, Palo Alto, CA) according to the manufacturer's protocol. After amplification, cDNAs were purified using the QIAquick PCR Purification Kit (Qiagen) and eluted with TE buffer. Labeling was performed using Label IT® (Mirus) following the manufacturer's instructions. Briefly, labeling reactions were prepared by mixing 10X Mirus Labeling Buffer A (10 µL), purified cDNA (3.5µg), Cy5 (or Cy3) dye (5 µL) in a total volume of 100 µL. After incubating the reaction mix at 37°C for 1 hr, the two resulting probes were purified by passing through SigmaSpin columns followed by Qiaquick columns. The purified Cy-3 and Cy-5 DNA probes were then combined and concentrated using micron YM 50 columns. Microarray analysis was performed by using cDNA microarrays made at AECOM. About 27,000 mouse genes (Incyte Genomics) were precisely spotted onto a single glass slide. Detailed descriptions of microarray hardware and procedures are available from http://129.98.70.229/. Microarray analysis was performed in three independent repeats. Details of slide hybridization, washing and image collection were described in previous studies (Wang et al., 2003; Wang et al., 2002).

Quality control and data analysis for microarrays. The scanned images were analyzed using the software Genepix (Axon Instruments, Inc. CA) and an absolute intensity value was obtained for each of the channels for the reference RNA and the RNA derived from the cells. The entire raw data set was filtered to accommodate a requirement of at least two good quality measurements for each triplicate experiment. Values from only the good quality measurements (where the signal strength was more than twice the standard deviation of the background plus the background) were considered for further analysis. Two types of normalization were performed routinely in tandem on all the experiments using the GeneSpring software package (Silicon Genetics, Redwood City, CA). First, intensity-based-normalization was performed which takes

into consideration the overall signal strength of both channels and normalizes the signal strength between all the different chips, reducing the chance of chip-to-chip variability due to the experiment being performed on different days. Second, a reference-channel-based normalization was performed which takes into consideration the reference channel (which in this case is pooled reference RNA) and normalizes the values in all the spots. This reduces the chance of spot to spot variability. The final data was a result of both these types of normalization.

In order to determine the significance of upregulated and downregulated genes, we calculated the standard deviation of the reference channel in all of the chips and found it to be 0.18 and used 5X standard deviation as the cutoff, indicating a high level of fidelity in our data above 2-fold. Genes that were up- or down-regulated in the arrays performed on control samples (FACS sorted cells which were treated with Matrigel and EGF) were removed from the final list of genes specific to the invasive subpopulation of tumor cells.

Real time PCR confirmation. To verify the data obtained from microarrays, QRT-PCR analysis of selected overexpressed and underexpressed genes was performed by using the iCycler Apparatus (Bio-Rad) with sequence-specific primer pairs for all genes tested (see Supplementary Table 3 for primer sequences, amplicon size and Tm) as described previously (Wang et al., 2002). The SYBR Green PCR Core Reagents system (Perkin-Elmer Applied Biosystems) was used for real-time monitoring of amplification.

Plasmid construction, cell culture, transfection, infection and generation of ZBP-1 stable expression cell lines. FLAG-ZBP-1 (Farina et al., 2003) was digested with BamHI/XbaI and inserted into the BamHI/XbaI sites of EGFP-C1 (Clontech). The EGFP-FLAG-ZBP-1, which encodes a fusion protein, was then isolated as Eco47III/XbaI restriction fragment, blunt ended and inserted into a filled XhoI site of pMCSVneo (Clontech). This vector contains a viral packaging signal, neomycin resistance gene, and the 5' and 3' long terminal repeats from the murine PCMV virus. As a result, the LTR drives high-level constitutive expression of the EGFP-FLAG-ZBP-1 gene. PHOENIX cells were cultured under standard conditions (Dal Canto et al., 1999) and were transfected with EGFP-FLAG-ZBP-1 using FUGENE (Roche). Retroviral supernatant was harvested and used to infect MTLn3 cells as previously described (Dal Canto et al., 1999). Stable MTLn3 cells were selected in the presence of neomycin.

Microchemotaxis chamber assay. A 48-well microchemotaxis chamber (Neuroprobe) was used to study the chemotactic response to EGF, following the manufacturer's instructions and as described previously (SEGALL ET AL., 1996).

Blood burden, single cells in the lung, and metastases. MTLn3-ZBP-1 or MTLn3-GFP cells were injected into the mammary fat pads of female Fischer 344 rats. Tumor cell blood burden was determined as described previously (Wyckoff et al., 2000a). After blood removal and

euthanization of the rat, the lungs were removed and the visible metastatic tumors near the surface of the lungs were counted. For measurement of metastases, excised lungs were placed in 3.7% formaldehyde, mounted in paraffin, sectioned, and stained with H&E. Slices were viewed using a 20X objective, and all metastases in a section containing more than five cells were counted (Wyckoff et al., 2000a).

Results

Gene expression patterns unique to invasive tumor cells. GFP-labeled tumor cells were injected into rat mammary fat pads, and primary tumors were allowed to grow for 2– 2.5 weeks. To provide insight into the pattern of gene expression associated with chemotactic and invasive carcinoma cells *in vivo*, we compared the gene expression profile of the subpopulation of invasive tumor cells collected from the primary tumor by chemotaxis into a microneedle with that of the general population of GFP-expressing tumor cells sorted from the whole primary tumor by FACS (FIG. 5B). Hereafter, the former population of cells will be called the invasive cells, and the latter the general population, respectively. The invasive subpopulation of tumor cells was collected into microneedles filled with EGF and Matrigel that were held in the primary tumor for up to 4 hours as described previously (Wyckoff et al., 2000b; Wang et al., 2003). The collection of the invasive cells was monitored by imaging the GFP-expressing cells with a multiphoton microscope as they migrated to the EGF containing microneedles (FIG. 5A). This allowed direct confirmation that collection was due to cell migration and not a passive process.

The collected cells were a mixture of carcinoma cells (75%) and macrophages (25%) as shown previously (Wang et al., 2003). Macrophages were removed by binding to magnetic beads conjugated with anti-MAC-1, giving a greater than 96% pure population of carcinoma cells for analysis (Wang et al., 2003). The general population of primary tumor cells was collected by FACS sorting and plated either on matrigel or matrigel and EGF for 4 hours, the interval of time required for microneedle collection, to mimic the collection conditions prior to purification of the RNA. These controls were done to subtract patterns of gene expression resulting from stimulating cells with matrigel and EGF, and allowed identification of the gene expression signature of the invasive cells (FIG. 5B).

Differential gene expression analysis comparing the invasive and general populations of tumor cells revealed 1366 genes that were differentially expressed (Supplementary Table 4). As shown in FIG. 6, genes with known functions were divided into eleven different functional categories based on definitions provided by the gene-ontology consortium (Mariadason et al., 2002), (http://www.geneontology.org).

In order to determine the significance of changes in gene expression in each of the functional categories of the genes represented in our arrays, Chi-square or SAM analysis were

performed. The functional categories of Cell Cycle, Apoptosis, Metabolism, Protein Metabolism, Cytoskeleton & ECM, Growth Factor & Signal Transduction and Nucleic Acid Chemistry were found to be statistically significant in the invasive cells by Chi-square (Zigeuner et al., 2004) or SAM analysis (Tusher et al., 2001). Random sets of equal numbers of genes did not generate the same pattern of up and down regulation indicating that the pattern was not observed by chance ($P< 0.05$). Similarly, clustering the results from all genes of the general population in the same space of all genes on the microarray did not yield an outcome similar to the invasion signature ($P> 0.05$). A detailed table indicating each of the functional categories and the significant analysis is given as a supplementary table (Supplementary Table 5) indicating the number of genes printed on the microarray and the number regulated in invasive cells.

It is interesting to note that the number of genes whose expression is regulated up or down in the functional category called cell cycle (FIG. 6, #1) is reduced in the invasive cells compared to the general population. In addition, there is a reduction in the number of regulated genes of the Nucleic Acid Chemistry category (FIG. 6, #10), which includes genes necessary for DNA synthesis. These may indicate that the cell proliferation activity of invasive cells is repressed (Bravo et al., 2003) and the cell cycle is arrested (Nishitani and Lygerou, 2002). The increase in the number of genes regulated in both the General Metabolism and the protein metabolism categories (FIG. 6, #5 and 6, respectively) may indicate that invasive cells are very active metabolically, probably utilizing more energy and having a fast turnover of proteins (Larsen et al., 2003). The number of genes regulated in the Apoptosis category (FIG. 6, #2) is significantly higher in the invasive cells. A closer inspection of the genes involved shows that the pro-apoptotic genes are downregulated and the anti-apoptotic genes are upregulated. This may indicates that these cells have a survival advantage over the general population. Conversely, the genes involved in the Growth Factors and Signal Transduction group (FIG. 6, #9) is markedly reduced. These, taken together with the Cell Cycle genes (FIG. 6, #1), jointly indicate a significant reduction in the proliferative nature of these cells (Supplementary Table 5).

Finally, there is an increase in the number of regulated genes in the Cytoskeleton and Extracellular Matrix category (FIG. 6, #7). This is of particular relevance to the migratory behavior of the tumor cells that is important in their invasion (discussed next).

Genes involved in invasion. In order to be collected by the microneedle, the carcinoma cells must be capable of moving toward and crawling into the extracellular matrix of the microneedle within the 4 hr. collection interval. If a cell moves 2 cell diameters during this interval to gain entry to the microneedle it would have a minimum speed of 0.2 μm/min, similar to the velocity of carcinoma cells *in vitro*. However, carcinoma cells move in the primary tumor at speeds up to 10X this minimum value (Condeelis and Segall, 2003) indicating that cells from

hundreds of microns away from the microneedle can be recruited for collection and that the cells may penetrate the extracellular matrix in the collecting microneedle. Consistent with this prediction is the observation that carcinoma cells are found within the matrix of the collecting microneedle, indicating that cells have traveled hundreds of microns during the collection interval. This indicates speeds much greater than 0.2 μm/min *in vivo*.

The motility cycle of chemotactic crawling cells is composed of 5 steps; signal sensing, protrusion toward the signal source, adhesion, contraction and tail retraction (Bailly and Condeelis, 2002). As shown in Table 1 and FIG. 7, based on the microarray analysis, many genes associated with motility are upregulated in the invasive cells compared to the general population of cells. We verified the array results using real time PCR for selected genes representing the 5 steps of the motility cycle. As shown in FIG. 7A, the same pattern of expression was observed in the invasive cells with both microarray and real time PCR analysis.

Table 1. List of motility related genes differentially expressed in the invasive sub-population of tumor cells. Genes associated with motility are displayed in this table and the ratios on the right indicated the level of expression in the invasive compared to the general population of cells of the primary tumor.

Gene Description	Needle/FACS
Capping protein alpha 1	4.34
Cell division cycle 42	3.96
Capping Protein alpha 2	3.89
Moesin	3.67
Rho interactin protein 3	3.33
LIM-kinase 1	3.24
Palladin	3.12
Zyxin	2.93
Tropomyosin alpha chain	2.86
Rho-associated coiled-coil forming kinase 1	2.71
Testis expressed gene 9	2.67
Phosphatidylinositol-4-phosphate 5-kinase type II alpha	2.60
Epidermal growth factor receptor	2.59
Capping protein (actin filament), gelsolin-like	2.53
Annexin A5	2.47
CRIPT protein	2.32
Protein kinase C, zeta	2.30
Arp 2/3 complex subunit p21	2.22
RAB25, member RAS oncogene family	2.19
Vinculin	2.16
Kinesin family member 5B	2.13
Catenin beta	2.08
Chaperonin subunit 4 (delta)	2.06
Chaperonin subunit 3 (gamma)	2.06
Tubulin Alpha-4 chain	2.05
Integrin beta 1 (fibronectin receptor beta)	2.00
Cofilin 1, non-muscle	1.98
Arp 2/3 complex subunit p16	1.93
Kinectin 1	1.91
Downstream of Tyrosine Kinase 1	1.91
Burkitt lymphoma receptor 1	1.90
Wave 3	1.89
Rho-associated coiled-coil forming kinase 2	1.63
Cadherin 1	1.51
Fibroblast growth factor receptor 1	0.54
Zip code binding protein 1	0.25
Alpha-Actinin, smooth muscle isoform	0.21

The protrusion of a pseudopod toward the chemotactic signal initiating the motility cycle is the key step in defining the leading edge of the cell and therefore its direction during migration (Bailly and Condeelis). Protrusion is driven by actin polymerization-based pushing against the

cell membrane and this requires the minimum motility machine composed of cofilin, Arp2/3 complex and capping protein acting on their common downstream effector, β-actin (Mogilner and Edelstein-Keshet, 2002). The elevated expression of any one of these three effectors is expected to significantly enhance the speed of migration of cells since doubling the amount of either Arp2/3 complex, capping protein or cofilin in the reconstituted minimum motility machine can increase protrusion rate by 10x (Loisel et al., 1999). Therefore, it is significant, as shown in FIG. 7B, that the genes coding for all three end-stage effectors, the Arp2/3 complex (the p16 and p21 subunits), capping protein and cofilin, are up regulated by at least two-fold each. Furthermore, the genes coding for the pathways regulating the activities of Arp2/3 complex (WAVE3), capping protein and cofilin are coordinately upregulated in the invasive cell population. In the cofilin pathway, genes for ROCK1 and ROCK2, LIMK 1 and PKCζ are upregulated along with cofilin. LIM-kinase is activated either by PAK which is regulated by Cdc42-GTP and Rac-GTP or by ROCK which is regulated by Rho-GTP. Either PAK (Edwards et al., 1999) or ROCK (Ohashi et al., 2000) can phosphorylate LIM-kinase thereby activating it to increase cofilin phosphorylation. Inhibition of LIM-kinase activity is PKC dependent and this involves one of the unconventional PKC isoforms (Edwards et al., 1999). As shown in FIG. 7B, PKCζ gene expression, the inhibitory branch of the LIM-kinase inhibitory pathway, is elevated along with that of the activating branch of the pathway involving ROCK and PAK.

Similar increases in both the stimulatory and inhibitory parts of the capping protein pathway are upregulated in invasive carcinoma cells (FIG. 7B). The expression of both the alpha and beta subunits of capping protein is increased. In addition, genes that antagonize capping protein function such as the type II alpha isoform of PI4, 5 kinase and Mena are upregulated (Cooper and Schafer, 2000; Bear et al., 2002).

Genes coding for proteins involved in myosin mediated contraction and tail retraction (tropomyosin, ROCK1, and calpain), gelsolin-like protein (CAPG) and adhesion molecules (zyxin, vinculin, and integrin β1) are up regulated, as well (Table 1). ROCK plays a crucial role in cell adhesion and motility and is linked to pathogenesis and progression of several human tumors (Sahai and Marshall, 2003). Integrin β1 has previously been implicated in the ability of an experimentally transformed fibroblast cell line to metastasize (Brakebusch et al., 1999), and its expression is increased in upper aerodigestive tract and cervical squamous cell carcinomas (Van Waes et al., 1995).

ZBP-1 as a master gene regulating cell polarity. A gene that is strongly downregulated in invasive cells is Zip-code binding protein (ZBP-1) (Table 1 and FIG. 7). ZBP-1 is a 68 kD RNA-binding protein that binds to the mRNA zipcode of β-actin mRNA and functions to localize the mRNA to the leading edge of crawling cells. β-actin is the preferred isoform of actin for the

polymerization of filaments at the leading edge of cells and, therefore, is acted on by the cofilin, capping protein and Arp2/3 pathways (Shestakova et al., 2001). β-actin mRNA localization is required for the generation of intrinsic cell polarity that is characteristic of normal fibroblasts and epithelial cells. Disruption of ZBP-1-mediated β-actin mRNA targeting leads to cells without stable cell polarity (Shestakova et al., 2001), and loss of β-actin mRNA targeting is correlated with the polarity of carcinoma cell lines *in vitro* and *in vivo* (Shestakova et al., 1999; 2001). Therefore, ZBP-1 is a candidate invasion suppressor gene required for normal cell polarity by determining the sites in cells where the Arp2/3 complex, capping protein and cofilin pathways converge by controlling the sites of targeting of β-actin mRNA and the location of β-actin protein that is the common downstream effector of these pathways (FIG. 7B).

To test the hypothesis that ZBP-1 expression can suppress invasion, the full length ZBP-1 gene was subcloned in a pMCSVneo vector (FIG. 8A) and transfected into the parental MTLn3 cells. Data from Western blot analysis (FIG. 8B) confirmed that stable clones transfected with pEGFP-FLAG-ZBP-1 expressed higher levels of ZBP-1 compared to untransfected cells. To account for any effects that might arise from the introduction of EGFP into cells, MTLn3 cells transfected with pGreenLantern-1 vector (Life Technologies, Inc.) were used as control.

To investigate the chemotactic properties of the ZBP-1 overexpressing cells, two independent clones of ZBP-1 overexpressing cell lines were characterized. Chemotaxis was measured in a Boyden chamber. ZBP-1 overexpressing cells migrated through the filter in response to EGF poorly compared to the parental MTLn3 cells (FIG. 9A), indicating that chemotaxis was inhibited. This was true for both ZBP-1 clones and is consistent with previous data showing the enhanced intrinsic cell polarity of ZBP-1 expressing cells (Shestakova et al., 1999; 2001). Furthermore, the ability of carcinoma cells to invade microneedles placed into primary tumors derived from MTLn3 cells over expressing ZBP-1 was greatly reduced (FIG. 9B) further indicating a reduction in chemotaxis.

Injection of the ZBP-1 over expressing cells into the mammary fat pads of rats resulted in tumors that were less metastatic. The metastatic potential of these tumors was characterized as the number of tumor cells present in circulating blood (FIG. 10A), and the number of lung metastatic tumors (FIG. 10B). However, as shown in FIG. 10C, tumor growth was not affected by increasing the expression of ZBP-1. In addition, primary tumors derived from control and ZBP-1 overexpressing cell lines were indistinguishable as judged by their histology upon multiphoton imaging of GFP-expressing tumor cells (data not shown).

Discussion

Signature of invasive carcinoma cells. By comparing gene expression patterns of invasive cells to those of the general population of carcinoma cells in the same primary tumor, we were able to find patterns in the regulation of gene expression unique to the invasive subpopulation of cells. Our results indicate that the regulation of genes involved in cell division, metabolism, signal transduction at the membrane, cell survival and cell motility was most dramatically changed in invasive cells predicting a population that is neither proliferating nor apoptotic but intensely metabolically active and motile. While increased cell proliferation during tumor development has been associated with poor prognosis in patients (Evan and Vousden, 2001), the results reported both here and in previous studies (Wyckoff et al., 2000a) indicate that tumor size is neither correlated with invasion nor the ability of cells to metastasize to distant organs. In addition, invasive cells show down regulation of genes associated with apoptosis and up regulation of genes for cell survival. This is consistent with previous work where it was shown that cell survival genes were up regulated in metastatic tumors as compared to non-metastatic tumors (Wang et al., 2002) and suggests that the invasive subpopulation may contribute disproportionally to this expression profile in whole metastatic tumors.

In a previous study, the genes differentially expressed between metastatic and non-metastatic cells in culture and the tumors derived from them by orthotopic injection of the cells into the mammary gland were compared. We found that those coding for molecules involved in cell adhesion, motility, cell polarity, and signal transduction were most different. Comparing the gene expression patterns in non-metastatic tumors to metastatic tumors from the previous study (20), with the differences between the invasive cell population and general population of the same tumor defined here, we have found that a subset of genes (Table 2), maintain the same patterns of regulation in both studies. This suggests that the invasive subpopulation of cells collected from primary tumors with microneedles has enhanced an expression pattern of a subset of genes that is characteristic of the differences between metastatic and non-metastatic cell lines and tumors. This is emphasized by the fact that the invasive subpopulation of cells collected by chemotaxis into microneedles is from tumors derived from a single cell line, the MTLn3 cell line. This indicates that as the tumor progresses, highly invasive cells are selected in which a pattern of gene expression present in metastatic cells and tumors is enhanced over the pattern of expression of the cells that remain behind in the primary tumor.

Table 2: Differentially expressed genes common to invasive cells identified in this study and to metastatic tumors and cell lines identified in a previous study. Common genes regulated in a similar way in all the three samples are displayed here. Dark shading indicates overexpression and light shading represents repression. Taken together these genes outline a signature of invasion and indicate that a number of interacting pathways are involved in invasion.

Gene name	Met/non met, Cell line*	Met/non met, Tumor**	Needle/FACS***	Gene function
Collagen, type III, alpha 1	0.01	0.15	0.19	ECM Composition
G-protein coupled receptor 26	0.14	0.2	0.46	Signal transduction
Zip code binding protein 1	0.08	0.03	0.25	Cell polarity
Fibroblast growth factor receptor 1	0.32	0.35	0.53	Signal transduction
ARP 2/3 COMPLEX 16 KD SUBUNIT.	6.31	5.45	1.93	Minimum motility machine
Tight junction protein 2	2.96	2.16	3.4	Adhesion Molecules
Member Ras oncogene family	7.99	6.38	2.18	Signal transduction
Epidermal growth factor receptor	20.12	3.0	2.6	Signal transduction

* Metastatic cell line = MTLn3, non-metastatic cell line = MTC;
** Tumor derived from injection of MTLn3 or MTC;
*** Needle = cells collected into needle by chemotaxis = invasive; FACS = cells obtained from whole tumor by FACS = general population.

Cell motility genes and their roles in cancer invasion. Chemotaxis to EGF is required for collection of cells into the microneedle because significant numbers of cells are not collected in the absence of EGF (Wyckoff et al., 2000b), and EGF-R activity is required for the collection of carcinoma cells. Therefore, the motility related genes that are differentially expressed in the invasive population may also contribute to EGF-dependent chemotaxis and enhanced migration in the primary tumor. A major result of this study is the finding that genes from the pathways associated with the minimum motility machine are greatly up regulated, predicting that protrusion velocity will be increased. Since protrusion sets cell direction and, therefore, defines chemotaxis, this step in the motility cycle may be key in determining invasive potential. Furthermore, as seen in FIG. 7B, genes coding for key components of the pathways regulating the end stage effectors of the minimum motility machine are up regulated together, from the receptor through the key kinases and finally the end stage effectors themselves. By upregulating these entire pathways, receptor-ligand stimulated motility would be greatly enhanced leading to increased invasiveness. These results are consistent with the 10-fold higher velocity of cell migration toward blood vessels and EGF filled microneedles, both sources of chemoattractant, observed in primary tumors of un-dissected live rats and mice compared to their cultured cell counterparts (Wyckoff et al., 2000a; 2000b; Farina et al., 1998b; Wang et al., 2002; Condeelis and Segall, 2003). Consistent with these results are the finding that inhibition of the nucleation activity of Arp2/3

complex in carcinoma cells in culture inhibits chemotaxis to EGF (Bailly et al., 2001) and that cofilin activity is required for cell motility in carcinoma cells (Chan et al., 2000).

Our results show that cofilin, LIM-kinase 1, ROCK 1, 2 and PKCζ are all over expressed in highly invasive carcinoma cells. In previous studies, LIM-kinase 1 was shown to be over expressed in metastatic breast and prostate tumors (Davila et al., 2003; Yoshioka et al., 2003). Over expression of LIM Kinase 1 in tumor cell lines increased their motility and invasiveness *in vitro* (Davila et al., 2003) and *in vivo* (Yoshioka et al., 2003). Reduction in the expression of LIM-kinase 1 in metastatic prostate cell lines deceased invasiveness in matrigel invasion assays (Davila et al., 2003). These results are consistent with ours shown here that LIM-kinase 1 is more highly expressed in the invasive cell population.

In contrast, it has been reported that increased expression of LIM-kinase 1 in carcinoma cells significantly reduces their cell motility as the phosphorylation of cofilin by LIM-kinase 1 abolishes EGF induced actin nucleation and polymerization (Zebda et al., 2000). Our study may resolve this paradox by demonstrating that in invasive cells collected from primary tumors both the stimulatory and inhibitory pathways to LIM-kinase 1 and cofilin are over expressed together thereby increasing the steady state rate of cofilin activation in invasive carcinoma cells resulting in enhanced cell motility as predicted previously (Davila et al., 2003; Yoshioka et al., 2003; Zebda et al., 2000; Sahai et al., 2001).

ZBP-1 in metastasis. In general, cells that lack a fixed intrinsic polarity are more chemotactic to exogenous gradients presumably because there is no intrinsic polarity to be overcome by the exogenous chemotactic signal and the cell can turn in any direction to respond to a gradient (Parent and Devreotes, 1999; Iijima et al., 2002). The presence of intrinsic polarity in carcinoma cells in tumors is correlated with the stable polarization of actin polymerization at one end of the cell only, resulting in polarized locomotion. In contrast, carcinoma cells in metastatic MTLn3 tumors are unpolarized except when they are near blood vessels where they become polarized toward the blood space (Shestakova et al 1999; Wyckoff et al., 2000a). These results suggest that cells that have proceeded through the epithelial mesenchymal transition (EMT) to the point where all remnants of the intrinsic cell polarity of the original epithelium are lost, such as MTLn3 cells, are more efficient at responding to external chemotactic signals and more attracted to blood vessels in the primary tumor.

A key difference between metastatic and non-metastatic cells that may explain the inverse correlation between intrinsic cell polarity and metastasis is loss of the ability by metastatic cells to localize mRNA and proteins that define cell polarity (Shestakova et al., 1999). The mechanism relating β-actin mRNA targeting to the leading edge and intrinsic cell polarity involves the localization of β-actin nucleation to the leading edge during motility. Disruption of mRNA

targeting to the leading edge using oligonucleotides that disrupt the interaction between ZBP-1 and the targeting sequence in the mRNA, the zip-code, results in delocalization of mRNA and β-actin nucleation sites, and the disruption of cell polarity (Shestakova et al., 2001). Highly metastatic cells have lost the ability to target mRNA for β-actin, which may be required to maintain a localized supply of β-actin protein to support a stable leading edge in response to the activity of the minimum motility machine. Without a stable leading edge, the intrinsic polarity of the metastatic cell is lost and cell direction is determined by signals from blood vessels, resulting in chemotaxis toward blood vessels and intravasation (Wyckoff et al., 2000a; Condeelis and Segall, 2003). Molecular profiling of MTLn3 and MTC cells and tumors using both cDNA arrays and QRT-PCR demonstrates that non-metastatic MTC cells and tumors express much higher levels of ZBP-1 than the metastatic MTLn3 cells and tumors (Wang et al., 2002). Furthermore, in the present study, invasive tumor cells isolated from primary mammary tumors using chemotaxis express much lower levels of ZBP-1 than cells that remain behind in the primary tumor even though both cell populations were derived from the same progenitor MTLn3 cells (Table 2). Furthermore, as shown in the current study, invasive carcinoma cells expressing experimentally increased levels of ZBP-1 after transfection with ZBP-1 expression vectors exhibit decreased chemotaxis, and invasion into microneedles, and the tumors made from cell grafts of these ZBP-1 expressing cells are much less metastatic by several criteria.

The results reported here indicate that ZBP-1 is a 'metastasis repressor' and, together with mRNA targeting status and analysis of tumor cell polarity around blood vessels discussed above, might be used in prognosis and therapy.

In view of the above, it will be seen that the several advantages of the invention are achieved and other advantages attained.

As various changes could be made in the above methods and compositions without departing from the scope of the invention, it is intended that all matter contained in the above description and shown in the accompanying drawings shall be interpreted as illustrative and not in a limiting sense.

All references cited in this specification are hereby incorporated by reference. The discussion of the references herein is intended merely to summarize the assertions made by the authors and no admission is made that any reference constitutes prior art. Applicants reserve the right to challenge the accuracy and pertinence of the cited references.

Supplemental Table 1

ID	Acc No	Gene	Description	N/F ratio
1,13,7	AW554270	Hnrpu	heterogeneous nuclear ribonucleoprotein U	6.96244698
1,15,6	AW557056		ESTs	9.8276436
1,20,17	AW536795	Clk	CDC-like kinase	2.52297812
1,8,19	AA404094	C11orf17	C11orf17	2.89863435
10,10,16	AW537281		ESTs	2.05025384
10,11,8	AW550681		ESTs	1.67198708
10,12,23	AA060863		Mus musculus TSC22-related inducible leucine zipper 1b (Tilz1b) mRNA,	2.5675062
10,14,14	C87169			1.74212657
10,14,9	AW546455		ESTs, Moderately similar to nuclear factor of activated T-cells, cytoplasmi	3.70859768
10,18,7	AW553938		ESTs	1.78494589
10,19,13	AU023882	Brca2	breast cancer 2	2.11786605
10,19,8	AW551966		ESTs	1.69399525
10,2,11	AU015358	Ubl1a2-pendi	ubiquitin-like 1 (sentrin) activating enzyme subunit 2	5.36511446
10,2,7	AW552108		ESTs, Highly similar to SUCCINATE DEHYDROGENASE CYTOCHROM	2.6570659
10,2,9	AU042207		ESTs, Weakly similar to N-methyl-D-aspartate receptor glutamate-binding	3.27248879
10,21,7	AW554737		ESTs, Weakly similar to KIAA0512 protein [H.sapiens]	2.51486794
10,22,9	AW547900		ESTs	1.70219737
10,23,9	AW547928		ESTs	4.42609651
10,3,10	AU040764		ESTs	2.30582743
10,3,17	AW543960		EST	1.98385959
10,3,6	AW554947		ESTs, Highly similar to translation initiation factor IF2 [H.sapiens]	3.62564427
10,6,10	AU040830		ESTs, Weakly similar to 60S RIBOSOMAL PROTEIN L30A [Saccharomyc	4.09184393
10,6,16	AW537188			2.91355459
10,6,8	AW549332		ESTs	2.02373543
10,8,16	AW537237	Arl6ip	ADP-ribosylation-like factor 6 interacting protein	3.42711503
10,8,21	AA240506		ESTs	1.72389261
10,8,26	AA386680	Kif5b	kinesin family member 5B	2.13080531
10,9,18	AW538432	Rhoip3-pendi	Rho interacting protein 3	3.33021601
11,14,15	C80446		ESTs	6.59773219
11,15,8	AW551715			2.6189542
11,17,9	AW547189		ESTs, Weakly similar to membrane glycoprotein [M.musculus]	1.87280539
11,22,18	AW543115		ESTs	3.00521981
11,22,7	AW555297		ESTs	2.1674956
11,3,7	AW552496			2.87792419
11,3,9	AU042851			2.23592148
11,4,12	AU018955		ESTs	2.19569146
11,6,22	AA138394		ESTs	2.16917767
11,8,10	AU043242		ESTs, Weakly similar to ORF YKR081c [S.cerevisiae]	2.34050104
12,10,18	AW538403		Mus musculus formin binding protein 11 (FBP11) mRNA, complete cds	3.04888214
12,11,10	AU043911		ESTs, Weakly similar to UBIQUITIN-CONJUGATING ENZYME E2-17 KD	2.76954033
12,11,6	AW555759	Phb	prohibitin	2.76169976
12,13,18	AW538517		ESTs	4.50704838
12,14,3	AI448261		Mus musculus serine-threonine kinase receptor-associated protein mRNA	1.96213955
12,15,13	AU023751		ESTs, Highly similar to HPBRII-7 protein [H.sapiens]	5.42622482
12,16,17	AW545323			5.84397302
12,16,9	AW546487	Mns1	meiosis-specific nuclear structural protein 1	1.78819183
12,18,6	AW556673	Anxa7	annexin A7	2.03695246
12,18,9	AW547603		ESTs	3.80861968
12,19,6	AW556706		ESTs	3.09489644
12,2,11	AU015298		ESTs, Moderately similar to dJ30M3.3 [H.sapiens]	1.99824462
12,20,9	AW547693		ESTs	3.55440963
12,21,18	AW539791		ESTs, Weakly similar to coded for by C. elegans cDNAs GenBank: [C.ele	6.21796016
12,21,7	AW554706		ESTs, Highly similar to hypothetical protein [H.sapiens]	2.35747851
12,22,18	AW539811	Cdc10	cell division cycle 10 homolog (S. cerevisiae)	3.90212531
12,22,7	AW554761		ESTs	2.54196101
12,23,7	AW554784		ESTs, Weakly similar to Cxorf5 [H.sapiens]	2.14798017
12,3,12	AU024765			4.02111663
12,3,18	AA529949		ESTs	2.02716114
12,4,10	AU040750		ESTs, Highly similar to VACUOLAR ASSEMBLY PROTEIN VPS41 HOMC	1.7668606
12,4,3	AI427886		ESTs, Highly similar to RAS-RELATED PROTEIN RAB-28 [R.norvegicus]	2.6941002
12,5,16	AW537132	Gdap2	ganglioside-induced differentiation-associated-protein 2	3.00246852

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12,8,19	AA285584		Mus musculus strain Swiss Webster/NIH actin-associated protein palladin	3.12462418
13,15,7	AW554567	Fkbp1a	FK506 binding protein 1a (12 kDa)	2.65395775
13,17,7	AW554607	Ptk9r-pendin	related protein	2.08852506
13,18,12	AU015048		ESTs	3.33465439
13,2,10	AU043380		ESTs, Highly similar to RER1 PROTEIN [Saccharomyces cerevisiae]	1.92262948
13,2,14	C85794		ESTs, Weakly similar to myelin transcription factor 1-like [M.musculus]	2.14278605
13,2,16	AW537070		ESTs	1.93209692
13,20,9	AW548914		Mus musculus receptor activity modifying protein 2 mRNA, complete cds	3.22966737
13,21,8	AW552636			1.65124352
13,22,16	C78511	Biklk	Bcl2-interacting killer-like	2.2503145
13,23,8	AW552679		ESTs	2.16211139
13,3,10	AU043443		ESTs, Highly similar to TRAM PROTEIN [Canis familiaris]	4.01129823
13,4,7	AW553519		ESTs, Highly similar to DNA-DIRECTED RNA POLYMERASE II 19 KD P	1.72758381
13,5,11	AU016361		EST	2.10796295
14,1,3	AI429145		ESTs	4.8127654
14,11,12	AU020132	Odc	ornithine decarboxylase, structural	2.89009249
14,11,18	AW538715	Ass1	arginosuccinate synthetase 1	4.6092053
14,13,12	AU020218	Zrf2	zuotin related factor 2	2.62741328
14,14,11	AU017036		ESTs, Highly similar to UBIQUITIN-CONJUGATING ENZYME E2-17 KD	2.0788242
14,14,16	C76660		ESTs, Moderately similar to KIAA0663 protein [H.sapiens]	2.17228735
14,15,14	C87551	Eif4e-ps	eukaryotic translation initiation factor 4E	1.96683492
14,15,24	AA030786		ESTs	2.24037307
14,18,18	AW541471	Tfg	Trk-fused gene	1.67868784
14,20,10	AU046294	Magoh	mago-nashi homolog, proliferation-associated (Drosophila)	2.35313884
14,20,9	AW548203		ESTs	3.09092408
14,22,13	AU018430		ESTs	3.81890328
14,7,20	AA220617	Bak	Bc12 homologous antagonist/killer	2.46129103
14,8,16	AW537454		ESTs	2.21447486
14,9,17	AW544435			2.00018963
15,10,13	AU023604		ESTs, Weakly similar to SEX-LETHAL PROTEIN, FEMALE-SPECIFIC [D	2.56911034
15,12,18	AW539416		ESTs	2.34887616
15,13,24	AA031056	Mcmd5	mini chromosome maintenance deficient 5 (S. cerevisiae)	2.39168943
15,14,5	AI326287		ESTs, Highly similar to TUBULIN ALPHA-4 CHAIN [Gallus gallus]	2.05448175
15,15,18	AW539519		ESTs	2.34152702
15,16,18	AW539538		ESTs	2.61191657
15,22,17	AW536987	Snta1	syntrophin, acidic 1	2.4648536
15,23,14	AU022589		ESTs	1.82446202
15,3,12	AU019284		ESTs	2.05917438
15,6,15	C79548		ESTs	1.69012907
15,6,26	AA415370		ESTs	2.25790098
15,9,18	AW539347		ESTs	4.44707202
16,10,5	AI323620	Hkp1	House-keeping protein 1	1.64033149
16,10,6	AW555997		EST	1.63067441
16,12,18	AW538700		ESTs	2.61753856
16,12,24	AA027451			2.61431094
16,13,7	AW553990		ESTs	4.108365
16,14,24	AA030061			2.6212084
16,15,11	AU017015			3.50279732
16,15,16	C76678		Mus musculus mRNA for Sid6061p, complete cds	3.72002855
16,16,14	C87531		ESTs	2.99145001
16,17,10	AU046028		ESTs, Moderately similar to RNA polymerase II transcription factor SIII p1	2.46786006
16,17,15	C80210		ESTs	7.29568703
16,17,17	AW545676		ESTs	2.59138366
16,18,9	AW548061		ESTs, Weakly similar to unknown [C.elegans]	3.03251314
16,19,11	AU018045			3.21985786
16,2,12	AU018486	Ssb	Sjogren syndrome antigen B	3.97953644
16,20,18	AW541494	Surf4	surfeit gene 4	3.59187439
16,21,10	AU041374			1.7844772
16,21,17	AW536576	Tex9	testis expressed gene 9	2.67155044
16,23,13	AU018409	ArhA	Rho family GTPase	3.53026877
16,3,11	AU015646	Rex3	reduced expression 3	2.07164441
16,4,9	AU042578			2.01540733
16,6,14	C86226			5.44261442

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16,8,14	C86301		ESTs	2.17929475
16,8,15	C79036		EST	3.8756934
16,9,14	C86367		ESTs, Weakly similar to BAT2 [M.musculus]	2.37598823
17,17,6	AW557130	Xist	inactive X specific transcripts	1.6978919
17,18,8	AW551743		ESTs, Moderately similar to WD-REPEAT PROTEIN SAZD [H.sapiens]	1.80777802
17,20,14	C88038			1.80890073
17,22,6	AW558021		ESTs	2.21967907
17,23,18	AW543447			3.02886602
17,6,11	AU016133		ESTs, Weakly similar to MSSP [M.musculus]	2.21300981
18,22,6	AW557547			2.43243053
18,7,16	AW537221	Fgfrp	fibroblast growth factor regulated protein	2.64855873
19,1,16	AW536849	Ccnb1-rs1	cyclin B1, related sequence 1	3.25510854
19,10,12	AU020382			6.58930398
19,13,12	AU020575		ESTs, Moderately similar to HYPOTHETICAL 27.1 KD PROTEIN CCE1-(	2.03756993
19,14,17	AW536101		Mus musculus mRNA for phosphorylated adaptor for RNA export (PHAX ç	3.31362291
19,15,24	AA030810		ESTs, Highly similar to AF161432_1 HSPC314 [H.sapiens]	2.04362708
19,16,17	AW536142		ESTs, Weakly similar to unknown [R.norvegicus]	1.98133946
19,18,6	AW557108		ESTs	1.98176254
19,19,18	AW542930		ESTs	1.95321647
19,19,8	AW552398		ESTs, Moderately similar to TRANSCRIPTION INITIATION FACTOR TFII	4.26378752
19,20,19	AA276043	Fbp1	fructose bisphosphatase 1	1.81520728
19,22,8	AW552461		ESTs, Weakly similar to SKD1 PROTEIN [Mus musculus]	1.62993678
19,23,15	C85347			5.69154099
19,23,9	AW548671		ESTs	1.88113666
19,3,26	AA388122	Mem3	Maternal embryonic message 3	2.37455611
19,5,15	C79184	Kpna2	karyopherin (importin) alpha 2	4.48319301
19,5,16	AW537587			4.45813595
19,5,8	AW549980		ESTs, Highly similar to UBIQUITIN-CONJUGATING ENZYME E2-17 KD	3.30468034
19,6,25	W82690		ESTs	2.09784801
19,7,11	AU016110		Mus musculus heat shock protein (HSPC030) mRNA, complete cds	3.03138332
19,7,14	C86564			1.7333449
19,8,7	AW553398		EST	4.02468789
2,1,11	AU015271		ESTs	2.71447848
2,10,16	AW537279	Macs	myristoylated alanine rich protein kinase C substrate	5.47595949
2,13,11	AU016670		ESTs	2.48053812
2,14,9	AW546453		ESTs	2.73290518
2,15,7	AW553809	Rnaseli	ribonuclease L (2', 5'-oligoisoadenylate synthetase-dependent) inhibitor	3.12701979
2,16,12	AU021072		ESTs, Weakly similar to unknown [R.norvegicus]	3.69119996
2,16,13	AU023815		ESTs, Weakly similar to (defline not available 5901816) [D.melanogaster]	2.31844668
2,21,15	C81194	Hsp105	heat shock protein, 105 kDa	2.79345821
2,22,11	AU017931		ESTs, Highly similar to ALPHA-1,6-MANNOSYL-GLYCOPROTEIN BETA	2.05061784
2,22,18	AW540941		ESTs, Highly similar to CYTOCHROME C OXIDASE POLYPEPTIDE VIB	2.11548466
2,22,8	AW552025		ESTs	1.86359682
2,23,14	AU021850	Semcap2	semaF cytoplasmic domain associated protein 2	1.83549489
2,3,23	AA034561	Fen1	Flap structure specific endonuclease 1	2.58741717
2,7,11	AU015537		ESTs, Highly similar to H<BETA>58 PROTEIN [Mus musculus]	1.73006318
20,1,13	AU021834		ESTs	2.80269482
20,10,18	AW538407	Slc20a1	solute carrier family 20, member 1	2.76768172
20,13,14	C87110		ESTs	3.32776214
20,16,14	C87205		ESTs, Weakly similar to C44B9.1 [C.elegans]	3.70199032
20,17,13	AU023806	Rock1	Rho-associated coiled-coil forming kinase 1	2.71453544
20,17,17	AW545339	Ate1	arginine-tRNA-protein transferase 1	2.0166932
20,17,25	W87153		ESTs, Moderately similar to HYPOTHETICAL 21.5 KD PROTEIN C08B1'	1.92812079
20,18,12	AU021126		ESTs	4.03038879
20,18,17	AW536320	Orc4	origin recognition complex, subunit 4	2.55331517
20,18,8	AW550920		ESTs	3.16437003
20,18,9	AW547604		ESTs, Weakly similar to ORF YOL071w [S.cerevisiae]	2.7049388
20,19,19	AA066250		ESTs, Weakly similar to BC-2 protein [H.sapiens]	3.43011637
20,19,8	AW551944		ESTs, Highly similar to Similar to D.melanogaster parallel sister chromatic	2.76726728
20,2,26	AA413090		ESTs, Moderately similar to unknown protein IT12 [H.sapiens]	2.08408988
20,20,8	AW551959	Cul1	cullin 1	3.04082811
20,21,19	AA068436		ESTs, Highly similar to unknown [R.norvegicus]	5.64768422
20,22,7	AW554765		ESTs, Moderately similar to tpr protein [H.sapiens]	2.23120297

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20,23,14	AU021819	Top1	topoisomerase (DNA) I	3.54840029
20,3,3	AI427786		EST	2.05554644
20,3,5	AW557661	Taldo1	transaldolase 1	3.57376954
20,6,22	AA154465		ESTs, Highly similar to similar to human DNA-binding protein 5. [H.sapien	3.12509279
20,6,8	AW549269		ESTs	2.55555586
20,7,13	AU022791			3.77694698
20,7,15	C78755		ESTs	3.38255
20,7,16	AW537202	Dhfr	dihydrofolate reductase	2.653293
20,9,11	AU016480		ESTs, Highly similar to 40S RIBOSOMAL PROTEIN S25 [Homo sapiens;	2.43409271
20,9,17	AW544140	D10Wsu52e	DNA segment, Chr 10, Wayne State University 52, expressed	4.68301819
20,9,9	AU042440		ESTs, Weakly similar to BRAIN SPECIFIC POLYPEPTIDE PEP-19 [Rattu	3.11453505
21,1,9	AU042135		ESTs, Moderately similar to protocadherin-3 [R.norvegicus]	2.5390447
21,16,17	AW536295			1.81921122
22,1,8	AW548397		ESTs, Weakly similar to cDNA EST EMBL:T01421 comes from this gene	2.63643756
22,12,14	C86478			7.93096055
22,14,9	AW546813		EST	1.54052025
22,16,23	AA073695	Mea1	male enhanced antigen 1	3.68124867
22,23,18	AW542425		ESTs	3.11225586
22,9,17	AW544437		ESTs	2.28118451
23,1,6	AW555565	Zyx	zyxin	2.92901591
23,1,7	AW552671		ESTs	1.80066851
23,1,8	AW549119	RIE2	RIE2 protein	2.108802
23,11,7	AW553643		ESTs, Highly similar to LZIP-1 and LZIP-2 [M.musculus]	1.72760253
23,12,10	AU045213		ESTs	1.57541576
23,12,15	C80749		ESTs	2.025627
23,12,17	AW536194		ESTs, Highly similar to CGI-35 protein [H.sapiens]	5.04586204
23,12,6	AW556475		ESTs	2.7187435
23,14,13	AU024490		ESTs, Highly similar to PROTEIN TRANSLATION FACTOR SUI1 HOMO	6.64658114
23,14,26	AA052404	CRIPT	CRIPT protein	2.31831023
23,16,15	C80954			2.05158328
23,16,25	W97837	D10Ertd322e	DNA segment, Chr 10, ERATO Doi 322, expressed	2.49482644
23,18,22	AA183803		ESTs, Weakly similar to envelope polyprotein□ [M.musculus]	1.73268827
23,2,12	AU019219		EST	2.10823042
23,2,16	AW537048	Ets2	E26 avian leukemia oncogene 2, 3' domain	3.32507873
23,2,7	AW552709		Mus musculus brain protein 44-like protein (Brp44l) mRNA, complete cds	2.52172331
23,20,14	C88330		ESTs, Weakly similar to weak similarity to the yeast SSM4 protein [C.eleg	2.28243719
23,20,17	AW536945		ESTs, Weakly similar to female sterile homeotic-related protein Frg-1 [M.r	3.37311499
23,21,10	AU042018		ESTs	3.02452904
23,22,16	C78481	Eif3	eukaryotic translation initiation factor 3	5.42442604
23,23,17	AW537006		ESTs	1.69659304
23,4,6	AW555631		ESTs, Highly similar to PUTATIVE RECEPTOR PROTEIN [Homo sapien	2.48889274
23,5,15	C79506			2.4202114
23,5,9	AW545976	Cops7a	COP9 (constitutive photomorphogenic), subunit 7a (Arabidopsis)	2.29782307
23,6,16	AW537694		ESTs, Highly similar to HYPOTHETICAL 109.5 KD PROTEIN IN PPA1-D	4.23891808
23,7,3	AI426727		ESTs, Weakly similar to 5'-AMP-ACTIVATED PROTEIN KINASE, GAMM/	2.61712024
23,7,6	AW556339		ESTs, Highly similar to RN protein [R.norvegicus]	2.31101609
23,8,11	AU017390		ESTs	1.80278618
23,8,14	C86919			4.01688942
23,8,24	AA017991		ESTs	2.4834124
24,1,14	C85101		ESTs	1.52794038
24,1,7	AW552230		ESTs	2.37684894
24,12,7	AW553979		ESTs, Highly similar to TYROSINE-PROTEIN KINASE JAK1 [Homo sapi	2.11242201
24,14,7	AW554059		ESTs, Weakly similar to HYPOTHETICAL 15.9 KD PROTEIN IN GLNA-FI	2.94508646
24,17,11	AU017987		ESTs, Weakly similar to NADH-CYTOCHROME B5 REDUCTASE [R.norv	2.01692806
24,18,11	AU018029		ESTs, Highly similar to cbp146 [M.musculus]	3.42804304
24,18,19	AA080156	Kap	kidney androgen regulated protein	3.15890138
24,22,25	AA000038	Usp23	ubiquitin specific protease 23	3.13740756
24,3,13	AU022218	Ptp4a1	protein tyrosine phosphatase 4a1	2.45987735
24,5,14	C86208		ESTs	4.60351847
24,5,16	AW537358		ESTs, Weakly similar to cDNA EST yk338g10.5 comes from this gene [C.	4.42410766
24,7,24	AA013832	Clpx	caseinolytic protease X (E.coli)	3.18328772
24,8,16	AW537419		ESTs	2.2968508
24,9,21	AA209964	D11Moh34	DNA segment, Chr 11, KL Mohlke 34	7.59017857

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25,18,17	AW536755		ESTs, Highly similar to similar to nuclear domain 10 protein NDP52 [H.sa	7.5093238
25,19,8	AW552431	Scp2	sterol carrier protein 2, liver	4.81820219
25,22,7	AW555335			2.1614645
26,10,9	AW546296		ESTs	2.76472101
26,19,16	C77513		ESTs, Highly similar to GUANINE NUCLEOTIDE-BINDING PROTEIN G(I	1.93596646
26,19,8	AW551969	Prtb	proline rich protein expressed in brain	3.39962483
26,20,9	AW547818	Fmr1	fragile X mental retardation syndrome 1 homolog	3.18414807
26,21,24	AA031120	Psma1	proteasome (prosome, macropain) subunit, alpha type 1	2.66376533
26,8,17	AW544153		ESTs	1.87750286
27,1,17	AW543439	Fkbp4	FK506 binding protein 4 (59 kDa)	3.25474097
27,10,15	C79409			1.66090225
27,10,16	AW537744		Mus musculus protein inhibitor of activated STAT protein PIAS1 mRNA, c	2.15944042
27,10,17	AW545798	D13Abb1e	DNA segment, Chr 13, Abbott 1 expressed	1.77967958
27,11,12	AU020432		ESTs	2.38379328
27,11,20	AA265845		Mus musculus mRNA for heterogeneous nuclear ribonucleoprotein H	2.18570225
27,12,14	C86757		ESTs	1.70687597
27,12,26	W36917	D17Wsu155e	DNA segment, Chr 17, Wayne State University 155, expressed	1.96735624
27,13,17	AW536071			2.57404337
27,15,14	C87823		ESTs, Weakly similar to cDNA EST EMBL:T01156 comes from this gene	2.44670577
27,15,7	AW554328		ESTs, Highly similar to RSP5 PROTEIN [Saccharomyces cerevisiae]	3.91361709
27,17,9	AW547193			2.22215744
27,18,19	AA403949	Capn12	calpain 12	2.38344367
27,18,6	AW557115			3.25273021
27,2,8	AW548748		ESTs, Weakly similar to proline-rich protein [M.musculus]	2.84041662
27,20,16	C78065		ESTs	1.70716822
27,20,18	AW542945		ESTs	1.83234873
27,21,18	AW543112			1.91026009
27,23,4	AI426498		Mus musculus radio-resistance/chemo-resistance/cell cycle checkpoint cc	4.00732871
27,4,15	C79174		ESTs	4.05893627
27,6,12	AU019031	Hist4	histone 4 protein	2.34117834
27,6,26	AA415519		ESTs, Weakly similar to HYPOTHETICAL 40.4 KD PROTEIN R06F6.5 IN	2.10134942
27,7,21	AA189879		ESTs, Weakly similar to similar to Zinc finger, C2H2 type [C.elegans]	1.87840796
27,8,23	AA057995		ESTs, Moderately similar to AF151892_1 CGI-134 protein [H.sapiens]	2.14756865
27,8,25	W81857		ESTs, Highly similar to HYPOTHETICAL 39.7 KD PROTEIN C34E10.2 IN	2.45832094
27,9,16	AW537685		ESTs, Highly similar to HYPOTHETICAL 83.2 KD PROTEIN IN CHA1-AF	2.34299929
27,9,17	AW544704		ESTs, Weakly similar to CGI-90 protein [H.sapiens]	1.86491349
27,9,26	W14928	Smpd1	Sphingomyelin phosphodiesterase 1, acid lysosomal	2.03589216
28,11,23	AA051256	Cbx5	chromobox homolog 5 (Drosophila HP1a)	1.99435809
28,12,18	AW538480		ESTs, Moderately similar to serine proteinase inhibitor 6 [M.musculus]	4.92457718
28,17,14	C87270		ESTs	2.58381273
28,17,5	AI327096		Mus musculus neuronal calcium sensor-1 (NCS-1) mRNA, complete cds	4.6763181
28,18,17	AW536321		ESTs	1.67994555
28,19,6	AW556708		ESTs	1.42637305
28,19,7	AW553932		EST	1.63732816
28,21,12	AU021314		Mus musculus KOI-4 gene, partial cds	3.06495231
28,22,19	AA068665		ESTs, Weakly similar to AF152841_1 polymyositis scleroderma overlap s	3.05957507
28,23,12	AU015222		ESTs	2.79592277
28,23,9	AW547880			3.23970231
28,4,17	AW543978		ESTs	3.96983188
28,6,10	AU040813		ESTs, Weakly similar to T23G11.9 [C.elegans]	2.30954932
28,6,2	AI449074		ESTs	4.4970497
28,7,7	AW552851		ESTs	2.13912406
28,9,18	AW538390			1.83399874
29,10,18	AW539386		ESTs	7.00805039
29,10,9	AW547284		ESTs, Weakly similar to PYRROLINE-5-CARBOXYLATE REDUCTASE [(	2.0491818
29,11,13	AU023662			20.5984082
29,14,17	AW536258	Tpp2	tripeptidyl peptidase II	1.83550641
29,15,4	AI427491		ESTs, Highly similar to PROBABLE UBIQUITIN CARBOXYL-TERMINAL	2.39417765
29,18,10	AU041939		Mus musculus TBX1 protein mRNA, complete cds	2.22193251
29,19,15	C81124	Hsp60	heat shock protein, 60 kDa	1.96854487
29,20,10	AU042003			2.44102461
29,3,10	AU043450	Msh2	mutS homolog 2 (E. coli)	2.65990107
3,1,10	AU041246		ESTs, Highly similar to 26S PROTEASE REGULATORY SUBUNIT 4 HO	7.57599128

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3,1,17	AW543415		Mus musculus secretory carrier membrane protein 4 mRNA, complete cds	3.64366353
3,11,17	AW545809	Mdu1	antigen identified by monoclonal antibodies 4F2	1.79142854
3,13,16	C76908			6.20352697
3,13,17	AW536067	Aop2	anti-oxidant protein 2	2.42567808
3,13,7	AW554240		ESTs, Highly similar to OLIGOSACCHARYL TRANSFERASE STT3 SUB	2.75246722
3,14,10	AU044892		ESTs	1.70531929
3,14,24	AA030271		ESTs	2.48351778
3,14,6	AW556999		ESTs, Moderately similar to hypothetical protein [H.sapiens]	2.84061777
3,15,15	C80485	Zfr	zinc finger RNA binding protein	4.20498132
3,17,20	AA260352		Mus musculus cerebellar postnatal development protein-1 (Cpd1) mRNA,	3.26803395
3,18,9	AW548431		ESTs, Highly similar to CYTOCHROME C OXIDASE POLYPEPTIDE VIIE	4.00909626
3,19,18	AW542927	Bcap31	B-cell receptor-associated protein 31	5.06678767
3,19,6	AW557152		ESTs, Highly similar to spliceosomal protein SAP 155 [H.sapiens]	2.70613649
3,19,9	AW548470		ESTs	12.8845812
3,2,11	AU015947		ESTs	1.78824793
3,20,8	AW552411	Ech1	enoyl coenzyme A hydratase 1, peroxisomal	2.31504488
3,23,12	AU015879		Mus musculus LIM-kinase1 (Limk1) gene, complete cds; Wbscr1 (Wbscr1	3.23910865
3,3,12	AU018928		ESTs, Highly similar to TRAF4-associated factor 2 [H.sapiens]	5.51004896
3,4,11	AU016022	Anxa4	annexin A4	3.44828013
3,4,12	AU018954			3.27206923
3,5,26	AA413831	LOC56463	p100 co-activator	7.85093068
3,5,5	AW558170		ESTs	1.84131912
3,6,22	AA172774	D16Wsu83e	DNA segment, Chr 16, Wayne State University 83, expressed	7.71686883
3,6,24	AA015136	LOC56046	hypothetical protein	3.59627177
3,6,26	AA422809		ESTs, Highly similar to KIAA0368 [H.sapiens]	4.1731865
3,7,8	AW550056		ESTs	5.47894293
3,9,2	AI666581		RIBOSOMAL PROTEIN S6 KINASE II ALPHA 1	2.01602961
30,1,11	AU015616		ESTs, Weakly similar to cDNA EST yk338f6.5 comes from this gene [C.el	2.33028873
30,1,14	C85143			2.94027965
30,1,16	AW536713		ESTs	2.28356006
30,10,5	AI893564	Anx5	Annexin V	2.03267402
30,11,7	AW553280	Itgb1	integrin beta 1 (fibronectin receptor beta)	2.00370896
30,12,14	C86480	Plp	proteolipid protein (myelin)	2.74602712
30,14,12	AU020233	Arf1	ADP-ribosylation factor 1	3.99152601
30,16,12	AU021489	Omd	osteomodulin	2.59384895
30,16,16	C76750	Hnrpa1	heterogeneous nuclear ribonucleoprotein A1	4.58236322
30,19,14	C87694		ESTs, Weakly similar to acid ceramidase [M.musculus]	1.87973161
30,2,15	C78024			1.97370615
30,2,19	AA472933		ESTs, Highly similar to unknown [H.sapiens]	2.60253647
30,20,8	AW552159	Atp2a2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	2.40955193
30,21,11	AU018151		ESTs	1.91390077
30,21,19	AA068842	Ubc2e	ubiquitin conjugating enzyme 2e	2.43579854
30,22,15	C85070		ESTs	2.17760937
30,22,8	AW552205	Zfp101	zinc finger protein 101	1.84567109
30,23,9	AW548330		ESTs, Moderately similar to NADH-UBIQUINONE OXIDOREDUCTASE C	2.64689279
30,3,14	C85216			48.9719617
30,3,16	AW537334		ESTs, Weakly similar to signal recognition particle 54K protein [M.musculi	2.64741235
30,5,7	AW553103		ESTs, Weakly similar to es 64 [M.musculus]	2.47043219
30,7,16	AW537446	Tcea1	transcription elongation factor A (SII), 1	3.35375659
30,9,13	AU023128		ESTs, Highly similar to CAMP-DEPENDENT PROTEIN KINASE TYPE I-	2.97162728
31,1,5	AW558291		ESTs	2.31484213
31,1,7	AW552672	Btd	biotinidase	1.87360737
31,1,8	AW549121	Hmg14	high mobility group protein 14	5.30516699
31,11,7	AW553645	Slc12a2	solute carrier family 12, member 2	5.20922584
31,12,7	AW554493			2.1083931
31,12,9	AW547310		ESTs	2.72482755
31,13,8	AW551817	Madh4	MAD homolog 4 (Drosophila)	2.75722936
31,14,15	C80862		ESTs, Moderately similar to (defline not available 5931553) [M.musculus]	3.09077696
31,14,18	AW539487	Pabpc1	poly A binding protein, cytoplasmic 1	3.2298131
31,15,24	AA030846	Coq7	demethyl-Q 7	2.01374888
31,18,10	AU041887		ESTs, Highly similar to HYPOTHETICAL 30.3 KD PROTEIN IN APE1/LA	5.57332473
31,18,8	AW551918	Ube2i	ubiquitin-conjugating enzyme E2I	3.50095995
31,2,8	AW548978			3.41685873

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31,22,14	AU022550		ESTs	2.05932698
31,3,11	AU016270		ESTs, Highly similar to CYCLIN-DEPENDENT KINASES REGULATORY	3.39581265
31,6,26	AA414612	Cappa1	capping protein alpha 1	4.33595632
31,8,12	AU020667	Uchl3	ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	3.22520008
31,8,13	AU023550	Fin14	fibroblast growth factor inducible 14	2.19594103
31,8,20	AA272115		ESTs	2.3927419
31,9,7	AW553602		ESTs, Weakly similar to (defline not available 6016842) [M.musculus]	2.28557359
32,10,13	AU023139		ESTs, Weakly similar to natural killer cell tumor-recognition protein [M.mu	2.06147099
32,18,17	AW536519		ESTs, Weakly similar to lens epithelium-derived growth factor [H.sapiens]	2.62322524
32,21,11	AU018130		ESTs, Weakly similar to cholesterol 25-hydroxylase [M.musculus]	6.33573576
32,23,6	AW557836		ESTs	8.74090491
32,9,16	AW537469		ESTs, Moderately similar to BB1	2.05226764
33,11,19	AA423209	Psme3	Proteaseome (prosome, macropain) 28 subunit, 3	2.22293967
33,15,17	AW536140	Hsp86-1	heat shock protein, 86 kDa 1	3.22006954
33,15,7	AW554376	Dlgh1	discs, large homolog 1 (Drosophila)	3.04957435
33,18,15	C80708		ESTs, Weakly similar to 62D9.a [D.melanogaster]	2.11948459
33,18,18	AW542919		ESTs, Highly similar to KIAA0398 [H.sapiens]	2.04958634
33,19,14	C88028		ESTs, Highly similar to small membrane protein 1 [H.sapiens]	3.66566524
33,2,8	AW548794		ESTs	1.86124923
33,21,5	AI327246		ESTs, Weakly similar to titin [M.musculus]	3.50724343
33,3,8	AW549937	Hdac2	histone deacetylase 2	2.2928649
33,6,11	AU016137	Fth	ferritin heavy chain	2.46495945
33,6,8	AW550050			4.27791285
33,8,15	C79363		Mus musculus hsp40 mRNA for heat shock protein 40, complete cds	1.62376072
33,9,18	AW538992		Mus musculus mRNA for 26S proteasome non-ATPase subunit	4.76789816
34,10,14	C86107	Actn3	actinin alpha 3	2.5209022
34,13,17	AW545272			1.64775098
34,18,18	AW539649		ESTs, Highly similar to DEK PROTEIN [Homo sapiens]	2.54249509
34,18,20	AA266868		ESTs, Highly similar to RIBOSOMAL PROTEIN S6 KINASE [Homo sapie	2.36462731
34,2,14	C81381		ESTs, Weakly similar to BcDNA.GH03108 [D.melanogaster]	2.2321414
34,2,15	C77692		EST	2.0046599
34,2,26	AA543829		ESTs, Weakly similar to CG17593 gene product [D.melanogaster]	1.77033364
34,21,8	AW552022	Nudt5	nudix (nucleoside diphosphate linked moiety X)-type motif 5	2.15526038
34,23,21	AA213017	Fmo3	flavin containing monooxygenase 3	1.94008494
34,6,9	AU042383		ESTs	2.9220976
35,11,17	AW545818		ESTs, Weakly similar to /prediction	3.33983595
35,13,14	C87726		Mus musculus mitotic checkpoint component Mad2 mRNA, complete cds	2.39134431
35,4,15	C79176		ESTs, Weakly similar to TYROSINE-PROTEIN KINASE JAK3 [M.musculu	2.82666014
35,8,9	AU043040			2.28926461
36,12,7	AW553719		ESTs	2.38365423
36,12,9	AW546347		Mus musculus geminin mRNA, complete cds	2.18189942
36,15,12	AU021009		Mus musculus cleavage and polyadenylation specificity factor 73 kDa sub	1.73127069
36,16,3	AI451984	Prim1	DNA primase, p49 subunit	2.25030209
36,2,8	AW548009		ESTs, Highly similar to PTD014 [H.sapiens]	2.34643201
36,3,16	AW537083		ESTs, Highly similar to cellular apoptosis susceptibilty protein [H.sapiens]	2.7665325
36,3,8	AW549140		ESTs, Weakly similar to Peter Pan [D.melanogaster]	2.37970593
36,4,11	AU015435		ESTs	2.654766
36,5,10	AU040801		ESTs, Highly similar to rer [M.musculus]	3.23611164
36,5,25	W62229	Ube1c	ubiquitin-activating enzyme E1C	5.47716315
37,11,18	AW539443			4.63619909
37,12,6	AW556511		ESTs	1.84141389
37,14,12	AU020998	Plat	plasminogen activator, tissue	2.59992149
37,14,2	AI451597		EST	2.74058252
37,16,6	AW557336	Vti1b-pendin	vesicle transport through interaction with t-SNAREs 1b homolog	1.87783553
37,17,18	AW543524	Ghrh	growth hormone releasing hormone	3.7312984
37,7,11	AU016461	Ssfa1	sperm specific antigen 1	2.51212865
37,8,14	C86958		ESTs	2.44494556
37,8,22	AA161815		ESTs	4.12389804
38,1,5	AW557863		ESTs	2.491298
38,18,14	C87642		ESTs, Weakly similar to coded for by C. elegans cDNAs GenBank:M8886	1.86906723
38,20,12	AU021687		ESTs	1.80303815
38,20,2	AI464450		ESTs	2.20420204
38,3,5	AW557915	Ezh1	enhancer of zeste homolog 1 (Drosophila)	2.4168558

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38,3,7	AW552394		ESTs	2.48791469
38,4,9	AU042629		ESTs	2.39206021
38,5,12	AU018693			1.98372833
38,5,5	AW557968		EST	3.51417458
39,12,20	AA265633		ESTs	3.0875993
39,14,25	W97741			1.86720634
39,15,18	AW539528	D13Wsu177e	DNA segment, Chr 13, Wayne State University 177, expressed	1.97046078
39,19,17	AW536910		ESTs, Moderately similar to chromosome-associated protein-E [H.sapiens	2.36518598
39,19,18	AW543636	Anxa5	annexin A5	2.47144291
39,21,3	AI447815		ESTs, Moderately similar to LUTHERAN BLOOD GROUP GLYCOPROTE	2.20379027
39,4,17	AW544818	Rab18	RAB18, member RAS oncogene family	3.10934705
39,7,24	AA014196	Glud	Glutamate dehydrogenase	3.2382491
39,8,24	AA020034		ESTs, Weakly similar to cleft lip and palate transmembrane protein 1 [H.s	2.37690372
4,1,10	AU040633			6.85111934
4,1,5	AW557574	Lrpap1	low density lipoprotein receptor related protein, associated protein 1	3.78963637
4,10,17	AW545006	Psmb1	proteasome (prosome, macropain) subunit, beta type 1	4.27778141
4,10,8	AW549474		ESTs, Moderately similar to unknown [H.sapiens]	3.31482474
4,11,17	AW545119		ESTs	7.99450458
4,11,18	AW538456		ESTs	1.80382642
4,11,6	AW555755		ESTs	2.56214384
4,12,18	AW538474		ESTs, Highly similar to PUTATIVE SERINE/THREONINE-PROTEIN KIN/	2.24782634
4,12,7	AW553714	Tlk	Tousled-like kinase (Arabidopsis)	2.51067102
4,13,17	AW545033		ESTs, Moderately similar to KIAA0007 [H.sapiens]	5.42429029
4,15,9	AW546427		ESTs, Highly similar to RAS-LIKE PROTEIN TC21 [Homo sapiens]	2.78308135
4,16,25	W83959		ESTs	3.01450973
4,18,10	AU045568		ESTs, Weakly similar to IgG Fc binding protein [M.musculus]	3.36250158
4,18,18	AW539607		ESTs, Weakly similar to All-1 protein +GTE form [M.musculus]	3.09932421
4,2,26	AA545607	Mtf2	metal response element binding transcription factor 2	3.77711247
4,20,11	AU017822		ESTs, Weakly similar to NSP-like 1 [M.musculus]	3.22678447
4,21,14	AU021740		ESTs, Weakly similar to POSSIBLE GLOBAL TRANSCRIPTION ACTIVA	4.12897995
4,23,11	AU017911		ESTs, Weakly similar to implantation-associated protein [R.norvegicus]	1.97675348
4,3,5	AW557657	Idh1	isocitrate dehydrogenase 1 (NADP+), soluble	8.1065632
4,4,23	AA041834	Tk1	Thymidine kinase 1	8.48004271
4,4,6	AW554926		ESTs, Highly similar to PTB-ASSOCIATED SPLICING FACTOR [Homo s	4.1812777
4,6,17	AW544040		ESTs	5.62841401
4,6,21	AA208818	Fxr1h	fragile X mental retardation gene, autosomal homolog	2.57488284
40,12,18	AW538705			3.20268152
40,13,8	AW551167		ESTs	2.08503773
40,14,18	AW538766		ESTs, Weakly similar to HYPOTHETICAL UOG-1 PROTEIN [M.musculus	2.62514043
40,17,11	AU017992	Ktn1	kinectin 1	1.91062916
40,2,16	AW536696	Ndufv1	NADH dehydrogenase flavoprotein 1	3.16947838
40,22,12	AU014587		ESTs, Highly similar to POLYADENYLATE-BINDING PROTEIN [Xenopus	2.98336473
40,23,18	AW542401		ESTs	4.62270774
40,4,26	AA473234		ESTs	1.87955934
40,5,13	AU022276	Ask-pending	activator of S phase kinase	1.80182586
40,7,22	AA154888			2.04574146
41,10,13	AU023417	Xnp	X-linked nuclear protein	2.30515632
41,10,17	AW545835		Mus musculus Smt3A protein mRNA, complete cds	4.7826417
41,13,10	AU044944	Rab11a	RAB11a, member RAS oncogene family	3.25702722
41,14,10	AU044964			2.56107295
41,15,7	AW554377		ESTs	3.21044986
41,18,18	AW542924		ESTs, Highly similar to hSgt1p [H.sapiens]	1.66131839
41,19,8	AW552438		ESTs, Moderately similar to (defline not available 5714400) [M.musculus]	2.08490079
41,23,17	AW536843	Cct4	chaperonin subunit 4 (delta)	2.06085563
41,3,16	AW537566		ESTs, Highly similar to HYPOTHETICAL PROTEIN C22G7.01C IN CHR(	4.12527961
41,6,17	AW544660		ESTs	1.66698823
41,6,26	AA422973		ESTs, Moderately similar to AF161556_1 HSPC071 [H.sapiens]	2.65258149
41,7,26	AA465980		ESTs, Highly similar to HYPOTHETICAL 51.6 KD PROTEIN F59B2.5 IN	4.08396113
41,8,26	AA413694	Rab7	RAB7, member RAS oncogene family	2.9484156
41,9,11	AU017162	Rpl5	ribosomal protein L5	1.69424694
42,1,11	AU015293		ESTs	2.4905226
42,11,18	AW538500			2.19910947
42,11,9	AW546328			1.83845987

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42,14,7	AW553808		ESTs, Weakly similar to (defline not available 5579011) [M.musculus]	1.76652845
42,16,16	C76345			1.89458467
42,18,17	AW536342		ESTs, Weakly similar to RSP-1 PROTEIN [Mus musculus]	2.54286613
42,18,19	AA105717	Ddx20	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 20	1.90908814
42,19,17	AW536359		ESTs, Highly similar to UNR PROTEIN [Rattus norvegicus]	4.79845364
42,2,8	AW548051		ESTs	2.87413737
42,21,2	AI465270		ESTs	1.93143913
42,22,17	AW536450		ESTs	2.60324142
42,22,6	AW557553		ESTs	4.42376372
42,23,18	AW541003		ESTs	2.28301633
42,23,9	AW547945		ESTs, Weakly similar to ZIP-kinase [M.musculus]	3.23486994
42,5,11	AU015486	Cappa2	capping protein alpha 2	3.89440112
42,6,17	AW544098		ESTs	1.80028519
42,6,25	W67062		ESTs, Weakly similar to CST1_HUMAN CLEAVAGE STIMULATION FAC	3.27251103
42,6,26	AA467238		ESTs, Moderately similar to AF155107_1 NY-REN-37 antigen [H.sapiens]	2.02584311
43,14,24	AA024255	Slc22a5	solute carrier family 22 (organic cation transporter), member 5	1.88023183
43,15,19	AA396298		Mus musculus mRNA for RNase 4, complete cds	3.47095734
43,15,9	AW547111	Myhca	myosin heavy chain, cardiac muscle, adult	3.15565354
43,16,4	AI431019		ESTs	3.15836334
43,18,6	AW557123	Dok1	downstream of tyrosine kinase 1	1.90696059
43,19,14	C87993	Mtf1	metal response element binding transcription factor 1	1.99812319
43,20,14	C88019		EST	2.32051899
43,22,15	C85340		ESTs	2.94188799
43,22,17	AW536816		ESTs, Weakly similar to ZW10 interactor Zwint [H.sapiens]	3.21107378
43,23,18	AW543413		ESTs	2.8263413
43,23,8	AW552337		ESTs, Highly similar to RAS-RELATED PROTEIN RAB-6 [Homo sapiens	2.6412205
43,5,22	AA162800	Cul3	cullin 3	4.18974017
44,14,13	AU023746	Tacc3	transforming, acidic coiled-coil containing protein 3	4.17677389
44,2,16	AW536480		ESTs	2.67138219
44,22,17	AW536428		ESTs, Moderately similar to BLEOMYCIN HYDROLASE [Oryctolagus cur	2.17062519
44,6,16	AW537169		ESTs, Weakly similar to misato [D.melanogaster]	3.14060625
45,1,8	AW549019		ESTs	2.2203287
45,10,17	AW536183	Cct3	chaperonin subunit 3 (gamma)	2.05541031
45,13,11	AU017619	Ak3	adenylate kinase 3	3.18650819
45,18,17	AW536926		ESTs, Highly similar to KIAA0601 protein [H.sapiens]	2.28215731
45,4,10	AU043481		ESTs	3.30981186
45,4,11	AU016359		ESTs, Weakly similar to G PROTEIN PATHWAY SUPPRESSOR 1 [R.nor	1.9497425
45,7,14	C86941			15.3163935
45,7,6	AW556373		ESTs, Highly similar to HAM1 PROTEIN [Saccharomyces cerevisiae]	2.22896598
45,7,9	AW546162		ESTs, Weakly similar to CARG-BINDING FACTOR-A [M.musculus]	2.18948222
45,9,18	AW539377			2.06575072
45,9,9	AW546244		ESTs, Weakly similar to G protein-coupled receptor kinase 6, splice variar	1.67151599
46,10,5	AI573427	Catnb	Catenin beta	2.08164667
46,10,6	AW556036		ESTs, Weakly similar to Weak similarity in middle of protein to HIV-1 TAT	1.69352257
46,14,10	AU044566		ESTs, Highly similar to VACUOLAR ATP SYNTHASE SUBUNIT D [Bos t	2.89741757
46,16,11	AU018011		Mus musculus truncated SON protein (Son) mRNA, complete cds	2.7298613
46,16,18	AW538862		ESTs, Weakly similar to P9513.2 gene product [S.cerevisiae]	3.05492777
46,17,18	AW541468		ESTs, Highly similar to HYPOTHETICAL 64.5 KD PROTEIN ZK652.9 IN	2.98503799
46,2,12	AU018547		EST, Weakly similar to NaPi-2 beta [R.norvegicus]	2.58032425
46,2,16	AW536727		ESTs, Highly similar to HYPOTHETICAL 18.5 KD PROTEIN C12G12.05(	2.25494534
46,20,7	AW555047		Mus musculus major histocompatibility complex region NG27, NG28, RPS	3.29025801
46,22,3	AI447150		Mus musculus insulin-like growth factor I receptor mRNA, complete cds	1.80548672
46,22,9	AW548322	Pctk1	PCTAIRE-motif protein kinase 1	12.057525
47,1,13	AU022611			2.77641552
47,1,16	AW537042		ESTs	1.72983218
47,1,3	AI426662		EST	4.15642291
47,10,17	AW536175	Adh5	alcohol dehydrogenase 5	2.65013451
47,11,9	AW547270		ESTs, Weakly similar to Smarce1-related protein [M.musculus]	1.62495168
47,12,17	AW536197		Mus musculus Tera (Tera) mRNA, complete cds	8.19234776
47,12,6	AW556482		ESTs, Moderately similar to hypothetical protein [H.sapiens]	2.30339462
47,13,18	AW539474		ESTs	2.19134929
47,13,8	AW551820		ESTs, Highly similar to HYPOTHETICAL 37.2 KD PROTEIN C12C2.09C	2.73609738
47,14,14	C88094		ESTs, Weakly similar to teg292 protein [M.musculus]	14.3187898

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47,15,18	AW539529		ESTs	2.64445063
47,15,2	AI451613		ESTs, Highly similar to CYP4B1 [M.musculus]	2.31891323
47,15,8	AW551863			2.64717189
47,19,26	W59202	Stat3ip1-penc	signal transducer and activator of transcription 3 interacting protein 1	5.10228177
47,2,15	C78609		ESTs, Highly similar to EUKARYOTIC INITIATION FACTOR 4 GAMMA [(	2.62128716
47,22,18	AW543722		ESTs, Highly similar to ARGINYL-TRNA SYNTHETASE [Cricetulus longi(	7.6437739
47,3,10	AU043407		ESTs, Highly similar to elongation factor SIII p15 subunit [R.norvegicus]	3.0792624
47,3,9	AW545936	Cks1	cyclin-dependent kinase regulatory subunit 1	3.20253236
47,4,11	AU016321		ESTs	1.94331632
47,6,7	AW553551		ESTs, Highly similar to calcium-independent alpha-latrotoxin receptor hom	2.23517007
47,7,15	C79581	Msn	moesin	3.67038537
47,8,8	AW550493	Dbi	diazepam binding inhibitor	2.55549282
47,8,9	AW546174	Tgfb1i4	transforming growth factor beta 1 induced transcript 4	5.66898842
48,12,7	AW553985		ESTs	1.83971483
48,14,15	C80147	Hdgf	hepatoma-derived growth factor	2.57961845
48,15,7	AW554081	Adnp	activity-dependent neuroprotective protein	3.05598933
5,14,12	AU020992		ESTs	2.56816926
5,14,5	AI894273		ESTs, Moderately similar to HIGH MOBILITY GROUP-LIKE NUCLEAR P	13.4694908
5,15,14	C88181		ESTs, Moderately similar to CCR4-ASSOCIATED FACTOR 1 [M.musculu	2.04916356
5,15,18	AW539545		ESTs	1.80420641
5,16,24	AA030995	Ppib	peptidylprolyl isomerase B	5.33570443
5,17,12	AU015031		ESTs	1.8703351
5,17,18	AW543515		ESTs, Highly similar to TRNA-PROCESSING PROTEIN SEN3 [Saccharc	2.60061248
5,2,12	AU019262		ESTs, Weakly similar to DNAJ PROTEIN HOMOLOG MTJ1 [M.musculus]	4.08465973
5,22,18	AW543750		M.musculus mRNA for glutamyl-tRNA synthetase	3.03806317
5,3,16	AW537799		Mus musculus SIK similar protein mRNA, complete cds	2.63669536
5,4,12	AU019331		ESTs	2.09219857
5,6,24	AA016759	Mcmd6	mini chromosome maintenance deficient 6 (S. cerevisiae)	3.94222873
5,8,26	AA547555	Cks1	CDC28 protein kinase 1	2.84216385
6,1,18	AA475488		ESTs, Highly similar to KIAA1008 protein [H.sapiens]	1.90779251
6,10,11	AU016865	Zpk	zipper (leucine) protein kinase	1.87496068
6,11,6	AW556065			5.78033428
6,12,6	AW556081		ESTs	2.22898364
6,15,13	AU023995		Mus musculus chromosome segregation protein SmcB (SmcB) mRNA, cc	2.53048623
6,17,18	AW541455		ESTs, Weakly similar to anillin [D.melanogaster]	1.75224982
6,17,9	AW546860		ESTs	2.57607044
6,19,18	AW541501		ESTs, Highly similar to CLATHRIN HEAVY CHAIN [Rattus norvegicus]	2.11748542
6,19,8	AW552139	Adcy6	adenylate cyclase 6	3.73120192
6,22,10	AU041439	Gnai2	guanine nucleotide binding protein, alpha inhibiting 2	2.87168005
6,22,9	AW548297	Gtse1	G two S phase expressed protein 1	1.95946572
6,3,5	AW557901		ESTs, Weakly similar to C54G7.4 gene product [C.elegans]	2.52237792
6,5,8	AW549706	Nedd4	neural precursor cell expressed, developmentally down-regulated gene 4	2.32708497
6,6,7	AW553142			2.08668967
6,6,8	AW549721	Hspa9a	heat shock protein, 74 kDa, A	2.53548012
6,7,8	AW549786	Atp5b	ATP synthase, H+ transporting mitochondrial F1 complex, alpha subunit	3.88348655
6,8,8	AW549817	Blr1	Burkitt lymphoma receptor 1	1.90463473
6,9,10	AU044286		ESTs	2.42699522
7,1,11	AU016189		ESTs	2.01345543
7,1,6	AW555561	Mybl2	myeloblastosis oncogene-like 2	2.46749273
7,10,7	AW553629		ESTs, Moderately similar to LEYDIG CELL TUMOR 10 KD PROTEIN [Ra	1.78861896
7,12,7	AW554486	Unp	ubiquitous nuclear protein	1.96744634
7,16,8	AW551867	Csrp2	cysteine-rich protein 2	1.64296726
7,16,9	AW547491		ESTs, Highly similar to nuclear pore complex glycoprotein p62 [M.muscul	1.75162793
7,20,17	AW536943		ESTs	5.96558728
7,23,25	AA003258		ESTs	3.03415059
7,3,11	AU016261		ESTs	2.13057935
7,6,16	AW537692		ESTs, Highly similar to AUXIN-RESISTANCE PROTEIN AXR1 [Arabidop	4.82857308
7,6,26	AA437614		ESTs, Highly similar to S1-1 protein [R.norvegicus]	2.58076889
7,7,16	AW537731		ESTs	3.0261222
7,8,10	AU043672		ESTs, Highly similar to PUTATIVE ATP-DEPENDENT RNA HELICASE (	2.12334628
7,8,12	AU020664		Mus musculus dUB-type TGT mRNA for deubiquitinating enzyme, comple	3.72216489
7,8,22	AA168656	D5Ertd363e	DNA segment, Chr 5, ERATO Doi 363, expressed	3.19904375
7,9,10	AU045064		ESTs, Highly similar to SOH1 PROTEIN [Saccharomyces cerevisiae]	2.03529119

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8,1,20	AA241756	sid2057p	small acidic protein sid2057p	3.15579129
8,10,7	AW553223		ESTs	2.42843107
8,12,17	AW545455		ESTs	2.12149376
8,12,5	AI573460	Chd1	Chromodomain helicase DNA binding protein 1	2.5508808
8,14,8	AW551176			3.98411086
8,16,18	AW538820	Ak4	adenylate kinase 4	5.59041224
8,2,5	AW557865	Rad50	RAD50 homolog (S. cerevisiae)	2.71088834
8,21,11	AU018118	Nap1l1	nucleosome assembly protein 1-like 1	4.57766989
8,21,7	AW555020		ESTs, Highly similar to UBIQUINOL-CYTOCHROME C REDUCTASE CC	3.13400887
8,22,18	AW542335		ESTs, Highly similar to MICROSOMAL SIGNAL PEPTIDASE 21 KD SUB	2.43673469
8,23,3	AI452358		ESTs	2.78553944
8,5,26	AA474386		ESTs	3.47257915
8,6,17	AW544320		ESTs, Highly similar to G10 PROTEIN [Xenopus laevis]	3.66608286
8,6,6	AW555813		ESTs	2.35836881
8,8,24	AA014445	Fl10	FL10	3.94046683
8,9,6	AW555985	Rpa2	replication protein A2	2.49051478
9,1,15	C78280			2.91666907
9,1,5	AW558079		ESTs, Weakly similar to PPAR gamma coactivator [M.musculus]	2.59690006
9,11,16	C76867		ESTs, Moderately similar to TROPOMYOSIN ALPHA CHAIN, SKELETAL	2.862564
9,12,11	AU017259	eed	embryonic ectoderm development	3.34313099
9,13,11	AU017276	Ntan1	N-terminal Asn amidase	2.5715129
9,13,7	AW554273		ESTs, Weakly similar to VRK2 [H.sapiens]	1.64732082
9,14,23	AA086829	Mssk1	muscle-specific serine kinase 1	2.10008711
9,16,11	AU018261		ESTs	4.2328248
9,17,11	AU040108			2.16353765
9,17,8	AW551726	Wbp5	WW domain binding protein 5	2.49664457
9,2,6	AW555464		ESTs, Weakly similar to neuronal-specific septin 3 [M.musculus]	2.85764954
9,20,17	AW536798		ESTs	2.04520746
9,21,10	AU041740		M.musculus mRNA for fibromodulin	2.01868023
9,22,10	AU041756		ESTs	2.55472592
9,22,8	AW552312			1.97837746
9,3,9	AU042878	Psmc3ip	proteasome (prosome, macropain) 26S subunit, ATPase 3, interacting prc	2.06986302
9,4,16	AW537568		ESTs, Weakly similar to similar to yeast heat shock protein STI1 [C.elegar	2.21201049
9,5,25	W82194	LOC57423	hypothetical protein, clone:2-31	3.00433236
9,6,22	AA144221	Hic53	hydrogen peroxide inducible protein 53	1.61390639
9,7,17	AW544666		ESTs	1.57368062
24,13,17	AW545557			0.28978191
11,23,13	AU018762	gMCK2	Mus musculus casein kinase 2 beta subunit	0.21318857
37,21,16	C78503	Ask-pending	activator of S phase kinase	0.19321852
2,18,12	AU021170	Abca1	Macrophage specific gene	0.39018671
8,10,15	C79113		weakly simmilar to casein kinase 2 beta subunit	0.19558858
38,15,18	AW538851		ESTs	0.18013489
39,5,15	C79508		ESTs	0.28888507
37,7,13	AU023540			0.16773535
12,10,7	AW552972		ESTs, Highly similar to ATP-DEPENDENT PROTEASE LA 2 [Myxococcu	0.29737297
11,2,12	AU018863	Klf4	Kruppel-like factor 4 (gut)	0.40306527
24,17,15	C80212		ESTs	0.33812652
17,20,15	C85300	unp	Mus musculus ubiquitin-specific protease	0.32300436
43,13,2	AI451378		ESTs	0.45472196
31,7,13	AU023508		Mus musculus uroporphyrinogen III synthase gene, promoter,	0.16844858
24,22,13	AU018397	Nek7	Mus musculus NIMA (never in mitosis gene a)-related expressed kinase 7	0.35983929

Supplemental Table 2: Primers used in Quantitative RT- PCR (QRT-PCR).

Gene Name	Primer type	Primer sequence 5'-3'	Annealing Temperature (°C)	Product Size (bp)
Apoptosis Inhibitor 4	Forward	accttcaagaactggcccttt	60	117
	Reverse	aaaacactgggccaaatcag		
Breast Cancer Associated Protein 2	Forward	ttggacaacccccaattaaa	60	100
	Reverse	ctggagtgctttttgaaggc		
Defender Against Death 1	Forward	ttgctggatgcctatctcct	60	147
	Reverse	gcaaaccgctaagatgaagc		
Heat Shock Protein 60	Forward	acacaaatgaagaggctggg	60	106
	Reverse	actggattagcccctttgct		
Integrin Beta 1	Forward	cagtgaacagcaagggtgaa	60	115
	Reverse	taagaacaattccggcaacc		
Macrophage Migration Inhibitory Factor 1	Forward	ttcatcgtgaacaccaatgt	60	147
	Reverse	aaaagtcatgagctggtccg		
Ornithine Decarboxylase 1	Forward	catccaaaggcaaagttggt	60	104
	Reverse	agcctgctggttttcagtgt		
Beta-actin	Forward	gatctggcaccacaccttct	60	144
	Reverse	ggggtgttgaaggtctcaaa		
GAPDH	Forward	gaagggctcatgaccacagt	60	125
	Reverse	ggatgcagggatgatgttct		

Supplemental Table 3: Primers used in Quantitative Real Time PCR (QRT-PCR).

Primer name		Sequence 5'-3'	Product size (bp)	Annealing temperature (°C)
ZBP1	Forward	tcaagattgctccaccagaa	91	60
	Reverse	cttccctgagccttgaactg		
Arp2/3, p21	Forward	ttcaaggccaacgtcttctt	120	60
	Reverse	tctggagttgcacttttgga		
Actin gamma	Forward	actgggacgacatggagaag	114	60
	Reverse	tgttagctttggggttcagg		
LIMK 1	Forward	tcatcaagagcatggacagc	113	60
	Reverse	gaggtctcggtggatgatgt		
Actn3	Forward	gcaggagcagaacatcatca	112	60
	Reverse	catgctgtagaccgtgtgct		
CFL1	Forward	gtcaagatgctgccagacaa	102	60
	Reverse	ggcccagaaaatgaatacca		
TMOD	Forward	cgagggttaaaggggaaaag	102	60
	Reverse	gacaggcatcgttctcccta		
MNS1	Forward	ctgccgatctctcatcctct	100	60
	Reverse	gagcacaagccactctgaca		
Cap 1	Forward	gaaagccaccagtttcaacc	105	60
	Reverse	cttgagcactccaaccacct		
Rock 1	Forward	ttcaagccgactaacggtatg	114	60
	Reverse	gctcgaggaattctggaaga		
Arp2/3, p16	Forward	gctaggctcgctgaagaaga	117	60
	Reverse	tattcgtccacgtccacctt		
Beta-actin	Forward	gatctggcaccacaccttct	144	60
	Reverse	ggggtgttgaaggtctcaaa		
GAPDH	Forward	gaagggctcatgaccacagt	125	60
	Reverse	ggatgcagggatgatgttct		

Supplemental Table 4

Acc No	Gene	Description	N/F ratio
AW536875		ESTs, Highly similar to 60S RIBOSOMAL PROTEIN L15 [Rattus norvegicus]	28.07042798
C88094		ESTs, Weakly similar to teg292 protein [M.musculus]	14.31878982
AI894273		ESTs, Moderately similar to HIGH MOBILITY GROUP-LIKE NUCLEAR PROTEIN 2 [	13.46949084
AW555456		Mus musculus centrin (Cetn2) gene, complete cds	12.38855512
AW548322	Pctk1	PCTAIRE-motif protein kinase 1	12.057525
C86468	Kcnn4	potassium intermediate/small conductance calcium-activated channel, subfamily N, m	11.02530152
AU019118		ESTs, Moderately similar to unknown [H.sapiens]	9.327888895
AA041834	Tk1	Thymidine kinase 1	8.480042707
AW536197		Mus musculus Tera (Tera) mRNA, complete cds	8.192347763
AW557657	Idh1	isocitrate dehydrogenase 1 (NADP+), soluble	8.106563202
AW537075		ESTs, Weakly similar to SIG41 [M.musculus]	7.942965646
AA172774	D16Wsu83e	DNA segment, Chr 16, Wayne State University 83, expressed	7.71686883
AW543722		ESTs, Highly similar to ARGINYL-TRNA SYNTHETASE [Cricetulus longicaudatus]	7.643773902
AA209964	D11Moh34	DNA segment, Chr 11, KL Mohlke 34	7.590178566
AU041246		ESTs, Highly similar to 26S PROTEASE REGULATORY SUBUNIT 4 HOMOLOG [S	7.575991278
AW536755		ESTs, Highly similar to similar to nuclear domain 10 protein NDP52 [H.sapiens]	7.509323804
AU019152	Zfr	zinc finger RNA binding protein	7.187804716
AW554270	Hnrpu	heterogeneous nuclear ribonucleoprotein U	6.962446985
AU024490		ESTs, Highly similar to PROTEIN TRANSLATION FACTOR SUI1 HOMOLOG [Anopl	6.646581144
AU018130		ESTs, Weakly similar to cholesterol 25-hydroxylase [M.musculus]	6.335735765
AW539791		ESTs, Weakly similar to coded for by C. elegans cDNAs GenBank: [C.elegans]	6.21796016
AU017180		ESTs, Highly similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN K [	6.088798225
AI464376		M.musculus mRNA for ribosomal protein S5	6.087358987
AW544204	Cct8	chaperonin subunit 8 (theta)	6.014885062
AW546174	Tgfb1i4	transforming growth factor beta 1 induced transcript 4	5.668988417
AA068436		ESTs, Highly similar to unknown [R.norvegicus]	5.647684222
AW538820	Ak4	adenylate kinase 4	5.590412241
AW549255		ESTs, Weakly similar to unknown [R.norvegicus]	5.576813364
AU041887		ESTs, Highly similar to HYPOTHETICAL 30.3 KD PROTEIN IN APE1/LAP4-CWP1 II	5.573324729
AW547924	Rbbp7	retinoblastoma binding protein 7	5.560647246
AU018928		ESTs, Highly similar to TRAF4-associated factor 2 [H.sapiens]	5.510048965
W62229	Ube1c	ubiquitin-activating enzyme E1C	5.477163155
AW537279	Macs	myristoylated alanine rich protein kinase C substrate	5.47595949
C78877	Psmc5	protease (prosome, macropain) 26S subunit, ATPase 5	5.462141323
AW548086	Ptma	prothymosin alpha	5.460385354
AU023751		ESTs, Highly similar to HPBRII-7 protein [H.sapiens]	5.426224824
C78481	Eif3	eukaryotic translation initiation factor 3	5.424426041
AW545033		ESTs, Moderately similar to KIAA0007 [H.sapiens]	5.424290287
AU041313	Etl1	enhancer trap locus 1	5.38413569
AU015358	Ubl1a2-pendi	ubiquitin-like 1 (sentrin) activating enzyme subunit 2	5.365114455
AW543409	DXWsu72e	DNA segment, Chr X, Wayne State University 72, expressed	5.350172937
AA030995	Ppib	peptidylprolyl isomerase B	5.335704428
AW549121	Hmg14	high mobility group protein 14	5.305166988
AW553645	Slc12a2	solute carrier family 12, member 2	5.209225843
AW536460	Sfrs3	splicing factor, arginine/serine-rich 3 (SRp20)	5.140661094
W59202	Stat3ip1-penc	signal transducer and activator of transcription 3 interacting protein 1	5.10228177
AW542927	Bcap31	B-cell receptor-associated protein 31	5.066787673
AW536194		ESTs, Highly similar to CGI-35 protein [H.sapiens]	5.045862039
AW538480		ESTs, Moderately similar to serine proteinase inhibitor 6 [M.musculus]	4.92457718
AW539467	Eif3	eukaryotic translation initiation factor 3	4.892017699
AW544515	Arl6ip	ADP-ribosylation-like factor 6 interacting protein	4.837717593
AW537692		ESTs, Highly similar to AUXIN-RESISTANCE PROTEIN AXR1 [Arabidopsis thaliana	4.828573083
AW552431	Scp2	sterol carrier protein 2, liver	4.818202195
AW536911	Cd97	CD97 antigen	4.810474487
AW536359		ESTs, Highly similar to UNR PROTEIN [Rattus norvegicus]	4.798453644
AW544502	Atp1b1	ATPase, Na+/K+ transporting, beta 1 polypeptide	4.787962787
AW545835		Mus musculus Smt3A protein mRNA, complete cds	4.7826417
AW538992		Mus musculus mRNA for 26S proteasome non-ATPase subunit	4.76789816
AW545393		ESTs, Highly similar to TRANSLATION INITIATION FACTOR EIF-2B GAMMA SUBU	4.68467069
AW544140	D10Wsu52e	DNA segment, Chr 10, Wayne State University 52, expressed	4.683018189
AI327096		Mus musculus neuronal calcium sensor-1 (NCS-1) mRNA, complete cds	4.676318103

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AW541474	Ncl	nucleolin	4.657700504
AW537584	Krt2-8	keratin complex 2, basic, gene 8	4.6321245
AW557019		ESTs, Moderately similar to TRANSCRIPTION INITIATION FACTOR IIA SMALL CH/	4.63152
AW538715	Ass1	arginosuccinate synthetase 1	4.609205297
AW544376		ESTs, Weakly similar to predicted using Genefinder [C.elegans]	4.596454455
C76750	Hnrpa1	heterogeneous nuclear ribonucleoprotein A1	4.582363217
AU018118	Nap1l1	nucleosome assembly protein 1-like 1	4.577669891
AA166336		ESTs, Moderately similar to DRIM protein [H.sapiens]	4.515841853
C79184	Kpna2	karyopherin (importin) alpha 2	4.483193007
AW538863		Mus musculus mRNA for mitochondrial acyl-CoA thioesterase, clone 1	4.480301436
AW547148		ESTs, Highly similar to LL5 protein [R.norvegicus]	4.473954317
AW536137	Cct5	chaperonin subunit 5 (epsilon)	4.469320692
AU044379	Arl6ip	ADP-ribosylation-like factor 6 interacting protein	4.456690776
AA272363		ESTs, Highly similar to KINESIN-II 85 KD SUBUNIT [Strongylocentrotus purpuratus]	4.451371032
AW537358		ESTs, Weakly similar to cDNA EST yk338g10.5 comes from this gene [C.elegans]	4.424107656
AU040277	Rpms7	ribosomal protein, mitochondrial, S7	4.42173964
AU015699		ESTs, Highly similar to SPLICING FACTOR U2AF 35 KD SUBUNIT [Homo sapiens]	4.396787304
AU043252		Mus musculus succinyl-CoA synthetase (Sucla1) mRNA, complete cds	4.389745409
AU043400	Supt4h	suppressor of Ty 4 homolog (S. cerevisiae)	4.346211791
AA414612	Cappa1	capping protein alpha 1	4.335956318
AW558053	Ugt1a1	UDP-glucuronosyltransferase 1 family, member 1	4.324788648
AW539780	H3f3b	H3 histone, family 3B	4.312364694
AW545006	Psmb1	proteasome (prosome, macropain) subunit, beta type 1	4.277781412
AW555779	Mapk3	mitogen activated protein kinase 3	4.26598905
AW552398		ESTs, Moderately similar to TRANSCRIPTION INITIATION FACTOR TFIID 28 KD SU	4.263787523
AW537694		ESTs, Highly similar to HYPOTHETICAL 109.5 KD PROTEIN IN PPA1-DAP2 INTER	4.238918085
C80485	Zfr	zinc finger RNA binding protein	4.204981315
AW539102		ESTs, Weakly similar to EUKARYOTIC TRANSLATION INITIATION FACTOR 3 BET/	4.200882302
W75853		ESTs, Moderately similar to SIGNAL RECOGNITION PARTICLE 19 KD PROTEIN [H	4.198748472
AW542909	Hmg14	high mobility group protein 14	4.195667397
AA162800	Cul3	cullin 3	4.189740174
AW554926		ESTs, Highly similar to PTB-ASSOCIATED SPLICING FACTOR [Homo sapiens]	4.181277703
AW545839	Nap1l1	nucleosome assembly protein 1-like 1	4.179882367
AU023746	Tacc3	transforming, acidic coiled-coil containing protein 3	4.176773893
AA422809		ESTs, Highly similar to KIAA0368 [H.sapiens]	4.173186503
AW537017	Odc	ornithine decarboxylase, structural	4.144399442
AW553526	Npm1	nucleophosmin 1	4.140352223
AW538686	Ubce7	ubiquitin-conjugating enzyme 7	4.138451568
AU021740		ESTs, Weakly similar to POSSIBLE GLOBAL TRANSCRIPTION ACTIVATOR SNF2L	4.128979953
AW537566		ESTs, Highly similar to HYPOTHETICAL PROTEIN C22G7.01C IN CHROMOSOME	4.125279614
AW548258	P4ha1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha 1 pc	4.107549035
AU040830		ESTs, Weakly similar to 60S RIBOSOMAL PROTEIN L30A [Saccharomyces cerevisi	4.091843934
AA033344	Slc12a2	solute carrier family 12, member 2	4.088397442
AU019262		ESTs, Weakly similar to DNAJ PROTEIN HOMOLOG MTJ1 [M.musculus]	4.084659729
AA465980		ESTs, Highly similar to HYPOTHETICAL 51.6 KD PROTEIN F59B2.5 IN CHROMOS	4.083961131
AW549711		Mus musculus fallotein mRNA, complete cds	4.0677901
C80966	Timm8b	translocase of inner mitochondrial membrane 8 homolog b (yeast)	4.044729993
AW556206	Hsp84-1	heat shock protein, 84 kDa 1	4.022387626
AU043443		ESTs, Highly similar to TRAM PROTEIN [Canis familiaris]	4.011298228
AW545939	Rps12	ribosomal protein S12	4.009116425
AW548431		ESTs, Highly similar to CYTOCHROME C OXIDASE POLYPEPTIDE VIIB PRECURS	4.009096262
AI426498		Mus musculus radio-resistance/chemo-resistance/cell cycle checkpoint control protei	4.007328711
AI429136		ESTs, Highly similar to transforming acidic coiled-coil containing protein 3 [M.muscul	4.00493038
AU020233	Arf1	ADP-ribosylation factor 1	3.991526009
AU041628		ESTs, Weakly similar to ORF2 [M.musculus]	3.98385943
AU018486	Ssb	Sjogren syndrome antigen B	3.979536441
AW536140	Hsp86-1	heat shock protein, 86 kDa 1	3.972152303
AI323926	Fau	Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (fox d	3.970764464
C86592	Fn1	fibronectin 1	3.964340966
AW556230	Cdc42	cell division cycle 42 homolog (S. cerevisiae)	3.958094748
AI324227		Mus musculus 14-3-3 protein gamma mRNA, complete cds	3.946899417
AA016759	Mcmd6	mini chromosome maintenance deficient 6 (S. cerevisiae)	3.942228729
AA014445	Fl10	FL10	3.940466825

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C78998	Rpl27	ribosomal protein L27	3.935127734
AA008189		ESTs, Highly similar to KINESIN-II 85 KD SUBUNIT [Strongylocentrotus purpuratus]	3.921010056
AW554328		ESTs, Highly similar to RSP5 PROTEIN [Saccharomyces cerevisiae]	3.913617092
AU042788		ESTs, Moderately similar to phosphoenolpyruvate carboxykinase [M.musculus]	3.912511036
AW539228	Fasl	Fas antigen ligand	3.910933775
AW556588	Tpi	triosephosphate isomerase	3.903538184
AU045251	Ranbp1	RAN binding protein 1	3.903340068
AW539811	Cdc10	cell division cycle 10 homolog (S. cerevisiae)	3.902125311
AW555157		ESTs, Highly similar to C-1-TETRAHYDROFOLATE SYNTHASE, CYTOPLASMIC [H	3.896907728
AU015486	Cappa2	capping protein alpha 2	3.894401118
C87887	Etl1	enhancer trap locus 1	3.89073106
AW542408	Pea15	phosphoprotein enriched in astrocytes 15	3.887421434
AW549786	Atp5b	ATP synthase, H+ transporting mitochondrial F1 complex, alpha subunit	3.883486547
AW537480	Atp5a1	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit, isoform 1	3.879801077
AW555675		ESTs, Highly similar to ALCOHOL DEHYDROGENASE [Homo sapiens]	3.873714959
AA423312	Ga17-pending	dendritic cell protein GA17	3.848176993
AW544122	Nap1l1	nucleosome assembly protein 1-like 1	3.846161333
AW548354		Mus musculus elongation factor 1-beta homolog mRNA, complete cds	3.799007315
C79212		ESTs, Weakly similar to R32611_2 [H.sapiens]	3.7976083
AW558177		ESTs, Weakly similar to head-elevated expression in 0.9 kb [D.melanogaster]	3.796955936
AW556707		ESTs, Moderately similar to PTB-ASSOCIATED SPLICING FACTOR [Homo sapiens	3.794530279
AW557574	Lrpap1	low density lipoprotein receptor related protein, associated protein 1	3.789636371
AA545607	Mtf2	metal response element binding transcription factor 2	3.777112474
AW545354		Mus musculus mRNA for sid2057p, complete cds	3.771481148
AW553405	Ube1x	ubiquitin-activating enzyme E1, Chr X	3.743347278
AW543524	Ghrh	growth hormone releasing hormone	3.731298401
AU020664		Mus musculus dUB-type TGT mRNA for deubiquitinating enzyme, complete cds	3.722164894
C76678		Mus musculus mRNA for Sid6061p, complete cds	3.720028548
AW546455		ESTs, Moderately similar to nuclear factor of activated T-cells, cytoplasmic 3 [H.sapie	3.70859768
C87205		ESTs, Weakly similar to C44B9.1 [C.elegans]	3.701990317
AU021072		ESTs, Weakly similar to unknown [R.norvegicus]	3.691199965
AA073695	Mea1	male enhanced antigen 1	3.681248673
C87164	Ier3	immediate early response 3	3.675300717
AW547244	Rpl10a	ribosomal protein L10A	3.671527312
C79581	Msn	moesin	3.670385369
AW546184	Atp6d	ATPase, H+ transporting, lysosomal (vacuolar proton pump), 42 kDa	3.669772578
AW544320		ESTs, Highly similar to G10 PROTEIN [Xenopus laevis]	3.666082859
C88028		ESTs, Highly similar to small membrane protein 1 [H.sapiens]	3.66566524
AW553254	Zfp207	zinc finger protein 207	3.651732585
AW539757	Zfp36	zinc finger protein 36	3.649425165
AU020890		ESTs, Weakly similar to CARG-BINDING FACTOR-A [Mus musculus]	3.645112149
AW543415		Mus musculus secretory carrier membrane protein 4 mRNA, complete cds	3.643663528
C87445		ESTs, Highly similar to PROBABLE 3-OXOADIPATE COA-TRANSFERASE SUBUN	3.635344195
AW554947		ESTs, Highly similar to translation initiation factor IF2 [H.sapiens]	3.625644265
AW545835		Mus musculus Smt3A protein mRNA, complete cds	3.606723188
AW554157	Nsmaf	neutral sphingomyelinase (N-SMase) activation associated factor	3.602107632
C77976		ESTs, Weakly similar to retinoblastoma-associated protein HEC [H.sapiens]	3.599674605
AW543839		ESTs, Moderately similar to AKAP450 protein [H.sapiens]	3.596313894
AA015136	LOC56046	hypothetical protein	3.596271768
AI324640	Amd3	S-adenosylmethionine decarboxylase 3	3.595274519
AW541494	Surf4	surfeit gene 4	3.591874393
AI450158		SIGNAL RECOGNITION PARTICLE 54 KD PROTEIN	3.578261456
AW557661	Taldo1	transaldolase 1	3.573769539
AA537161		ESTs, Highly similar to A55058 retinoic acid-regulated protein pH 34 - mouse [M.mus	3.573741952
AU043213	Ewsh	Ewing sarcoma homolog	3.565251777
AU021819	Top1	topoisomerase (DNA) I	3.548400292
AW537207		ESTs, Highly similar to transcription factor NF-AT 45K chain [H.sapiens]	3.53722457
C86331	H3f3b	H3 histone, family 3B	3.533490685
AW552131		ESTs, Highly similar to HYPOTHETICAL 109.5 KD PROTEIN IN PPA1-DAP2 INTER	3.530658429
AU018409	ArhA	Rho family GTPase	3.530268774
AI323675	Pctk3	PCTAIRE-motif protein kinase 3	3.521685781
AW536904	Ppia	peptidylprolyl isomerase A	3.507621504
AI327246		ESTs, Weakly similar to titin [M.musculus]	3.507243434

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AW544281		Mus musculus ASC-1 mRNA, complete cds	3.50215121
AW551918	Ube2i	ubiquitin-conjugating enzyme E2I	3.500959948
W48168	Hprt	Hypoxanthine guanine phosphoribosyl transferase	3.495738168
AU016813		ESTs, Highly similar to ubiquitin specific protease [H.sapiens]	3.494717718
AA396298		Mus musculus mRNA for RNase 4, complete cds	3.470957341
AW539445	Homer2-pend	homer, neuronal immediate early gene, 2	3.468546701
AW536666	Hmg1	high mobility group protein 1	3.462175648
AW549114	Dncic2	dynein, cytoplasmic, intermediate chain 2	3.461903637
AW544801	Nap1l1	nucleosome assembly protein 1-like 1	3.457665096
AW543791	Tbrg1	transforming growth factor beta regulated gene 1	3.456539482
AW538438	Rpl27a	ribosomal protein L27a	3.451778704
AU016022	Anxa4	annexin A4	3.448280131
C79628	Psme1	protease (prosome, macropain) 28 subunit, alpha	3.442541693
AA066250		ESTs, Weakly similar to BC-2 protein [H.sapiens]	3.430116366
AW542410	Psmc5	protease (prosome, macropain) 26S subunit, ATPase 5	3.429494424
AU018029		ESTs, Highly similar to cbp146 [M.musculus]	3.428043044
C85115		ESTs, Highly similar to NADH-CYTOCHROME B5 REDUCTASE [Rattus norvegicus]	3.427306351
AW556395	Oaz1	ornithine decarboxylase antizyme	3.418302938
AW536137	Cct5	chaperonin subunit 5 (epsilon)	3.417978956
AA517043	Rnf4	ring finger protein 4	3.409788494
AW551969	Prtb	proline rich protein expressed in brain	3.399624829
AU016270		ESTs, Highly similar to CYCLIN-DEPENDENT KINASES REGULATORY SUBUNIT 2	3.395812648
AW549909	Surf4	surfeit gene 4	3.393471399
AU044024	Tjp2	tight junction protein 2	3.392383317
AW546168	Rps5	ribosomal protein S5	3.391993373
AW538671	Col5a3	procollagen, type V, alpha 3	3.383446584
AI894263	Tuba2	Tubulin alpha 2	3.37781933
AW543832		ESTs, Highly similar to eukaryotic translation initiation factor eIF3, p35 subunit [H.sap	3.374834929
AW536945		ESTs, Weakly similar to female sterile homeotic-related protein Frg-1 [M.musculus]	3.37311499
AW536361		ESTs, Highly similar to KIAA0697 protein [H.sapiens]	3.364917242
AU045568		ESTs, Weakly similar to IgG Fc binding protein [M.musculus]	3.362501582
AW537446	Tcea1	transcription elongation factor A (SII), 1	3.353756593
AI666653		Mus musculus ubiquitin conjugating enzyme UBC9 mRNA, complete cds	3.347460034
AU017259	eed	embryonic ectoderm development	3.343130988
AI324671	Rpl30	Ribosomal protein L30	3.343001828
W09723		ESTs, Moderately similar to HAT1_HUMAN HISTONE ACETYLTRANSFERASE TYP	3.342429405
AW545818		ESTs, Weakly similar to /prediction	3.339835947
AA276878	H2-T23	histocompatibility 2, T region locus 23	3.334974918
AU014886	Gnb2-rs1	guanine nucleotide binding protein, beta-2, related sequence 1	3.333692828
AW538432	Rhoip3-pendi	Rho interacting protein 3	3.330216015
AW537357	Sdcbp	syndecan binding protein	3.329064842
AW537048	Ets2	E26 avian leukemia oncogene 2, 3' domain	3.325078728
AW549474		ESTs, Moderately similar to unknown [H.sapiens]	3.314824736
AW536101		Mus musculus mRNA for phosphorylated adaptor for RNA export (PHAX gene)	3.313622909
AW557102		ESTs, Moderately similar to INSULIN-DEGRADING ENZYME [R.norvegicus]	3.304747476
AW549980		ESTs, Highly similar to UBIQUITIN-CONJUGATING ENZYME E2-17 KD [Drosophila	3.304680342
AI413942		ESTs, Highly similar to UBIQUITIN-CONJUGATING ENZYME E2-17 KD [Drosophila	3.295674825
AW555047		Mus musculus major histocompatibility complex region NG27, NG28, RPS28, NADH	3.290258007
AA265636		ESTs, Highly similar to CALDESMON, SMOOTH MUSCLE [Gallus gallus]	3.286488615
AW557310	Kap	kidney androgen regulated protein	3.275864713
W67062		ESTs, Weakly similar to CST1_HUMAN CLEAVAGE STIMULATION FACTOR, 50 KI	3.272511033
C80438	Gart	phosphoribosylglycinamide formyltransferase	3.269100882
AA260352		Mus musculus cerebellar postnatal development protein-1 (Cpd1) mRNA, partial cds	3.268033947
AW536682	Impnb	importin beta	3.263591322
AU044944	Rab11a	RAB11a, member RAS oncogene family	3.257027215
AW555762	Tkt	transketolase	3.255445846
AW536849	Ccnb1-rs1	cyclin B1, related sequence 1	3.255108538
AW543439	Fkbp4	FK506 binding protein 4 (59 kDa)	3.254740967
AU042923		ESTs, Highly similar to dJ483K16.1 [H.sapiens]	3.250491765
AU045845	Ywhaq	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, theta pol	3.249673818
AW544115		ESTs, Weakly similar to NSP-like 1 [M.musculus]	3.245183948
AW539262	Etl1	enhancer trap locus 1	3.240855617
AW545451		ESTs, Moderately similar to ribonuclease P protein subunit p14 [H.sapiens]	3.240611299

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AU015879		Mus musculus LIM-kinase1 (Limk1) gene, complete cds; Wbscr1 (Wbscr1) gene, alte	3.239108652
AA014196	Glud	Glutamate dehydrogenase	3.238249096
AU040801		ESTs, Highly similar to rer [M.musculus]	3.236111635
AW547945		ESTs, Weakly similar to ZIP-kinase [M.musculus]	3.234869937
AW539487	Pabpc1	poly A binding protein, cytoplasmic 1	3.2298131
AW548914		Mus musculus receptor activity modifying protein 2 mRNA, complete cds	3.229667371
AU017822		ESTs, Weakly similar to NSP-like 1 [M.musculus]	3.226784472
AU020667	Uchl3	ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	3.225200079
AW536140	Hsp86-1	heat shock protein, 86 kDa 1	3.220069536
AA289001		ESTs, Weakly similar to DDX8_HUMAN PROBABLE ATP-DEPENDENT RNA HELIC	3.213217918
AW537501		ESTs, Weakly similar to hypothetical 43.2 kDa protein [H.sapiens]	3.212946254
AW536816		ESTs, Weakly similar to ZW10 interactor Zwint [H.sapiens]	3.211073781
AW536688	Tra1	tumor rejection antigen gp96	3.207785549
AW545936	Cks1	cyclin-dependent kinase regulatory subunit 1	3.202532356
AA168656	D5Ertd363e	DNA segment, Chr 5, ERATO Doi 363, expressed	3.199043745
AW550880	Txn	thioredoxin	3.194798752
AW557260		ESTs, Highly similar to testicular antigen [M.musculus]	3.194109779
AU017619	Ak3	adenylate kinase 3	3.186508194
AU022272	Rnaseli	ribonuclease L (2', 5'-oligoisoadenylate synthetase-dependent) inhibitor	3.184559303
AW547818	Fmr1	fragile X mental retardation syndrome 1 homolog	3.184148074
AA013832	Clpx	caseinolytic protease X (E.coli)	3.183287717
C86748	Tgfb2	transforming growth factor, beta 2	3.181199624
AW546704		ESTs, Highly similar to 40S RIBOSOMAL PROTEIN S13 [Homo sapiens; Rattus nor	3.179558602
AI325159		M.musculus mRNA for gas5 growth arrest specific protein	3.171264611
AW536696	Ndufv1	NADH dehydrogenase flavoprotein 1	3.16947838
AW552833		Mus musculus LNR42 mRNA, complete cds	3.160749904
AA080156	Kap	kidney androgen regulated protein	3.158901378
AA241756	sid2057p	small acidic protein sid2057p	3.155791289
AW547111	Myhca	myosin heavy chain, cardiac muscle, adult	3.155653539
AW536212		ESTs, Weakly similar to moesin [R.norvegicus]	3.150862062
AI327319		ESTs, Highly similar to CYTOCHROME B5 [Rattus norvegicus]	3.150293218
AW550836	Etl1	enhancer trap locus 1	3.148741977
AW537169		ESTs, Weakly similar to misato [D.melanogaster]	3.140606246
AA000038	Usp23	ubiquitin specific protease 23	3.137407556
AW539360		ESTs, Weakly similar to matrin cyclophilin [R.norvegicus]	3.135475267
AW536967	Etl1	enhancer trap locus 1	3.135171966
AW555020		ESTs, Highly similar to UBIQUINOL-CYTOCHROME C REDUCTASE COMPLEX CC	3.13400887
AW553809	Rnaseli	ribonuclease L (2', 5'-oligoisoadenylate synthetase-dependent) inhibitor	3.127019793
AA154465		ESTs, Highly similar to similar to human DNA-binding protein 5. [H.sapiens]	3.125092795
AA285584		Mus musculus strain Swiss Webster/NIH actin-associated protein palladin mRNA, pai	3.124624175
AW546078	Krt2-1	keratin complex 2, basic, gene 1	3.124299027
AU040705	Erp	endoplasmic reticulum protein	3.123823806
AI426510		Mus musculus mkf-1 mRNA, complete cds	3.116870544
AW549685		M.musculus mRNA for Pr22 protein	3.1146672
AU042440		ESTs, Weakly similar to BRAIN SPECIFIC POLYPEPTIDE PEP-19 [Rattus norvegicu	3.114535048
AW544818	Rab18	RAB18, member RAS oncogene family	3.109347054
AA237184	Ddx5	D-E-A-D (aspartate-glutamate-alanine-aspartate) box polypeptide 5	3.108934627
W85513		ESTs, Highly similar to KIAA0925 protein [H.sapiens]	3.1043914
C87631	Zfp68	Zinc finger protein 68	3.103182346
AU042346		ESTs, Moderately similar to serine/threonine protein kinase [M.musculus]	3.102909947
C81324		ESTs, Highly similar to ISOCITRATE DEHYDROGENASE [Bos taurus]	3.102708564
AI413150		HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1	3.101332766
AW544358		ESTs, Highly similar to PROTEIN DISULFIDE ISOMERASE PRECURSOR [Medicag	3.100578685
AW539607		ESTs, Weakly similar to All-1 protein +GTE form [M.musculus]	3.099324211
AW546793	Actg	actin, gamma, cytoplasmic	3.094036051
C80862		ESTs, Moderately similar to (defline not available 5931553) [M.musculus]	3.090776963
AW536256	Silg81	silica-induced gene 81	3.089849843
AW539609	Jup	junction plakoglobin	3.08822389
W98547	Bad	Bcl-associated death promoter	3.088183956
AW541488	B2m	beta-2 microglobulin	3.069100689
AW545318	Pcna	proliferating cell nuclear antigen	3.067845966
AW536215	Stip1	stress-induced phosphoprotein 1	3.065752133
AU021314		Mus musculus KOI-4 gene, partial cds	3.064952305

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AA175386		Mus musculus mRNA for partial LaXp180 protein	3.063948171
AA068665		ESTs, Weakly similar to AF152841_1 polymyositis scleroderma overlap syndrome [M	3.05957507
AW554081	Adnp	activity-dependent neuroprotective protein	3.055989327
AW538862		ESTs, Weakly similar to P9513.2 gene product [S.cerevisiae]	3.054927766
AW554376	Dlgh1	discs, large homolog 1 (Drosophila)	3.049574352
AW538403		Mus musculus formin binding protein 11 (FBP11) mRNA, complete cds	3.04888214
AW541446	D6Wsu137e	DNA segment, Chr 6, Wayne State University 137, expressed	3.044611755
AW551959	Cul1	cullin 1	3.040828115
AW548092		Mus musculus 14-3-3 protein beta mRNA, complete cds	3.039487463
AW543750		M.musculus mRNA for glutamyl-tRNA synthetase	3.038063168
AW538568	Rpl44	ribosomal protein L44	3.033122817
AW548061		ESTs, Weakly similar to unknown [C.elegans]	3.032513144
AU016110		Mus musculus heat shock protein (HSPC030) mRNA, complete cds	3.031383324
C81083	Hnrnpc	heterogeneous nuclear ribonucleoprotein C2	3.030135958
AW554393		ESTs, Weakly similar to RNA binding motif protein 7 [H.sapiens]	3.025632148
W13785		ribosomal protein S27	3.025322982
AW542456	Lmnb1	lamin B1	3.021908529
AW537278	Fmo5	flavin containing monooxygenase 5	3.01565301
AI326367		Mus musculus TCR beta locus from bases 250554 to 501917 (section 2 of 3) of the c	3.010492026
AU044431		Mus musculus DEBT-91 mRNA, complete cds	3.009214891
W82194	LOC57423	hypothetical protein, clone:2-31	3.004332364
AW537132	Gdap2	ganglioside-induced differentiation-associated-protein 2	3.002468515
AI465251		ESTs, Moderately similar to CALPONIN, ACIDIC ISOFORM [Rattus norvegicus]	2.998508138
AU015421		ESTs, Highly similar to unknown [H.sapiens]	2.988275793
AW541468		ESTs, Highly similar to HYPOTHETICAL 64.5 KD PROTEIN ZK652.9 IN CHROMOS	2.985037992
AU014587		ESTs, Highly similar to POLYADENYLATE-BINDING PROTEIN [Xenopus laevis]	2.983364731
AW536274		Mus musculus mRNA for Sid6061p, complete cds	2.975961818
AW554565	Aop1	anti-oxidant protein 1	2.975547979
AU016907	Supl15h	suppressor of Lec15 homolog (C.griseus)	2.97343761
AW557067	Dad1	defender against cell death 1	2.971833739
AU023128		ESTs, Highly similar to CAMP-DEPENDENT PROTEIN KINASE TYPE I-ALPHA RE(	2.971627282
AA036347	Klf9	Kruppel-like factor 9	2.968829965
AW536151	Hsp60	heat shock protein, 60 kDa	2.955737367
AW536963		ESTs, Highly similar to PUTATIVE ADENOSINE KINASE [Saccharomyces cerevisia(	2.950322741
AA413694	Rab7	RAB7, member RAS oncogene family	2.948415605
AW554059		ESTs, Weakly similar to HYPOTHETICAL 15.9 KD PROTEIN IN GLNA-FDHE INTER	2.945086458
AW558048	Cd24a	CD24a antigen	2.943485748
AW538527		ESTs, Moderately similar to R31341_1 [H.sapiens]	2.940115188
AW545662		ESTs, Highly similar to 26S PROTEASE REGULATORY SUBUNIT 7 [Homo sapiens	2.93417407
AW555565	Zyx	zyxin	2.929015914
W29492	Asns	asparagine synthetase	2.926212129
AA416435		ESTs, Highly similar to KIAA0095 gene is related to S.cerevisiae NIC96 gene. [H.sap	2.91604107
AI323814		Mouse mRNA for ARF4, complete cds	2.915172345
AI427441		M.musculus mRNA for neuronal protein 15.6	2.914821665
AW538481		ESTs, Highly similar to TRANSLATIONAL INITIATION FACTOR 2 BETA SUBUNIT [	2.905782415
AW552361		ESTs, Weakly similar to Similarity to Yeast YIP1 protein [C.elegans]	2.905297661
AU046228		ESTs, Highly similar to translation initiation factor IF2 [H.sapiens]	2.904375747
AU044835	Ppp1cc	protein phosphatase 1, catalytic subunit, gamma isoform	2.901544309
AA404094	C11orf17	C11orf17	2.898634353
W85166	Tacc3	transforming, acidic coiled-coil containing protein 3	2.897486584
AU044566		ESTs, Highly similar to VACUOLAR ATP SYNTHASE SUBUNIT D [Bos taurus]	2.897417571
AU020132	Odc	ornithine decarboxylase, structural	2.890092488
AW550627		Mus musculus drebrin E2 mRNA, complete cds	2.888730948
AU015096		ESTs, Weakly similar to nucleolin [R.norvegicus]	2.883466921
W10023	Catnb	catenin beta	2.882930209
C80267	Hnrnpc	heterogeneous nuclear ribonucleoprotein C2	2.882107319
C85471	Pdcd8	programmed cell death 8 (apoptosis inducing factor)	2.881679732
AU024091	Sucla2	succinate-Coenzyme A ligase, ADP-forming, beta subunit	2.881062765
AA044475	Nfe2l2	Nuclear, factor, erythroid derived 2, like 2	2.876121329
AW538967		Mus musculus mRNA for mDj3, complete cds	2.874346371
AU041439	Gnai2	guanine nucleotide binding protein, alpha inhibiting 2	2.87168005
AW544616		ESTs, Weakly similar to ZW10 interactor Zwint [H.sapiens]	2.870858344
AI414590	Srpk2	Serine/arginine-rich protein specific kinase 2	2.864730663

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C76867		ESTs, Moderately similar to TROPOMYOSIN ALPHA CHAIN, SKELETAL AND CARI	2.862563996
AI325958		ESTs, Highly similar to REPLICATION PROTEIN A 14 KD SUBUNIT [Homo sapiens	2.862534762
AW555464		ESTs, Weakly similar to neuronal-specific septin 3 [M.musculus]	2.857649535
AW536856		Mouse testis abundant mRNA sequence	2.857368245
C78835	Actx	melanoma X-actin	2.85448914
AU021567	Hip2	huntingtin interacting protein 2	2.850054551
AW554115	Crcp	calcitonin gene-related peptide-receptor component protein	2.847909648
AW556509		ESTs, Highly similar to similar to human DNA-binding protein 5. [H.sapiens]	2.847314257
AW558020		ESTs, Highly similar to CELL GROWTH REGULATING NUCLEOLAR PROTEIN [M.n	2.843396393
AW548709		ESTs, Moderately similar to EUKARYOTIC INITIATION FACTOR 4A [Caenorhabditis	2.843274915
AA547555	Cks1	CDC28 protein kinase 1	2.842163855
AW556999		ESTs, Moderately similar to hypothetical protein [H.sapiens]	2.840617772
AW546373		ESTs, Highly similar to 54K arginine-rich nuclear protein [H.sapiens]	2.840574103
AW548748		ESTs, Weakly similar to proline-rich protein [M.musculus]	2.840416615
AW536817		ESTs, Highly similar to ALPHA ENOLASE [Mus musculus]	2.840261891
AW539487	Pabpc1	poly A binding protein, cytoplasmic 1	2.84011637
AW537045		Mus musculus mRNA for initiation factor 2-associated 67kDa protein, complete cds	2.83718519
AW544601		ESTs, Weakly similar to cDNA EST EMBL:T00542 comes from this gene [C.elegans]	2.83318307
C79176		ESTs, Weakly similar to TYROSINE-PROTEIN KINASE JAK3 [M.musculus]	2.826660135
AA185258		ESTs, Highly similar to IDN3 [H.sapiens]	2.824275465
AW543973		ESTs, Highly similar to thyroid hormone receptor-associated protein complex compon	2.82307595
AW555383		ESTs, Highly similar to NADH-UBIQUINONE OXIDOREDUCTASE B22 SUBUNIT [B	2.820575628
AW549145	Fkbp3	FK506-binding protein 3 (25kD)	2.812895276
AW545658	Catns	catenin src	2.812160453
AW556635		ESTs, Weakly similar to splicing factor SC35 [M.musculus]	2.808058439
AW546855		M.musculus (C57 Black/6X CBA) LAL mRNA for lysosomal acid lipase	2.802794138
AW553068		ESTs, Weakly similar to KIAA0344 [H.sapiens]	2.799512259
W97442	Map3k12	mitogen activated protein kinase kinase kinase 12	2.798312097
AW536734		ESTs, Highly similar to EUKARYOTIC INITIATION FACTOR 4B [Homo sapiens]	2.79472633
C81194	Hsp105	heat shock protein, 105 kDa	2.79345821
AA537566		Histocompatibility 2, class II antigen A alpha	2.792318423
AW557878		M.musculus GAS 6 mRNA associated with growth-arrest	2.791570157
AW548139		Mus musculus mRNA, complete cds, clone:2-31	2.79079344
AW555176	D15Wsu59e	DNA segment, Chr 15, Wayne State University 59, expressed	2.784158457
AW546427		ESTs, Highly similar to RAS-LIKE PROTEIN TC21 [Homo sapiens]	2.78308135
AW537671		ESTs, Highly similar to similar to human DNA-binding protein 5. [H.sapiens]	2.779263429
C77223	Rpo2-1	RNA polymerase II 1	2.776921055
AA000318		ESTs, Highly similar to REPLICATION PROTEIN A 14 KD SUBUNIT [Homo sapiens	2.773773419
AW543985		ESTs, Weakly similar to MYELOID DIFFERENTIATION PRIMARY RESPONSE PRO	2.77132421
AW552638		Mouse mRNA for dbpA murine homologue, complete cds	2.769626773
AU043911		ESTs, Weakly similar to UBIQUITIN-CONJUGATING ENZYME E2-17 KD 2 [M.musc	2.769540325
AW543811		ESTs, Weakly similar to HYPOTHETICAL 86.9 KD PROTEIN ZK945.3 IN CHROMOS	2.767962067
AW538407	Slc20a1	solute carrier family 20, member 1	2.767681717
AW551944		ESTs, Highly similar to Similar to D.melanogaster parallel sister chromatids protein [H	2.767267283
AW537083		ESTs, Highly similar to cellular apoptosis susceptibilty protein [H.sapiens]	2.766532496
AW544737	Atpl	ATPase-like vacuolar proton channel	2.763759005
AW556977	Zpk	zipper (leucine) protein kinase	2.763133879
AW555759	Phb	prohibitin	2.761699761
AW536246		ESTs, Highly similar to PUTATIVE METHIONINE AMINOPEPTIDASE 1 [H.sapiens]	2.760259754
AW551817	Madh4	MAD homolog 4 (Drosophila)	2.757229361
AA146020		Mus musculus chromosome X contigB; X-linked lymphocyte regulated 5 gene, Zinc fi	2.756223603
AW554240		ESTs, Highly similar to OLIGOSACCHARYL TRANSFERASE STT3 SUBUNIT HOM	2.752467221
AU043122	Cox5b	cytochrome c oxidase, subunit Vb	2.751396487
AA265396	Lag	leukemia-associated gene	2.750567219
AW550641	Frg1	FSHD region gene 1	2.747989143
C86480	Plp	proteolipid protein (myelin)	2.746027119
AA399854		ESTs, Highly similar to PUTATIVE ASPARAGINYL-TRNA SYNTHETASE DED81 [S.	2.743198399
C76349	Sclip	Scgn10 like-protein	2.742268969
AA509855		ESTs, Highly similar to TROPOMYOSIN 4, EMBRYONIC FIBROBLAST ISOFORM [I	2.740953545
AI528760		Mouse mRNA for dbpA murine homologue, complete cds	2.739257165
AW551820		ESTs, Highly similar to HYPOTHETICAL 37.2 KD PROTEIN C12C2.09C IN CHROM	2.736097382
AW553001	Islr	immunoglobulin superfamily containing leucine-rich repeat	2.735275152
AI324702		60S RIBOSOMAL PROTEIN L19	2.733803162

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AU018011		Mus musculus truncated SON protein (Son) mRNA, complete cds	2.729861304
C87907	Mor2	malate dehydrogenase, soluble	2.728657356
AW556389	Cappb1	capping protein beta 1	2.727836531
AI661905		ESTs, Highly similar to similar to nuclear domain 10 protein NDP52 [H.sapiens]	2.72394245
AW537825		ESTs, Moderately similar to unknown protein IT12 [H.sapiens]	2.723239257
AA122891	Gapd	Glyceraldehyde-3-phosphate dehydrogenase	2.72255977
AW550518		Mus musculus acidic ribosomal phosphoprotein P1 mRNA, complete cds	2.722524256
AW546168	Rps5	ribosomal protein S5	2.722225631
AW549855	Scp2	sterol carrier protein 2, liver	2.72161746
AW555634	Dld	dihydrolipoamide dehydrogenase	2.72129
AW537250		ESTs, Weakly similar to damage-specific DNA binding protein 1 [M.musculus]	2.720679787
AW553320		Mus musculus mRNA for ribosomal protein L35a	2.720548204
AA547684		ESTs, Highly similar to translation initiation factor IF2 [H.sapiens]	2.719806487
AW545347		ESTs, Highly similar to HYPOTHETICAL 47.4 KD PROTEIN IN PAS1-MST1 INTERC	2.719059223
AA276030	Atpl	ATPase-like vacuolar proton channel	2.715993411
AW555415	Gtf2i	general transcription factor II I	2.714548958
AU023806	Rock1	Rho-associated coiled-coil forming kinase 1	2.714535436
AW557865	Rad50	RAD50 homolog (S. cerevisiae)	2.71088834
C77773		ESTs, Weakly similar to (defline not available 5453421) [M.musculus]	2.706432587
AW557152		ESTs, Highly similar to spliceosomal protein SAP 155 [H.sapiens]	2.706136493
AW547604		ESTs, Weakly similar to ORF YOL071w [S.cerevisiae]	2.704938801
AW555995	Lrpap1	low density lipoprotein receptor related protein, associated protein 1	2.70479575
AW556062	Tex10	testis expressed gene 10	2.704249677
AW536817		ESTs, Highly similar to ALPHA ENOLASE [Mus musculus]	2.700717507
AA050086	Ube2i	ubiquitin-conjugating enzyme E2I	2.699647334
AI427886		ESTs, Highly similar to RAS-RELATED PROTEIN RAB-28 [R.norvegicus]	2.694100196
AA032437		ESTs, Moderately similar to DUAL SPECIFICITY PROTEIN PHOSPHATASE PAC-1	2.688124354
AW551468		ESTs, Weakly similar to sorting nexin 1 [M.musculus]	2.684742798
AI451433	Abc2	ATP-binding cassette 2	2.67945398
AW538472	Biklk	Bcl2-interacting killer-like	2.677929061
AW546384	Psma3	proteasome (prosome, macropain) subunit, alpha type 3	2.675903592
AW550900	Emd	emerin	2.674320907
AU019004	Cd63	Cd63 antigen	2.673939197
AI326913		ESTs, Highly similar to CYCLIN-DEPENDENT KINASES REGULATORY SUBUNIT	2.672753295
AW536576	Tex9	testis expressed gene 9	2.671550442
AA031120	Psma1	proteasome (prosome, macropain) subunit, alpha type 1	2.663765326
AW544996	M6pr	mannose-6-phosphate receptor, cation dependent	2.661867728
AI451372		ESTs, Weakly similar to similar to kinensin-like protein [C.elegans]	2.661294957
AU022547		ESTs, Highly similar to ACTIVATOR 1 38 KD SUBUNIT [Homo sapiens]	2.660297025
AU043450	Msh2	mutS homolog 2 (E. coli)	2.659901068
AW536154	Ctps	CTP synthase	2.659526849
C76763		ESTs, Moderately similar to GOLIATH PROTEIN [Drosophila melanogaster]	2.657128663
AW554567	Fkbp1a	FK506 binding protein 1a (12 kDa)	2.653957746
AU018277		ESTs, Highly similar to OLIGOSACCHARYL TRANSFERASE STT3 SUBUNIT HOM	2.653900272
AW537202	Dhfr	dihydrofolate reductase	2.653293004
AW552167	Il1rak	interleukin 1 receptor-associated kinase	2.652630575
AA422973		ESTs, Moderately similar to AF161556_1 HSPC071 [H.sapiens]	2.652581493
AW536175	Adh5	alcohol dehydrogenase 5	2.650134514
AW549687		Mus musculus ribosomal protein L23 (Rpl23) gene, complete cds	2.649942368
AW537221	Fgfrp	fibroblast growth factor regulated protein	2.648558726
AW537334		ESTs, Weakly similar to signal recognition particle 54K protein [M.musculus]	2.647412355
AW548330		ESTs, Moderately similar to NADH-UBIQUINONE OXIDOREDUCTASE CHAIN 2 [M	2.646892785
AU019197	Bet3-pending	Bet3 homolog (S. cerevisiae)	2.644793591
AW552337		ESTs, Highly similar to RAS-RELATED PROTEIN RAB-6 [Homo sapiens]	2.641220499
AW537799		Mus musculus SIK similar protein mRNA, complete cds	2.636695362
AW548397		ESTs, Weakly similar to cDNA EST EMBL:T01421 comes from this gene [C.elegans]	2.636437564
C85373		ESTs, Highly similar to ARGINYL-TRNA SYNTHETASE, MITOCHONDRIAL PRECU	2.635279092
W64196		ESTs, Weakly similar to HG17_MOUSE NONHISTONE CHROMOSOMAL PROTEIN	2.63462814
W12375	Hnrpa2b1	heterogeneous nuclear ribonucleoprotein A2/B1	2.633808409
AW539363	Nsbp1	nucleosome binding protein 1	2.630394701
AU020218	Zrf2	zuotin related factor 2	2.627413283
AW537655	Gapd	glyceraldehyde-3-phosphate dehydrogenase	2.625964554
AW552715		ESTs, Weakly similar to DnaJ-like protein [M.musculus]	2.625449507

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AW538766		ESTs, Weakly similar to HYPOTHETICAL UOG-1 PROTEIN [M.musculus]	2.625140435
AI326146		ESTs, Highly similar to HYPOTHETICAL 23.3 KD PROTEIN ZK688.3 IN CHROMOS	2.62464727
AU040819		ESTs, Highly similar to VESICULAR INTEGRAL-MEMBRANE PROTEIN VIP36 PRE	2.624615038
AW536519		ESTs, Weakly similar to lens epithelium-derived growth factor [H.sapiens]	2.623225239
C78609		ESTs, Highly similar to EUKARYOTIC INITIATION FACTOR 4 GAMMA [Oryctolagus	2.621287161
AI662104		Mus musculus CYP2C40 (Cyp2c40) mRNA, complete cds	2.619833394
AW537395	Ube3a	ubiquitin conjugating enzyme E3A	2.619748772
AW554398	Tcea1	transcription elongation factor A (SII), 1	2.619234745
W09453		proton pump polypeptide [R. rattus]	2.618453637
AW544762	Fbln1	fibulin 1	2.617861014
AI426727		ESTs, Weakly similar to 5'-AMP-ACTIVATED PROTEIN KINASE, GAMMA-1 SUBUN	2.617120238
AW537625		ESTs, Highly similar to TRNA-PROCESSING PROTEIN SEN3 [Saccharomyces cere	2.615208114
AW537195		M.musculus mRNA for e1 protein	2.610502282
AW537401	Pk3	pyruvate kinase 3	2.609416814
AW549044		Mus musculus SPARC-related protein (SRG) mRNA, complete cds	2.609089766
AA274739	Pnn	pinin	2.604930495
AW556049	Aco2	aconitase 2, mitochondrial	2.602835974
AA472933		ESTs, Highly similar to unknown [H.sapiens]	2.602536474
AW543515		ESTs, Highly similar to TRNA-PROCESSING PROTEIN SEN3 [Saccharomyces cere	2.600612477
AU020998	Plat	plasminogen activator, tissue	2.599921486
AW545301	Dnpep	aspartyl aminopeptidase	2.598735375
AI324089		EST, Highly similar to PHOSPHATIDYLINOSITOL-4-PHOSPHATE 5-KINASE TYPE I	2.598540553
AW558079		ESTs, Weakly similar to PPAR gamma coactivator [M.musculus]	2.596900062
AU021489	Omd	osteomodulin	2.593848954
AI327309		Mus musculus clone TA-9 ATP synthase b chain homolog mRNA, partial cds	2.591834166
AI427644	Egfr	Epidermal growth factor receptor	2.591598589
AW544372		ESTs, Highly similar to pEachy [R.norvegicus]	2.591522355
AW537730		ESTs, Highly similar to PRE-MRNA SPLICING FACTOR PRP9 [Saccharomyces cer	2.589914483
AA034561	Fen1	Flap structure specific endonuclease 1	2.587417174
W98303	Sema3a	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphor	2.586437483
AI528850	Fasn	Fatty acid synthase	2.585878999
AW548198	Gpx3	glutathione peroxidase 3	2.584222275
C86630		ESTs, Highly similar to similar to nuclear domain 10 protein NDP52 [H.sapiens]	2.582573765
C87669	Mod1	malic enzyme, supernatant	2.581027133
AA437614		ESTs, Highly similar to S1-1 protein [R.norvegicus]	2.580768885
AU018547		EST, Weakly similar to NaPi-2 beta [R.norvegicus]	2.580324249
C80147	Hdgf	hepatoma-derived growth factor	2.579618455
AI322431		ESTs, Highly similar to MICROSOMAL SIGNAL PEPTIDASE 18 KD SUBUNIT [Cani	2.579173299
AW548906		ESTs, Highly similar to PROBABLE 60S RIBOSOMAL PROTEIN L14EB [Saccharom	2.579131557
AW546306	Hmg2	high mobility group protein 2	2.57498711
AA208818	Fxr1h	fragile X mental retardation gene, autosomal homolog	2.574882839
AU017276	Ntan1	N-terminal Asn amidase	2.571512897
AW536609	Eif3	eukaryotic translation initiation factor 3	2.57065592
AW548091		ESTs, Moderately similar to LAR PROTEIN PRECURSOR [Homo sapiens]	2.570578867
AU023604		ESTs, Weakly similar to SEX-LETHAL PROTEIN, FEMALE-SPECIFIC [Drosophila m	2.569110342
C81388	Slc16a1	solute carrier family 16 (monocarboxylic acid transporters), member 1	2.568588458
AA060863		Mus musculus TSC22-related inducible leucine zipper 1b (Tilz1b) mRNA, complete cr	2.567506201
AW555706	Ppia	peptidylprolyl isomerase A	2.564464822
AW551564		Mus musculus mRNA for sid2057p, complete cds	2.559018224
AW548086	Ptma	prothymosin alpha	2.558161157
AW550493	Dbi	diazepam binding inhibitor	2.555492823
AW544081	Rbbp7	retinoblastoma binding protein 7	2.554967829
AA003408	3-Sep	septin 3	2.553331559
AW536320	Orc4	origin recognition complex, subunit 4	2.55331517
AI324242		ESTs, Highly similar to HOMEOBOX PROTEIN OTX1 [M.musculus]	2.552903418
AI573460	Chd1	Chromodomain helicase DNA binding protein 1	2.550880804
AA061763		ESTs, Highly similar to HYPOTHETICAL 70.2 KD PROTEIN IN GSH1-CHS6 INTER(	2.550225644
AW549809	Abcd4	ATP-binding cassette, sub-family D (ALD), member 4	2.548870042
AW538647	Rps11	ribosomal protein S11	2.545085369
AW539270		ESTs, Highly similar to TUBULIN GAMMA CHAIN [Homo sapiens]	2.543404596
AW536342		ESTs, Weakly similar to RSP-1 PROTEIN [Mus musculus]	2.542866132
AW536182	Sec61a	SEC61, alpha subunit (S. cerevisiae)	2.542719816
AW539649		ESTs, Highly similar to DEK PROTEIN [Homo sapiens]	2.542495091

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AA426845	Sox15	SRY-box containing gene 15	2.54230538
Al427918		ESTs, Moderately similar to dJ206D15.3 [H.sapiens]	2.541668093
AW547546	Pmp20-pendi	peroxisomal membrane protein 20	2.540500727
AA266975	Cdc42	Cell division cycle 42	2.539715246
AW557331		ESTs, Weakly similar to F15D4.3 [C.elegans]	2.53958994
AU042135		ESTs, Moderately similar to protocadherin-3 [R.norvegicus]	2.539044703
AW555666		ESTs, Highly similar to CAMP-DEPENDENT PROTEIN KINASE TYPE I-ALPHA RE(	2.538023165
AW549721	Hspa9a	heat shock protein, 74 kDa, A	2.535480124
AU023995		Mus musculus chromosome segregation protein SmcB (SmcB) mRNA, complete cds	2.530486227
AW541453	Capg	capping protein (actin filament), gelsolin-like	2.530408897
AA222216	Tubb4	tubulin, beta 4	2.528905535
AW536795	Clk	CDC-like kinase	2.522978124
AW557901		ESTs, Weakly similar to C54G7.4 gene product [C.elegans]	2.522377919
AW552709		Mus musculus brain protein 44-like protein (Brp44l) mRNA, complete cds	2.521723313
AW536179		ESTs, Weakly similar to CGI-59 protein [H.sapiens]	2.521255841
C86107	Actn3	actinin alpha 3	2.520902204
AU044498	Bcap37	B-cell receptor-associated protein 37	2.518818666
AW547403	Adcyap1r1	adenylate cyclase activating polypeptide 1 receptor 1	2.518240435
AW554737		ESTs, Weakly similar to KIAA0512 protein [H.sapiens]	2.514867936
AA445435		ESTs, Moderately similar to PTD017 [H.sapiens]	2.512197233
AU016461	Ssfa1	sperm specific antigen 1	2.512128647
AA080011	Ywhae	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activatioprotein, epsilon pc	2.511644859
AU022118	Pnn	pinin	2.511460674
AW539549		ESTs, Highly similar to KIAA0095 gene is related to S.cerevisiae NIC96 gene. [H.sap	2.510991932
AW553714	Tlk	Tousled-like kinase (Arabidopsis)	2.510671023
C86454		ESTs, Weakly similar to SOX13 [M.musculus]	2.510141101
AA474681		ESTs, Moderately similar to A53770 growth factor-responsive protein, vascular smool	2.509526639
AW552886	Vcp	valosin containing protein	2.50801841
AU021911		ESTs, Moderately similar to ERYTHROID KRUEPPEL-LIKE TRANSCRIPTION FAC	2.507198715
AW539120		ESTs, Weakly similar to BETA-MANNOSIDASE PRECURSOR [H.sapiens]	2.505882042
AU042815	LOC53325	putative transcription factor	2.505471313
AW544505	Soat1	sterol O-acyltransferase 1	2.498847559
AW546367		Mus musculus CRIPT protein mRNA, complete cds	2.497650335
AW551726	Wbp5	WW domain binding protein 5	2.496644567
W97837	D10Ertd322e	DNA segment, Chr 10, ERATO Doi 322, expressed	2.494826439
AU016534		ESTs, Weakly similar to PARATHYMOSIN [Rattus norvegicus]	2.493713568
AW546141	Macs	myristoylated alanine rich protein kinase C substrate	2.492012377
AW547469	Ywhae	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activatioprotein, epsilon pol	2.491814894
AW539320	Pl1	placental lactogen 1	2.490879313
AW555985	Rpa2	replication protein A2	2.490514775
AA050684	Silg81	silica-induced gene 81	2.490476063
AW544374	Fin14	fibroblast growth factor inducible 14	2.490464918
AA016827		ESTs, Weakly similar to RING CANAL PROTEIN [Drosophila melanogaster]	2.489325106
AU015783		ESTs, Highly similar to unknown [H.sapiens]	2.489003752
AW555631		ESTs, Highly similar to PUTATIVE RECEPTOR PROTEIN [Homo sapiens]	2.488892742
C80070		ESTs, Moderately similar to hypothetical protein [H.sapiens]	2.488351328
AA016810	D15Wsu77e	DNA segment, Chr 15, Wayne State University 77, expressed	2.487746386
AA000223		Mus musculus SPARC-related protein (SRG) mRNA, complete cds	2.484495842
AU045850		ESTs, Highly similar to PUTATIVE ATP-DEPENDENT RNA HELICASE T26G10.1 IN	2.480950679
Al326091		Mus musculus antioxidant enzyme AOE372 mRNA, complete cds	2.480362721
AA014915	Hsp74	Heat shock protein, 74 kDa	2.479501024
AW544689		ESTs, Weakly similar to KIAA0869 protein [H.sapiens]	2.478339667
AW542349		ESTs, Highly similar to SIGNAL RECOGNITION PARTICLE 72 KD PROTEIN [Canis	2.474356881
Al426202		ESTs, Highly similar to leucine-rich-domain inter-acting protein 1 [M.musculus]	2.472494776
AW543636	Anxa5	annexin A5	2.471442908
AW553103		ESTs, Weakly similar to es 64 [M.musculus]	2.470432192
Al448428		ESTs, Weakly similar to Rigui [M.musculus]	2.470113702
AW546519	Trt	translationally regulated transcript (21 kDa)	2.469720709
AW539820	Lv	delta-aminolevulinate dehydratase	2.468434243
AU046028		ESTs, Moderately similar to RNA polymerase II transcription factor SIII p18 subunit [R	2.467860062
AW555561	Mybl2	myeloblastosis oncogene-like 2	2.467492726
AW543683	Ncl	nucleolin	2.466832971
W13561	Jag2	jagged 2	2.465200657

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AU016137	Fth	ferritin heavy chain	2.464959455
AW536987	Snta1	syntrophin, acidic 1	2.464853599
AW536435		ESTs, Moderately similar to KIAA0755 protein [H.sapiens]	2.463881083
AI327112		Mus musculus NADP-dependent isocitrate dehydrogenase (Idh) mRNA, complete cds	2.463800442
AA268327		ESTs, Highly similar to FIBRILLIN 1 PRECURSOR [Homo sapiens]	2.462447346
AI528700	Rab1	RAB1, member RAS oncogene family	2.46222509
AA220617	Bak	Bc12 homologous antagonist/killer	2.461291028
AW542307	Gtpbp	GTP binding protein 1	2.460990263
AU022218	Ptp4a1	protein tyrosine phosphatase 4a1	2.459877353
W81857		ESTs, Highly similar to HYPOTHETICAL 39.7 KD PROTEIN C34E10.2 IN CHROMO	2.458320944
C78257		ESTs, Highly similar to (defline not available 6012071) [R.norvegicus]	2.45776456
AW539362		ESTs, Highly similar to KIAA0515 protein [H.sapiens]	2.455566909
AA274915	U2af1-rs1	U2 small nuclear ribonucleoprotein auxiliary factor (U2AF), 35 kDa, related sequence	2.454199936
AW536155	Ddx5	DEAD (aspartate-glutamate-alanine-aspartate) box polypeptide 5	2.450399008
AI451115	Tcof1	Treacher Collins Franceschetti syndrome 1, homolog	2.449114592
AI415181		ESTs, Highly similar to adaptor protein [H.sapiens]	2.447784219
C87823		ESTs, Weakly similar to cDNA EST EMBL:T01156 comes from this gene [C.elegans]	2.446705774
AU045477		M.musculus ASF mRNA	2.44424645
C87175		ESTs, Highly similar to TUBULIN BETA CHAIN [Lytechinus pictus]	2.444103591
AW555877	Gdi3	guanosine diphosphate (GDP) dissociation inhibitor 3	2.443313285
AU023429		ESTs, Moderately similar to heat shock factor binding protein 1 HSBP1 [H.sapiens]	2.443174621
AW551192	Psme1	protease (prosome, macropain) 28 subunit, alpha	2.442839637
AW545938	Sap18	Sin3-associated polypeptide 18	2.441113088
AU016501	Ltbp3	latent transforming growth factor beta binding protein 3	2.439347726
AW551042		Mus musculus X chromosome: L1cam locus	2.438710922
AW552195		ESTs, Highly similar to MITOCHONDRIAL IMPORT RECEPTOR SUBUNIT TOM20 H	2.4386961
AW542335		ESTs, Highly similar to MICROSOMAL SIGNAL PEPTIDASE 21 KD SUBUNIT [Cani	2.436734688
AW547166		ESTs, Highly similar to UBIQUINOL-CYTOCHROME C REDUCTASE COMPLEX 14	2.436219154
AA068842	Ubc2e	ubiquitin conjugating enzyme 2e	2.435798543
AU016480		ESTs, Highly similar to 40S RIBOSOMAL PROTEIN S25 [Homo sapiens; Rattus nor	2.434092714
AU023232	Pigf	phosphatidylinositol glycan, class F	2.433935408
AA266531	AA930106	EST AA930106	2.43269159
AW548819		ESTs, Moderately similar to acidic 82 kDa protein [H.sapiens]	2.432596162
AA517431		ESTs, Moderately similar to GLYCOPROTEIN 25L PRECURSOR [Canis familiaris]	2.431952116
AA000842		ESTs, Highly similar to KINESIN-II 85 KD SUBUNIT [Strongylocentrotus purpuratus]	2.4312569
AU020424	Slc12a2	solute carrier family 12, member 2	2.42972381
W08137		ESTs, Weakly similar to HYPOTHETICAL 86.9 KD PROTEIN ZK945.3 IN CHROMOS	2.429186971
AW536067	Aop2	anti-oxidant protein 2	2.425678079
AW555001		Mus musculus RW1 protein mRNA, complete cds	2.422600237
AA274946	Eif1a	eukaryotic translation initiation factor 1A	2.420039228
AW557915	Ezh1	enhancer of zeste homolog 1 (Drosophila)	2.416855801
AA168536	Orc4	origin recognition complex, subunit 4	2.413722611
AW537427	Tstap91a	tissue specific transplantation antigen P91A	2.413410871
AI429159		ESTs, Weakly similar to ultra-high-sulfur keratin 1 [M.musculus]	2.413170232
AW536433	Hsp70-4	heat shock protein, 70 kDa 4	2.413114212
AW541013		ESTs, Moderately similar to HYPOTHETICAL PROTEIN HI0376 [Haemophilus influe	2.412854555
AA272821		ESTs, Highly similar to PUTATIVE ADENOSINE KINASE [Saccharomyces cerevisiae	2.412651495
AW552159	Atp2a2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	2.409551934
AW555351		Mus musculus domesticus mitochondrial carrier homolog 1 isoform a mRNA, complet	2.408853343
AI323543		Mus musculus (clone: pMAT1) mRNA, complete cds	2.40628791
AW536140	Hsp86-1	heat shock protein, 86 kDa 1	2.405500262
C76941	Tif1b	transcriptional intermediary factor 1, beta	2.40299958
AA414211		ESTs, Highly similar to RSP5 PROTEIN [Saccharomyces cerevisiae]	2.401776272
W08937		FAN protein	2.401104291
AW549671		ESTs, Weakly similar to SOX13 [M.musculus]	2.398051225
AA416246	Pmp22	Peripheral myelin protein, 22 kDa	2.394587625
AI427491		ESTs, Highly similar to PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDROLAS	2.394177647
AU015183	Ptprc	protein tyrosine phosphatase, receptor type, C	2.393529137
AA031056	Mcmd5	mini chromosome maintenance deficient 5 (S. cerevisiae)	2.391689429
C87726		Mus musculus mitotic checkpoint component Mad2 mRNA, complete cds	2.391344308
AW552558	Eif2s3x	eukaryotic translation initiation factor 2, subunit 3, structural gene X-linked	2.390411491
AW547239		ESTs, Highly similar to TRANSLOCON-ASSOCIATED PROTEIN, ALPHA SUBUNIT	2.388404892
AW552412		ESTs, Highly similar to TRANSLOCON-ASSOCIATED PROTEIN, BETA SUBUNIT F	2.385307516

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AU018839	Hmg14	high mobility group protein 14	2.384908256
AA403949	Capn12	calpain 12	2.38344367
C86052	Cnn1	calponin 1	2.380586251
AW549140		ESTs, Weakly similar to Peter Pan [D.melanogaster]	2.379705926
AA245492		ESTs, Moderately similar to AF151064_1 HSPC230 [H.sapiens]	2.379149074
AA466838		ESTs, Highly similar to Cdc5-like protein [R.norvegicus]	2.377796701
AW552727	Fasn	fatty acid synthase	2.377306081
AA020034		ESTs, Weakly similar to cleft lip and palate transmembrane protein 1 [H.sapiens]	2.376903716
AA023641	Madh3	MAD homolog 3 (Drosophila)	2.376148136
C86367		ESTs, Weakly similar to BAT2 [M.musculus]	2.375988234
AA388122	Mem3	Maternal embryonic message 3	2.374556107
AA004149		ESTs, Weakly similar to PROBABLE PEPTIDYL-TRNA HYDROLASE [Bacillus subtili	2.373057115
AW553203		Mus musculus mRNA, complete cds, clone:2-24	2.371518772
AW536206	Hsp86-1	heat shock protein, 86 kDa 1	2.370643703
W91463	Ddef1	development and differentiation enhancing	2.369512617
AW548540		Mus musculus SIK similar protein mRNA, complete cds	2.368814949
AA288977		ESTs, Moderately similar to GOLIATH PROTEIN [Drosophila melanogaster]	2.368498766
AA033138	Ant2	Adenine nucleotide translocator 2, fibroblast	2.36746577
AW536910		ESTs, Moderately similar to chromosome-associated protein-E [H.sapiens]	2.365185976
AW556217	Ash2l	ash2 (absent, small, or homeotic)-like (Drosophila)	2.364972967
AA266868		ESTs, Highly similar to RIBOSOMAL PROTEIN S6 KINASE [Homo sapiens]	2.364627315
C81301	Rbpsuh	recombining binding protein suppressor of hairless (Drosophila)	2.364326297
AA274539		Mus musculus mRNA for 26S proteasome non-ATPase subunit	2.362706461
AI325930		ESTs, Highly similar to CELL DIVISION CONTROL PROTEIN 23 [Saccharomyces ce	2.361095885
AW555373		Mus musculus short coiled coil protein SCOCO (Scoc) mRNA, complete cds	2.36056201
AW554706		ESTs, Highly similar to hypothetical protein [H.sapiens]	2.357478513
AW551989	Eef2	eukaryotic translation elongation factor 2	2.357184652
AA203922	Tmod3	tropomodulin 3	2.355290717
AU041196		ESTs, Highly similar to 60S RIBOSOMAL PROTEIN L22 [Tripneustes gratilla]	2.355169604
AA290484		ESTs, Weakly similar to SPORULATION-SPECIFIC PROTEIN 1 [Saccharomyces cer	2.354693252
AU046294	Magoh	mago-nashi homolog, proliferation-associated (Drosophila)	2.353138844
AA050900	Egr1	Early growth response 1	2.352134769
AW548009		ESTs, Highly similar to PTD014 [H.sapiens]	2.346432008
AU023893		ESTs, Highly similar to choline/ethanolaminephosphotransferase [H.sapiens]	2.343732092
AW537685		ESTs, Highly similar to HYPOTHETICAL 83.2 KD PROTEIN IN CHA1-APA1/DTP IN	2.342999287
AW540984	Api4	apoptosis inhibitor 4	2.342898046
C77892	Hba-a1	hemoglobin alpha, adult chain 1	2.342638604
AU019031	Hist4	histone 4 protein	2.341178338
AI414575		ESTs, Moderately similar to HISTONE ACETYLTRANSFERASE TYPE B CATALYTI	2.340858323
AU043242		ESTs, Weakly similar to ORF YKR081c [S.cerevisiae]	2.340501043
AW553194		Mus musculus Cope1 mRNA for nonclathrin coat protein epsilon-COP, complete cds	2.339239681
AW556204		ESTs, Weakly similar to ORF YGR200c [S.cerevisiae]	2.339173959
AU043007		M.musculus mRNA for neuronal protein 15.6	2.339134449
AW536641		ESTs, Highly similar to CLATHRIN HEAVY CHAIN [Rattus norvegicus]	2.338980841
AU040648		ESTs, Weakly similar to ORF YNL061w [S.cerevisiae]	2.337816604
AW558198	Emap2	endothelial monocyte activating polypeptide 2	2.335465842
AU043578	Tacc3	transforming, acidic coiled-coil containing protein 3	2.332924372
AW547363	Fmo5	flavin containing monooxygenase 5	2.330683655
W44162		ESTs, Moderately similar to N153_RAT NUCLEAR PORE COMPLEX PROTEIN NUP	2.330309625
AU015616		ESTs, Weakly similar to cDNA EST yk338f6.5 comes from this gene [C.elegans]	2.330288731
AI322439		ESTs, Moderately similar to SIGNAL RECOGNITION PARTICLE 19 KD PROTEIN [H	2.329157971
AW544876		ESTs, Highly similar to TRANSCRIPTION FACTOR BTF3 [Homo sapiens]	2.327613924
AW536151	Hsp60	heat shock protein, 60 kDa	2.327256569
AW549706	Nedd4	neural precursor cell expressed, developmentally down-regulated gene 4	2.327084972
AW555062		ESTs, Weakly similar to snRNP protein B [D.melanogaster]	2.322730091
AW556238		ESTs, Moderately similar to striatin [M.musculus]	2.321466801
AA444533		ESTs, Highly similar to G10 PROTEIN [Xenopus laevis]	2.319746228
AI451613		ESTs, Highly similar to CYP4B1 [M.musculus]	2.318913225
AU023815		ESTs, Weakly similar to (defline not available 5901816) [D.melanogaster]	2.318446678
AA052404	CRIPT	CRIPT protein	2.318310231
AW547917		ESTs, Highly similar to SINGLE-STRANDED DNA-BINDING PROTEIN, MITOCHON	2.317172841
AW536738	Klf9	Kruppel-like factor 9	2.316449053
AW537096		ESTs, Highly similar to GLUTAMINYL-TRNA SYNTHETASE [Homo sapiens]	2.316069284

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AW552222	H19	H19 fetal liver mRNA	2.315271509
AW552411	Ech1	enoyl coenzyme A hydratase 1, peroxisomal	2.315044879
AW556441		ESTs, Moderately similar to NY-REN-45 antigen [H.sapiens]	2.314566763
AW537615	Orc1	origin recognition complex, subunit 1 homolog (S. cerevisiae)	2.313001263
AW554187	G2an	alpha glucosidase 2, alpha neutral subunit	2.312088278
AW556339		ESTs, Highly similar to RN protein [R.norvegicus]	2.311016095
AW536573		ESTs, Weakly similar to similar to leucyl-tRNA synthetase [C.elegans]	2.311009258
AU044452	Nit1	nitrilase 1	2.31027286
AU040813		ESTs, Weakly similar to T23G11.9 [C.elegans]	2.309549316
AU021615		ESTs, Highly similar to SET PROTEIN [Homo sapiens]	2.30703954
AA444224		ESTs, Highly similar to UBP7_HUMAN UBIQUITIN CARBOXYL-TERMINAL HYDROL	2.305871297
AU023417	Xnp	X-linked nuclear protein	2.30515632
AW556482		ESTs, Moderately similar to hypothetical protein [H.sapiens]	2.303394618
AW546518	Erh	enhancer of rudimentary homolog (Drosophila)	2.303065378
AA268423	Rdh5	retinol dehydrogenase type 5	2.301249007
AA014771	Pkcz	protein kinase C, zeta	2.298782934
AW545976	Cops7a	COP9 (constitutive photomorphogenic), subunit 7a (Arabidopsis)	2.297823068
AU015592	Ybx1	Y box protein 1	2.296828893
AW552368		ESTs, Weakly similar to F42A6.6 [C.elegans]	2.296724442
AU016947	Rbbp6	retinoblastoma binding protein 6	2.293981468
AW539367		Mus musculus ribosomal protein L23 (Rpl23) gene, complete cds	2.293923928
AW549937	Hdac2	histone deacetylase 2	2.292864895
AW553303		ESTs, Highly similar to NADH-UBIQUINONE OXIDOREDUCTASE 19 KD SUBUNIT	2.292305877
AW557882	Anxa7	annexin A7	2.291896987
W34474		ESTs, Highly similar to HAM1 PROTEIN [Saccharomyces cerevisiae]	2.290024001
AW544089		ESTs, Highly similar to unknown [H.sapiens]	2.289029466
AW553526	Npm1	nucleophosmin 1	2.288099461
AA444943		ESTs, Highly similar to GLYCOPROTEIN 25L PRECURSOR [Canis familiaris]	2.28632601
AW553602		ESTs, Weakly similar to (defline not available 6016842) [M.musculus]	2.285573594
AW554909	Rpl8	ribosomal protein L8	2.285360197
AU020790		Mus musculus BAF53a (Baf53a) mRNA, complete cds	2.284270468
AU024674		ESTs, Highly similar to CITRATE SYNTHASE, MITOCHONDRIAL PRECURSOR [St	2.28323685
C88330		ESTs, Weakly similar to weak similarity to the yeast SSM4 protein [C.elegans]	2.282437195
AW536926		ESTs, Highly similar to KIAA0601 protein [H.sapiens]	2.282157312
W48017		ESTs, Highly similar to AF151859_1 CGI-101 protein [H.sapiens]	2.28097946
W13152		ESTs, Highly similar to CYCLIN-DEPENDENT KINASES REGULATORY SUBUNIT 2	2.280916964
AA388377	D5Ertd363e	DNA segment, Chr 5, ERATO Doi 363, expressed	2.280662428
AW536490	Usp5	ubiquitin specific protease 5 (isopeptidase T)	2.27846001
AW546788	Tgfbi	transforming growth factor, beta induced, 68 kDa	2.275899113
C80729	Catna1	catenin alpha 1	2.275074652
AI426199		ESTs, Weakly similar to stromal cell-derived factor 2 [M.musculus]	2.273575265
AW554921		ESTs, Weakly similar to KIAA0690 protein [H.sapiens]	2.270891671
AA541870		ESTs, Highly similar to arsenate resistance protein ARS2 [H.sapiens]	2.264516126
AW548210		ESTs, Highly similar to 40S RIBOSOMAL PROTEIN S25 [Homo sapiens; Rattus nor	2.262604986
AI427473		ESTs, Moderately similar to COP9 PROTEIN [Arabidopsis thaliana]	2.262114744
AW538852	Hmg14	high mobility group protein 14	2.259961047
AA030447	Prph1	Peripherin	2.25921575
AW536727		ESTs, Highly similar to HYPOTHETICAL 18.5 KD PROTEIN C12G12.05C IN CHROI	2.254945336
AW552406		Mus musculus ATP synthase gamma-subunit gene, nuclear gene encoding a mitoch	2.25252829
C78511	Biklk	Bcl2-interacting killer-like	2.2503145
AI451984	Prim1	DNA primase, p49 subunit	2.250302092
AW544726	Ywhaz	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta poly	2.248914858
AW538474		ESTs, Highly similar to PUTATIVE SERINE/THREONINE-PROTEIN KINASE A [Tryp	2.247826338
AW551451	Spnb2	beta-spectrin 2, non-erythrocytic	2.245979336
AW556933		ESTs, Weakly similar to PUTATIVE PRE-MRNA SPLICING FACTOR RNA HELICAS	2.245882244
AA049766		ESTs, Highly similar to KIAA0560 protein [H.sapiens]	2.244003084
AW552799		ESTs, Weakly similar to predicted using Genefinder [C.elegans]	2.243647865
AW536273	Mcmd5	mini chromosome maintenance deficient 5 (S. cerevisiae)	2.243088262
AA003951	Alas2	Aminolevulinic acid synthase 2, erythroid	2.241855839
AW544857		ESTs, Highly similar to ISOCITRATE DEHYDROGENASE [Bos taurus]	2.241748363
AA014456	Atp6k	ATPase, H+ transporting lysosomal (vacuolar proton pump), 9.2 kDa	2.23872792
AA254528	Magoh	mago-nashi homolog, proliferation-associated (Drosophila)	2.236163487
AU015485		ESTs, Weakly similar to PROBABLE PEROXISOMAL ENOYL-COA HYDRATASE [M	2.235591843

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AW553551		ESTs, Highly similar to calcium-independent alpha-latrotoxin receptor homolog 2 [R.n	2.235170069
AU024141		ESTs, Highly similar to UBIQUITIN [Homo sapiens; Bos taurus; Sus scrofa; Cavia po	2.232630685
C81381		ESTs, Weakly similar to BcDNA.GH03108 [D.melanogaster]	2.2321414
AW554765		ESTs, Moderately similar to tpr protein [H.sapiens]	2.231202975
AI323810		Mouse nucleolar protein N038 mRNA, complete cds	2.23056495
AW537485	Pla2g6	85 kDa calcium-independent phospholipase A2	2.230310343
AW556373		ESTs, Highly similar to HAM1 PROTEIN [Saccharomyces cerevisiae]	2.228965982
AU024437		ESTs, Weakly similar to rit [M.musculus]	2.228758058
AU023680		ESTs, Highly similar to SET PROTEIN [Homo sapiens]	2.228390926
W53962	Tgfb2	Transforming growth factor, beta 2	2.228071514
AW544412		ESTs, Highly similar to TUBULIN BETA CHAIN [Lytechinus pictus]	2.226024845
AA423209	Psme3	Proteaseome (prosome, macropain) 28 subunit, 3	2.222939666
AU042116		ESTs, Highly similar to 40S RIBOSOMAL PROTEIN S10 [Homo sapiens]	2.222175184
AU041939		Mus musculus TBX1 protein mRNA, complete cds	2.221932511
W83038	Csnk	casein kappa	2.220674318
AU016810		EST, Weakly similar to coxsackie and adenovirus receptor homologue [M.musculus]	2.220628518
AA272067	Fth	ferritin heavy chain	2.21966855
AW550222	Mc2r	melanocortin 2 receptor	2.219421336
AW546733		Mus musculus mRNA for Arp2/3 complex subunit p21-Arc, complete cds	2.219371653
AW549040	Rbmxrt	RNA binding motif protein, X chromosome retrogene	2.218222838
AW541478		ESTs, Highly similar to signal peptidase:SUBUNIT	2.217423992
AI447392	Dgcr6	DiGeorge syndrome chromosome region 6	2.216472345
AW549381	Rgds	ral guanine nucleotide dissociation stimulator	2.21318416
AU016133		ESTs, Weakly similar to MSSP [M.musculus]	2.213009807
AW537792	Grp78	glucose regulated protein, 78 kDa	2.212760746
AW551233	Ptp4a2	protein tyrosine phosphatase 4a2	2.212302179
AW537568		ESTs, Weakly similar to similar to yeast heat shock protein STI1 [C.elegans]	2.212010488
AW550650	Tctex1	t-complex testis expressed 1	2.210463986
AA016507	Eif2ak4	eukaryotic translation initiation factor 2 alpha kinase 4	2.209906084
AA510877	LOC56043	aldo-keto reductase	2.209674103
AW556506		ESTs, Weakly similar to contains similarity to human cyclin A/CDK2-associated prote	2.207942373
AA033417	Shd	src homology 2 domain-containing transforming protein D	2.207103949
AA270607	HIRIP5	HIRA-interacting protein 5	2.205698224
AI447815		ESTs, Moderately similar to LUTHERAN BLOOD GROUP GLYCOPROTEIN PRECUI	2.20379027
AW536587	Mkln1	muskelin 1, intracellular mediator containing kelch motifs	2.202865025
AA427166		ESTs, Weakly similar to BAZF [M.musculus]	2.202843556
C80427		ESTs, Weakly similar to HYPOTHETICAL 32.0 KD PROTEIN IN SAP190-SPO14 INT	2.202416221
AW537746	Atp6k	ATPase, H+ transporting lysosomal (vacuolar proton pump), 9.2 kDa	2.202077047
AW554292	Req	requiem	2.199587912
C76488	Ubce7	ubiquitin-conjugating enzyme 7	2.199583639
W11665		ESTs, Highly similar to LEUCYL-TRNA SYNTHETASE, CYTOPLASMIC [Saccharom	2.199309009
AW557050		ESTs, Highly similar to RADIAL SPOKE PROTEIN 3 [Chlamydomonas reinhardtii]	2.198522495
AI528531	Pdha1	Pyruvate dehydrogenase E1alpha subunit	2.198483601
AU023550	Fin14	fibroblast growth factor inducible 14	2.195941034
W62248	Cdh5	cadherin 5	2.193808943
AW536168	Rangap1	RAN GTPase activating protein 1	2.19351605
AW554767	Clk4	CDC like kinase 4	2.190991173
AA538228	Rab25	RAB25, member RAS oncogene family	2.189550785
AW546162		ESTs, Weakly similar to CARG-BINDING FACTOR-A [M.musculus]	2.189482216
AW539323		ESTs, Weakly similar to (defline not available 5852158) [M.musculus]	2.189245581
AU043933	Gapd	glyceraldehyde-3-phosphate dehydrogenase	2.189078854
C77465		ESTs, Moderately similar to ZINC FINGER PROTEIN MLZ-4 [Mus musculus]	2.188892377
AW536852	Fadk	focal adhesion kinase	2.188786742
AW536207		ESTs, Highly similar to TUBULIN BETA CHAIN [Sus scrofa]	2.188517011
W87197		ESTs, Highly similar to GLUTATHIONE S-TRANSFERASE P [Homo sapiens]	2.188470627
C79925	Cox5a	cytochrome c oxidase, subunit Va	2.187784867
AI325926	Pigf	Phosphatidylinositol glycan, class F	2.18771481
AW536073		ESTs, Weakly similar to cDNA EST yk338g10.5 comes from this gene [C.elegans]	2.187551361
AW555238		ESTs, Weakly similar to ORF YNL091w [S.cerevisiae]	2.187097387
AW546840		ESTs, Moderately similar to ubiquitin protein ligase [M.musculus]	2.18669825
AW544207	Ubce4	ubiquitin-conjugating enzyme 4	2.186399575
W11957		Sm protein F [H.sapiens]	2.185884275
AA265845		Mus musculus mRNA for heterogeneous nuclear ribonucleoprotein H	2.185702249

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C87751		Mus musculus sodium bicarbonate cotransporter isoform 3 kNBC-3 mRNA, complete	2.185545754
AW536982	Syn1	synapsin I	2.18521333
AA108797		ESTs, Highly similar to AF125100_1 HSPC039 protein [H.sapiens]	2.185013011
AU044169		ESTs, Weakly similar to TYROSINE-PROTEIN KINASE JAK3 [M.musculus]	2.184892665
AA105546		ESTs, Highly similar to CHROMOSOME REGION MAINTENANCE PROTEIN 1 [Sch	2.184752938
AW536192		Mus musculus mRNA similar to human Sua1, complete cds	2.184178135
AW556780	Cct3	chaperonin subunit 3 (gamma)	2.183029578
AW552502		ESTs, Weakly similar to RHO GDP-DISSOCIATION INHIBITOR 2 [M.musculus]	2.182648038
AA517533	Erf	Est2 repressor factor	2.181963644
AW546347		Mus musculus geminin mRNA, complete cds	2.181899423
AI414501		ESTs, Highly similar to citrin [H.sapiens]	2.180840196
AA521888	Neo1	neogenin	2.180793589
AW544317	Psma6	proteasome (prosome, macropain) subunit, alpha type 6	2.179852629
AU019946		Mus musculus E2F-like transcriptional repressor protein mRNA, complete cds	2.179418995
AA050169	Ppx	protein phosphatase X	2.177816479
AA111722	Ccnd1	cyclin D1	2.177805783
W83655	Prip	PPAR interacting protein PRIP	2.177488026
AA285673	Rbmx	RNA binding motif protein, X chromosome	2.17686901
AA036275	Gata1	GATA-binding protein 1	2.176573242
AW556431	Krt2-1	keratin complex 2, basic, gene 1	2.175571901
AW536811	H2afz	histone H2A.Z	2.173945499
C80066	Hn1	hematological and neurological expressed sequence 1	2.172659356
W08432	Brp44l	brain protein 44-like protein	2.17256098
C76660		ESTs, Moderately similar to KIAA0663 protein [H.sapiens]	2.172287352
C87299	Csnk1e	casein kinase 1, epsilon	2.167517796
AW553712	Ikbkb	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta	2.166514209
AU017536	Cox6a1	cytochrome c oxidase, subunit VI a, polypeptide 1	2.16607638
AW544371	Fin14	fibroblast growth factor inducible 14	2.165438344
W11746	Tuba4	tubulin alpha 4	2.164642273
AU020791		Mouse mRNA for TI-225, complete cds	2.164606896
C77018	G3bp2-pendir	ras-GTPase-activating protein (GAP<120>) SH3-domain-binding protein 2	2.164476129
AU040132	Shfdg1	split hand/foot deleted gene 1	2.164347535
AA275245		Mus musculus mRNA for vinculin, partial cds	2.164119226
AW547479		ESTs, Weakly similar to PERIPLASMIC DIVALENT CATION TOLERANCE PROTEIN	2.164045819
AW537551	Abcf3	ATP-binding cassette, sub-family F (GCN20), member 3	2.163970346
AI327284		ESTs, Highly similar to NADH-UBIQUINONE OXIDOREDUCTASE B15 SUBUNIT [B	2.161072251
AA182068		ESTs, Weakly similar to DEOXYRIBOSE-PHOSPHATE ALDOLASE [Escherichia coli	2.160741463
AU020241	Rps4x	ribosomal protein S4, X-linked	2.160120787
AW557678		ESTs, Moderately similar to CGI-147 protein [H.sapiens]	2.15947136
AW537744		Mus musculus protein inhibitor of activated STAT protein PIAS1 mRNA, complete cds	2.159440423
AW545312		M.musculus mRNA for GTP-binding protein	2.159318938
AW551617		ESTs, Weakly similar to HC1 ORF [M.musculus]	2.157995583
AW551441		Mus musculus carboxy terminus of Hsp70-interacting protein (Chip) mRNA, complete	2.157761101
AW552022	Nudt5	nudix (nucleoside diphosphate linked moiety X)-type motif 5	2.155260382
AW549360	Sfrs5	splicing factor, arginine/serine-rich 5 (SRp40, HRS)	2.154600128
AW552668	Lxn	latexin	2.154541717
AA204262		ESTs, Highly similar to ALPHA ENOLASE [Mus musculus]	2.153653659
AU021450		ESTs, Highly similar to step II splicing factor SLU7 [H.sapiens]	2.153638703
AI893442	Cox6a1	Cytochrome C oxidase, subunit VI a, polypeptide 1	2.152596602
AW537050		ESTs, Moderately similar to HYPOTHETICAL 49.7 KD PROTEIN IN GIN2-STE3 INT	2.152451561
W77190		ESTs, Weakly similar to 60S RIBOSOMAL PROTEIN L30A [Saccharomyces cerevisi	2.151613671
AA435101		ESTs, Highly similar to MDC-3.13 isoform 1 [H.sapiens]	2.149988061
AW556946		ESTs, Highly similar to TRANSCRIPTION INITIATION FACTOR IIF, ALPHA SUBUN	2.148972113
AW554745		ESTs, Weakly similar to LA PROTEIN HOMOLOG [Drosophila melanogaster]	2.148511594
AW554784		ESTs, Weakly similar to Cxorf5 [H.sapiens]	2.147980173
AA057995		ESTs, Moderately similar to AF151892_1 CGI-134 protein [H.sapiens]	2.147568646
C85330		Mus musculus mRNA for aldolase C, partial	2.146314267
AW553718		Mus musculus CRIPT protein mRNA, complete cds	2.146238796
W98278		ESTs, Highly similar to AF161434_1 HSPC316 [H.sapiens]	2.146162401
C85794		ESTs, Weakly similar to myelin transcription factor 1-like [M.musculus]	2.142786048
AW553739	Ttk	Ttk protein kinase	2.14258919
AA512757		ESTs, Weakly similar to cDNA EST EMBL:C08125 comes from this gene [C.elegans]	2.139749244
AW550795		ESTs, Highly similar to GUANINE NUCLEOTIDE-BINDING PROTEIN G(K), ALPHA !	2.137941679

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AU018994	Atp5l	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit g	2.137180545
AU040533		Mus musculus mRNA for mDj8, complete cds	2.136122453
AU043470		ESTs, Moderately similar to ubiquitin/60S ribosomal fusion protein [M.musculus]	2.135402569
AU041751	Wbp2	WW domain binding protein 2	2.13445614
AU040781		Mus musculus ring-box protein 1 (Rbx1) mRNA, complete cds	2.13360888
AU040559	Rpl3	ribosomal protein L3	2.133597012
AW546128	Gli2	GLI-Kruppel family member GLI2	2.133528553
AU040711		ESTs, Weakly similar to All-1 protein +GTE form [M.musculus]	2.132982988
AW545556	Rnps1	ribonucleic acid binding protein S1	2.131229452
AA386680	Kif5b	kinesin family member 5B	2.130805311
AA276752		ESTs, Weakly similar to AF104033_1 MUEL protein [M.musculus]	2.130751988
AW536420	Pfkl	phosphofructokinase, liver, B-type	2.130381062
AW537576	Usf2	upstream transcription factor 2	2.130169878
AI324141	Klc1	Kinesin light chain 1	2.129968869
AU023963		ESTs, Weakly similar to SIG41 [M.musculus]	2.127150277
W36959		ESTs, Weakly similar to AAKG_MOUSE 5'-AMP-ACTIVATED PROTEIN KINASE, G/	2.126333607
AA050135		ESTs, Highly similar to ISOCITRATE DEHYDROGENASE [Bos taurus]	2.126317392
AW537218		Mus musculus p53 apoptosis-associated target (Perp) mRNA, complete cds	2.124913489
AW554484	Hnrpa2b1	heterogenous nuclear ribonucleoprotein A2/B1	2.123621382
AW551889	Rnf4	ring finger protein 4	2.123489733
AU043672		ESTs, Highly similar to PUTATIVE ATP-DEPENDENT RNA HELICASE C22F3.08C I	2.123346276
AA183061		ESTs, Highly similar to RNA splicing-related protein [R.norvegicus]	2.119535349
C80708		ESTs, Weakly similar to 62D9.a [D.melanogaster]	2.119484585
W65230	Cldn13	claudin-13 gene	2.119015454
AA122896	Slc22a1l	solute carrier family 22 (organic cation transporter), member 1-like	2.118441117
AU023882	Brca2	breast cancer 2	2.117866055
AU019334		ESTs, Moderately similar to ACTIN-LIKE PROTEIN 14D [Drosophila melanogaster]	2.117797328
AW541501		ESTs, Highly similar to CLATHRIN HEAVY CHAIN [Rattus norvegicus]	2.117485424
AW557038		ESTs, Highly similar to TRANSCRIPTION INITIATION FACTOR TFIID 20/15 KD SUE	2.116385548
AW548472	Rps8	ribosomal protein S8	2.116104505
AW540941		ESTs, Highly similar to CYTOCHROME C OXIDASE POLYPEPTIDE VIB [Homo sap	2.115484663
AW545587		ESTs, Moderately similar to BIOTIN CARBOXYLASE [Anabaena pcc7120]	2.112747687
AW553979		ESTs, Highly similar to TYROSINE-PROTEIN KINASE JAK1 [Homo sapiens]	2.11242201
AW557096	Nfix	nuclear factor I/X	2.1119444
AU044022		ESTs, Weakly similar to predicted using Genefinder [C.elegans]	2.111675482
AW550624		Mouse mRNA for TI-225, complete cds	2.110955467
AI415012		ESTs, Weakly similar to F25H9.7 [C.elegans]	2.110875235
AA003927	Cct2	chaperonin subunit 2 (beta)	2.110823315
W89599	Eif2s3x	eukaryotic translation initiation factor 2, subunit 3, structural gene X-linked	2.109036647
AW549119	RIE2	RIE2 protein	2.108802
AA027675	Tbx15	T-box 15	2.107485233
AW555686		ESTs, Moderately similar to FAD SYNTHETASE [Saccharomyces cerevisiae]	2.107160343
AW536333	Tcfl1	transcription factor-like 1	2.105768299
AU015203	Pttg1	pituitary tumor-transforming 1	2.10557106
W34455		ESTs, Highly similar to NADH-UBIQUINONE OXIDOREDUCTASE B12 SUBUNIT [B	2.105042587
AU041434	Ulk1	Unc-51 like kinase 1 (C. elegans)	2.103857568
AU017038		ESTs, Highly similar to REPLICATION PROTEIN A 14 KD SUBUNIT [Homo sapiens	2.102934707
W14837	Prsc1	protease, cysteine, 1	2.102744346
AA163432		ESTs, Weakly similar to ANX7_MOUSE ANNEXIN VII [M.musculus]	2.102354444
AW544350		ESTs, Highly similar to ESS1 PROTEIN [Saccharomyces cerevisiae]	2.101933004
AU018835		Mus musculus claudin-10 mRNA, complete cds	2.101785421
AA415519		ESTs, Weakly similar to HYPOTHETICAL 40.4 KD PROTEIN R06F6.5 IN CHROMOS	2.101349422
AW538436		Mus musculus protein inhibitor of nitric oxide synthase (PIN) mRNA, complete cds	2.100694954
AA086829	Mssk1	muscle-specific serine kinase 1	2.100087115
AA212445	Stat5a	Signal transducer and activator of transcription 5A	2.099472632
AW555798	Ncor1	nuclear receptor co-repressor 1	2.098583834
AU041141		ESTs, Moderately similar to (defline not available 6118541) [M.musculus]	2.097620163
AA272878		ESTs, Highly similar to atypical PKC specific binding protein [R.norvegicus]	2.09748684
AA014127	D15Wsu77e	DNA segment, Chr 15, Wayne State University 77, expressed	2.094998947
AW544533	Tk1	thymidine kinase 1	2.093696405
AI528532		Mus musculus protein kinase C inhibitor (mPKCI) mRNA, complete cds	2.093394542
AU040509		ESTs, Weakly similar to Ring3 [M.musculus]	2.092999984
AA049416	His1a	histone H1	2.092964075

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AA268862	Saps-pending	SKAP55 homologue	2.092899653
C88157		Mus musculus RING finger protein AO7 mRNA, complete cds	2.092505596
AW536161	Ftl1	ferritin light chain 1	2.092408097
AA032709	D7Ertd462e	DNA segment, Chr 7, ERATO Doi 462, expressed	2.091456089
AW538753		ESTs, Highly similar to SORCIN [Cricetulus longicaudatus]	2.090595934
AW554607	Ptk9r-pendin	protein tyrosine kinase 9 related protein	2.088525057
AI325946		TESTIN 2 PRECURSOR	2.088224301
AW550148	Spint2	serine protease inhibitor, Kunitz type 2	2.088199037
AW555109	Chd1	chromodomain helicase DNA binding protein 1	2.088170924
AW557266		ESTs, Highly similar to MITOCHONDRIAL IMPORT RECEPTOR SUBUNIT TOM20 H	2.085963328
AW538548		ESTs, Highly similar to PHOSPHATIDYLSERINE DECARBOXYLASE PROENZYME	2.085827569
AW552438		ESTs, Moderately similar to (defline not available 5714400) [M.musculus]	2.084900792
AA413090		ESTs, Moderately similar to unknown protein IT12 [H.sapiens]	2.08408988
AI573427	Catnb	Catenin beta	2.08164667
AW551843		ESTs, Highly similar to (defline not available 5901572) [R.norvegicus]	2.081031756
AW549786	Atp5b	ATP synthase, H+ transporting mitochondrial F1 complex, alpha subunit	2.080499984
AW555377	Ahcy	S-adenosylhomocysteine hydrolase	2.080387755
AW545836		ESTs, Highly similar to GLUCOSE-6-PHOSPHATASE [Homo sapiens]	2.07946168
AW554408	Usp9x	ubiquitin specific protease 9, X chromosome	2.079410205
AU017036		ESTs, Highly similar to UBIQUITIN-CONJUGATING ENZYME E2-17 KD 3 [Homo sa	2.0788242
AU023795		ESTs, Weakly similar to formin binding protein 11 [M.musculus]	2.078771795
AU021910		ESTs, Highly similar to C-1 [H.sapiens]	2.078299566
AA066209		M.musculus mRNA for glutamyl-tRNA synthetase	2.078220839
AA028539	Pdgfc	platelet-derived growth factor, C polypeptide	2.078034358
AW545810		ESTs, Highly similar to P53-BINDING PROTEIN 53BP2 [M.musculus]	2.077868917
AW543954	Ubl1	ubiquitin-like 1	2.077687345
AU015235		Mus musculus pre-B-cell colony-enhancing factor mRNA, complete cds	2.077221503
AI450292		ESTs, Highly similar to signal peptidase:SUBUNIT	2.077147229
AU021030		Mus musculus mACS4 mRNA for Acyl-CoA synthetase 4, complete cds	2.076973921
AW548833		ESTs, Weakly similar to coronin-3 [M.musculus]	2.076920083
AA241780	Atp6s1	ATPase, H+ transporting, lysosomal (vacuolar proton pump), subunit 1	2.074155421
AU015646	Rex3	reduced expression 3	2.071644406
W34672	Sh3d2a	SH3 domain protein 2A	2.071075902
AU041272		ESTs, Weakly similar to cDNA EST EMBL:C08125 comes from this gene [C.elegans]	2.07070659
AW556256	Tcfcp2	transcription factor CP2	2.070422069
AI465224		ESTs, Highly similar to 60S RIBOSOMAL PROTEIN L15 [Rattus norvegicus]	2.06998501
AW555326	Smoh	smoothened homolog (Drosophila)	2.069871303
AU042878	Psmc3ip	proteasome (prosome, macropain) 26S subunit, ATPase 3, interacting protein	2.069863024
C78336	Cnn2	calponin 2	2.068042036
AW545645	Tpm5	tropomyosin 5	2.067947872
AW551315	Rps29	ribosomal protein S29	2.067794525
AI428885		ESTs, Weakly similar to /prediction	2.066416765
AW536068	Rrm1	ribonucleotide reductase M1	2.066220888
AI323636		Mus musculus eosinophil secondary granule protein (mEAR-2) mRNA, complete cds	2.065726689
AU042101	Plp	proteolipid protein (myelin)	2.065430884
C77213		ESTs, Moderately similar to PUTATIVE ORAL CANCER SUPPRESSOR [Mesocricet	2.065210238
AU023139		ESTs, Weakly similar to natural killer cell tumor-recognition protein [M.musculus]	2.061470989
AW536843	Cct4	chaperonin subunit 4 (delta)	2.060855635
AA221877		ESTs, Highly similar to GUAA_HUMAN GMP SYNTHASE [H.sapiens]	2.060478391
AU019894		ESTs, Highly similar to brain and reproductive organ-expressed protein [H.sapiens]	2.059614762
W59026		KIAA0857	2.05813772
AU042518	Hdc	histidine decarboxylase cluster	2.056638675
AW546468		ESTs, Highly similar to RIBONUCLEASE INHIBITOR [Rattus norvegicus]	2.055993345
AW536183	Cct3	chaperonin subunit 3 (gamma)	2.05541031
AI326287		ESTs, Highly similar to TUBULIN ALPHA-4 CHAIN [Gallus gallus]	2.054481753
AW551916		Mus musculus putative deubiquitinating enzyme UBPY (Ubpy) mRNA, complete cds	2.054332813
AW536647		ESTs, Highly similar to HYPOTHETICAL 25.7 KD PROTEIN IN MSH1-EPT1 INTERC	2.053538694
AW556964	Silg41	silica-induced gene 41	2.05313114
AW537469		ESTs, Moderately similar to BB1	2.052267636
AU017931		ESTs, Highly similar to ALPHA-1,6-MANNOSYL-GLYCOPROTEIN BETA-1,2-N-ACE	2.050617842
AW542919		ESTs, Highly similar to KIAA0398 [H.sapiens]	2.049586337
AW547284		ESTs, Weakly similar to PYRROLINE-5-CARBOXYLATE REDUCTASE [Glycine max	2.049181802
C88181		ESTs, Moderately similar to CCR4-ASSOCIATED FACTOR 1 [M.musculus]	2.049163559

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C85992	Tnni2	troponin I, skeletal, fast 2	2.046590193
AA124929		ESTs, Moderately similar to unnamed protein product [H.sapiens]	2.046014815
AA031105		ESTs, Weakly similar to nuclear protein ZAP [M.musculus]	2.0452411
AW547298		ESTs, Weakly similar to NG38 [M.musculus]	2.045099916
AW544241		ESTs, Highly similar to eukaryotic translation initiation factor eIF3, p35 subunit [H.sap	2.043937442
AA542348		ESTs, Weakly similar to SIK similar protein [M.musculus]	2.043764446
AA030810		ESTs, Highly similar to AF161432_1 HSPC314 [H.sapiens]	2.043627079
AA273426		ESTs, Moderately similar to nebulette [H.sapiens]	2.043366784
AI447370		ESTs, Highly similar to CAAX prenyl protein protease RCE1 [H.sapiens]	2.04179856
AA087193	Lcn2	Lipocalin 2	2.040902926
AW552069	Atp5f1	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit b, isoform 1	2.040618398
AW554249		ESTs, Weakly similar to microtubule-actin crosslinking factor [M.musculus]	2.040394297
AW552221	Hdgf	hepatoma-derived growth factor	2.039626815
AW547185	Arg1	arginase 1, liver	2.037574557
AU020575		ESTs, Moderately similar to HYPOTHETICAL 27.1 KD PROTEIN CCE1-CAP1 INTEI	2.037569931
AW545291	Calm	calmodulin	2.037514948
AU020225		Mus musculus mRNA for Sid393p, complete cds	2.037396367
AW556673	Anxa7	annexin A7	2.036952459
W14928	Smpd1	Sphingomyelin phosphodiesterase 1, acid lysosomal	2.035892157
AU045064		ESTs, Highly similar to SOH1 PROTEIN [Saccharomyces cerevisiae]	2.035291187
AU015736		ESTs, Moderately similar to KIAA0873 protein [H.sapiens]	2.035101764
AW554127	Ly84l	lymphocyte antigen 84 ligand	2.033282134
AI893564	Anx5	Annexin V	2.032674021
AI414985		ESTs, Highly similar to HYPOTHETICAL 109.5 KD PROTEIN IN PPA1-DAP2 INTER	2.032638418
AW536161	Ftl1	ferritin light chain 1	2.031483082
AW557154		ESTs, Highly similar to HYPOTHETICAL 64.5 KD PROTEIN ZK652.9 IN CHROMOS	2.030895392
AW544402		ESTs, Moderately similar to PROBABLE UBIQUITIN CARBOXYL-TERMINAL HYDR	2.028946654
AA058194	Ephb1	Eph receptor B1	2.028898148
AW536460	Sfrs3	splicing factor, arginine/serine-rich 3 (SRp20)	2.027993079
AU018866	Abcd3	ATP-binding cassette, sub-family D (ALD), member 3	2.027886388
W89491	Fus2	fusion 2 (human)	2.027721104
AW556539		Mus musculus mRNA for eIF3 p66, complete cds	2.026302738
W83009	D6Wsu137e	DNA segment, Chr 6, Wayne State University 137, expressed	2.026028375
AA467238		ESTs, Moderately similar to AF155107_1 NY-REN-37 antigen [H.sapiens]	2.025843113
W79958	Xnp	X-linked nuclear protein	2.025191263
AU019848	Ldb1	LIM domain binding 1	2.024274047
AA220582	Cyp2f2	Cytochrome P450, 2f2	2.023391931
C76118		Mus musculus carboxy terminus of Hsp70-interacting protein (Chip) mRNA, complete	2.022613159
AA016824	Cck	cholecystokinin	2.022490481
AI326325		ESTs, Weakly similar to CCAAT-BINDING TRANSCRIPTION FACTOR SUBUNIT A [	2.020679018
AA253928	S100a11	S100 calcium binding protein A11	2.019696914
AW541485	Ldlr	low density lipoprotein receptor	2.019565667
AW536904	Ppia	peptidylprolyl isomerase A	2.019439841
AW552486	Ube2i	ubiquitin-conjugating enzyme E2I	2.018883876
AU041740		M.musculus mRNA for fibromodulin	2.01868023
AI448352		ESTs, Highly similar to KIAA0670 protein [H.sapiens]	2.018648182
AW557886		ESTs, Highly similar to dJ30M3.2 [H.sapiens]	2.018168191
AW546615		ESTs, Highly similar to TRANSLATIONAL INITIATION FACTOR 2 ALPHA SUBUNIT	2.017143269
AW536942		Mus musculus mRNA for MSSP, complete cds	2.017088183
AU017987		ESTs, Weakly similar to NADH-CYTOCHROME B5 REDUCTASE [R.norvegicus]	2.016928064
C85531		Mus musculus TBX1 protein mRNA, complete cds	2.016803084
AW545339	Ate1	arginine-tRNA-protein transferase 1	2.016693199
AW546437	Rab6kifl	Rab6, kinesin-like	2.016652063
AI666581		RIBOSOMAL PROTEIN S6 KINASE II ALPHA 1	2.016029612
AI447773		Mus musculus BAF53a (Baf53a) mRNA, complete cds	2.015349198
AA537763		matrin cyclophilin (matrin-cyp) [R. rattus]	2.014990505
AA030846	Coq7	demethyl-Q 7	2.013748884
AW537679		ESTs, Highly similar to transcriptional co-activator CRSP77 [H.sapiens]	2.012445473
AW545196	Sui1-rs1	suppressor of initiator codon mutations, related sequence 1 (S. cerevisiae)	2.012217503
C78825		ESTs, Weakly similar to protein co-factor [M.musculus]	2.011284548
AW551014		ESTs, Highly similar to KIAA0594 protein [H.sapiens]	2.011053628
AW550287	Map2k7	mitogen activated protein kinase kinase 7	2.010008679
C79872	Psmd7	proteasome (prosome, macropain) 26S subunit, non-ATPase, 7	2.009904416

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AW538975		ESTs, Weakly similar to ladinin [H.sapiens]	2.009401476
AI666784		ESTs, Weakly similar to protein kinase C-binding protein RACK7 [H.sapiens]	2.00819018
C79697	Phgdh	3-phosphoglycerate dehydrogenase	2.00734278
AW536784		ESTs, Highly similar to HYPOTHETICAL PROTEIN KIAA0174 [H.sapiens]	2.005216822
AW552691		ESTs, Highly similar to KINESIN-II 85 KD SUBUNIT [Strongylocentrotus purpuratus]	2.004947093
W66889		ESTs, Highly similar to RABPHILIN-3A [Rattus norvegicus]	2.004938025
AW553280	Itgb1	integrin beta 1 (fibronectin receptor beta)	2.003708956
AI413372		ESTs, Highly similar to Rer1 protein [H.sapiens]	2.003211999
C77965	Fgfrp	fibroblast growth factor regulated protein	2.00177749
AA153905		ESTs, Weakly similar to CG17019 gene product [D.melanogaster]	2.000439106
AW544501	Hmox1	heme oxygenase (decycling) 1	0.498585892
W62969	Fyn	Fyn protooncogene	0.498473008
AW547534	Snrp116-pend	U5 small nuclear ribonucleoprotein 116 kDa	0.497942009
AW556002		ESTs, Weakly similar to open reading frame [M.musculus]	0.497906318
AW538495		ESTs, Moderately similar to GLYCOPROTEIN 25L PRECURSOR [Canis familiaris]	0.497505758
AU018809		ESTs, Weakly similar to cDNA EST EMBL:D70762 comes from this gene [C.elegans]	0.497360848
W34685	Rora	RAR-related orphan receptor alpha	0.496667567
AI426288		ESTs, Weakly similar to ultra-high-sulfur keratin [M.musculus]	0.496141712
AI324866		Mus musculus PEST phosphatase interacting protein mRNA, complete cds	0.495826245
AI893650	Usf2	Upstream transcription factor 2	0.49557731
AI426736		Mus musculus timeless homolog mRNA, complete cds	0.494513325
AA184214	Gabpb1	GA repeat binding protein, beta 1	0.494022907
AA017867		ESTs, Highly similar to CARCINOEMBRYONIC ANTIGEN CGM6 PRECURSOR [Hoi	0.493125955
AA268219	Mpeg1	macrophage expressed gene 1	0.492580225
AA239856	Omi	serine protease OMI	0.492467109
W16354		ESTs, Moderately similar to LAR PROTEIN PRECURSOR [Homo sapiens]	0.491968272
C87660		ESTs, Weakly similar to melastatin [M.musculus]	0.491744995
AW555781	C1qb	complement component 1, q subcomponent, beta polypeptide	0.490941625
AI428004		ESTs, Moderately similar to transporter protein [H.sapiens]	0.489481805
C77865		ESTs, Highly similar to major vault protein [R.norvegicus]	0.488832841
AI449541		ESTs, Highly similar to myc far upstream element-binding protein [H.sapiens]	0.488201357
W64937	Arp2-pending	angiopoietin related protein 2	0.486616378
AI327367	Cd28	CD28 antigen	0.486573305
AA413761	Epn2	epsin 2	0.48638791
AA511061		ESTs, Weakly similar to similar to kinensin-like protein [C.elegans]	0.485798066
AA462869	C2	Complement component 2 (within H-2S)	0.485770605
W30178		Platelet derived growth factoralpha	0.485512789
AW536657		ESTs, Highly similar to PHOSPHOENOLPYRUVATE CARBOXYKINASE, CYTOSOL	0.484491052
C81284		ESTs, Moderately similar to TYROSINE-PROTEIN KINASE JAK2 [M.musculus]	0.484285289
AI661346		ESTs, Moderately similar to estradiol 17beta-dehydrogenase [M.musculus]	0.484253534
AA064183	Pex16	peroxisome biogenesis factor 16	0.483919369
AI385600		Mus musculus cyclic nucleotide phosphodiesterase (PDE1A2) mRNA, complete cds	0.48335782
AI447349		ESTs, Moderately similar to hypothetical protein [H.sapiens]	0.483147225
AU045766		ESTs, Weakly similar to KIAA0926 protein [H.sapiens]	0.482947335
AA174729	D13Ertd275e	DNA segment, Chr 13, ERATO Doi 275, expressed	0.482851894
W82220	Rab3a	RAB3A, member RAS oncogene family	0.482386856
AI447993	H2-Aa	Histocompatibility 2, class II antigen A, alpha	0.48129597
AI327389	Stat4	Signal transducer and activator of transcription 4	0.481241844
AI427715		ESTs, Weakly similar to Rab8-interacting protein [M.musculus]	0.481160908
AI449408		RADIXIN	0.48100611
AA014942		ESTs, Weakly similar to RAS-like protein expressed in many tissues [M.musculus]	0.480372777
AA000726	Vipr2	Vasoactive intestinal peptide receptor 2	0.480224921
C81465	Taut	taurine/beta-alanine transporter	0.479566248
AI425920		ESTs, Weakly similar to HSPC010 [H.sapiens]	0.479378243
C77369		ESTs, Weakly similar to cDNA EST EMBL:C11678 comes from this gene [C.elegans]	0.47922836
C88320		ESTs, Weakly similar to RING1B protein [M.musculus]	0.47820664
AU040253		ESTs, Weakly similar to LR8 [M.musculus]	0.47742886
AA260747	Birc6	baculoviral IAP repeat-containing 6	0.476766539
AW544351	Kifap3	kinesin-associated protein 3	0.476693505
AU041202		Mus musculus mRNA, complete cds, clone:2-68	0.475319304
AU020028	Ier5	immediate early response 5	0.475163983
AI413118	Gng3lg	G protein gamma 3 linked gene	0.473543339
AA061278		ESTs, Weakly similar to KIAA0308 [H.sapiens]	0.473431725

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AU014897	Apc	adenomatosis polyposis coli	0.472956452
AA426926	D14Ertd817e	DNA segment, Chr 14, ERATO Doi 817, expressed	0.472580007
AA108640	Gdc1	Glycerolphosphate dehydrogenase 1, cytoplasmic adult	0.4722026
AA261368	Ywhaz	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta poly	0.471958974
AA435123		ESTs, Weakly similar to ZK1058.5 [C.elegans]	0.471909449
AU043840	Ccr4	carbon catabolite repression 4 homolog (S. cerevisiae)	0.471612261
AI450156		ESTs, Weakly similar to RING1B protein [M.musculus]	0.470602473
AW536169	Sparc	secreted acidic cysteine rich glycoprotein	0.468881114
AW552818		M.musculus mRNA for GTP-binding protein	0.466979012
C77414	Gpcr26	G-protein coupled receptor 26	0.466353125
AI449065		ESTs, Highly similar to SUSHI REPEAT-CONTAINING PROTEIN SRPX PRECURSC	0.4658412
AA260521	Ucp2	uncoupling protein 2, mitochondrial	0.465029569
AA200091		ESTs, Moderately similar to AF096286_1 pecanex 1 [M.musculus]	0.46491171
AI326894		ESTs, Moderately similar to HYPOTHETICAL 20.8 KD PROTEIN T09A5.6 IN CHROI	0.46346233
AA118392	Staf	selenocysteine tRNA gene transcription activating factor	0.460978805
AA200942	Slfn4	schlafen 4	0.460594202
AA275985		Rieske iron-sulfur protein [R.Rattus]	0.459911898
AI325975		ESTs, Highly similar to 65 KD YES-ASSOCIATED PROTEIN [Mus musculus]	0.459243061
AI323966		ESTs, Weakly similar to GOLIATH PROTEIN [Drosophila melanogaster]	0.458644321
W12425		ESTs, Highly similar to KIAA1533 protein [H.sapiens]	0.457391655
W81912	Crabp2	Cellular retinoic acid binding protein II	0.457211976
AA178121	Ctss	cathepsin S	0.457173001
W70924		PK-120 precursor (itih-4)	0.456587824
AA123853	Cast	calpastatin	0.456342311
AA230451	S100a8	S100 calcium binding protein A8 (calgranulin A)	0.456297242
AI430926		ESTs, Highly similar to KIAA1002 protein [H.sapiens]	0.455164376
W97303	Meg3	maternally expressed gene 3	0.454711379
AI426555		Mus musculus histone deacetylase mHDA1 mRNA, complete cds	0.454390478
AA061732	shrm	shroom	0.45390698
AU020551		ESTs, Moderately similar to NOF1 [H.sapiens]	0.45336961
AI429678	Capn5	Calpain 5	0.452911351
AA213015	Tstap35b	tissue specific transplantation antigen P35B	0.452689264
AU018982	C1s	complement component 1, s subcomponent	0.451660309
AA268592	Tgfbi	Transforming growth factor, beta induced, 68 kDa	0.451233977
C79673		ESTs, Weakly similar to TALIN [M.musculus]	0.451086496
AU019876		ESTs, Moderately similar to POLLEN SPECIFIC PROTEIN SF3 [Helianthus annuus]	0.450242321
W29855	ep	Pale ear	0.450183821
AI325516		ESTs, Highly similar to ASPARTOACYLASE [Homo sapiens]	0.449831178
AU016285	Unc5h3	UNC-5 homolog (C. elegans) 3	0.449107031
C81338	Col5a1	procollagen, type V, alpha 1	0.4484605
AA120639	D13Ertd372e	DNA segment, Chr 13, ERATO Doi 372, expressed	0.447735968
AI452234		ESTs, Weakly similar to Similar to aldehyde dehydrogenase [C.elegans]	0.447667176
AA073843		ESTs, Weakly similar to HYPOTHETICAL 29.5 KD PROTEIN C05B5.7 IN CHROMOS	0.446317848
AA189196		ESTs, Highly similar to T00325 hypothetical protein KIAA0546 - human [H.sapiens]	0.446285677
AA118626		ESTs, Highly similar to unnamed protein product [H.sapiens]	0.445541417
AI528706		Mus musculus MPS1 gene and mRNA, 3'end	0.443511276
AI324761		Mus musculus short-chain dehydrogenase CRAD2 mRNA, complete cds	0.442839884
W99968	Kcnn4	potassium intermediate/small conductance calcium-activated channel, subfamily N, m	0.441371237
AA435060	Lst1	leucocyte specific transcript 1	0.441296333
AA178076	Cd53	CD53 antigen	0.440591878
AU041801	Drr3	developmentally regulated repeat element-containing transcript 3	0.439266461
AU019411		ESTs, Highly similar to ARGININOSUCCINATE LYASE [Homo sapiens]	0.438910556
AI326924		ESTs, Highly similar to MYO-INOSITOL-1(OR 4)-MONOPHOSPHATASE [Xenopus l	0.43795106
AI450850		ESTs, Highly similar to 0-44 PROTEIN [Rattus norvegicus]	0.43692673
AA120432		Mus musculus prostaglandin transporter PGT mRNA, complete cds	0.436751727
AA110278		ESTs, Weakly similar to unknown [R.norvegicus]	0.43638582
AU042856		ESTs, Weakly similar to contains similarity to Saccharomyces cerevisiae MAF1 prote	0.43622857
AA003252	Myhca	myosin heavy chain, cardiac muscle, adult	0.434973545
AW546079		ESTs, Highly similar to HYPOTHETICAL 70.2 KD PROTEIN IN GSH1-CHS6 INTER(	0.434243151
C79931	jmj	jumonji	0.430266963
AI451309	Plxn3	Plexin 3	0.430074817
AI426259		ESTs, Weakly similar to high affinity immunoglobulin gamma Fc receptor I [M.muscul	0.429035689
AA474849		ESTs, Highly similar to KIAA1461 protein [H.sapiens]	0.42741177

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W82668	Spry1	sprouty homolog 1 (Drosophila)	0.426418559
AA161816	Api5	apoptosis inhibitory protein 5	0.425689953
AI323807		Mus musculus GDP-dissociation inhibitor mRNA, preferentially expressed in hematop	0.423803111
AA118878		ESTs, Highly similar to NEDD-4 PROTEIN [Homo sapiens]	0.423726623
AA212838	Psmb7	Proteasome (prosome, macropain) subunit, beta type 7	0.42279869
W46125		ESTs, Weakly similar to D29149 proline-rich protein - mouse [M.musculus]	0.422389477
AA144383	Clpx	caseinolytic protease X (E.coli)	0.422311709
AI385657	Ext1	Exostoses (multiple) 1	0.417206887
C86591	Sdfr2	stromal cell derived factor receptor 2	0.415674914
AU042151		ESTs, Highly similar to laminin B1 [M.musculus]	0.412353937
AI324011		ESTs, Weakly similar to BRAIN SPECIFIC POLYPEPTIDE PEP-19 [Rattus norvegicu	0.411873664
AI451431		ESTs, Highly similar to RAS-RELATED PROTEIN RAL-B [Rattus norvegicus]	0.410550864
AA175990		ESTs, Highly similar to P300_HUMAN E1A-ASSOCIATED PROTEIN P300□ [H.sapie	0.41013035
AA250039	Lgals9	lectin, galactose binding, soluble 9	0.409511422
AI326849		TRANSCRIPTIONAL REGULATOR PROTEIN HCNGP	0.406388099
C79775	Hba-a1	hemoglobin alpha, adult chain 1	0.40598605
C77913	Gdf3	growth differentiation factor 3	0.404203495
C77459		ESTs, Weakly similar to HYPOTHETICAL PROTEIN KIAA0008 [H.sapiens]	0.404184781
AW557391	Nedd5	neural precursor cell expressed, developmentally down-regulated gene 5	0.403827774
AU018863	Klf4	Kruppel-like factor 4 (gut)	0.403065274
AU042260	Cfi	complement component factor i	0.402491799
W34157		Secreted acidic cysteine rich glycoprotein SPARC	0.401851169
AA178132		Mus musculus PGES mRNA for prostaglandin E synthase, complete cds	0.401791284
W08086	Gba	Acid beta glucosidase	0.401380464
AA250238	Usp18	ubiquitin specific protease 18	0.401098929
AA048539		ESTs, Highly similar to INOSITOL 1,4,5-TRISPHOSPHATE-BINDING PROTEIN TYF	0.396520353
AA030377		ESTs, Highly similar to PDGF receptor beta-like tumor suppressor [H.sapiens]	0.395814313
C88171		ESTs, Weakly similar to KIAA0601 protein [H.sapiens]	0.395639563
AW549905	Hba-a1	hemoglobin alpha, adult chain 1	0.395434605
AU015378	Pde7a	phosphodiesterase 7A	0.395371322
AI429264		ESTs, Moderately similar to KIAA0948 protein [H.sapiens]	0.395320909
W87077		Cell cycle progression 2 protein (CPR2) [H. sapiens]	0.393842569
AI451393		ESTs, Weakly similar to HYPOTHETICAL PROTEIN HI1130 [Haemophilus influenzae	0.392399983
AI323471	Zfp147	Zinc finger protein 147	0.391742059
C79534	Cstf3	cleavage stimulation factor, 3' pre-RNA, subunit 3	0.389435064
AI573376	Fcer1g	Fc receptor, IgE, high affinity I, gamma polypeptide	0.385223818
AW549905	Hba-a1	hemoglobin alpha, adult chain 1	0.384703759
AU045698		Mus musculus SOCS box-containing WD protein SWiP-2 (Swip2) mRNA, complete c	0.384692305
W17967	Pon1	Paraoxonase 1	0.381300142
AA118886	H2-Oa	Histocompatibility 2, O region alpha locus	0.379646356
AA183698	Sell	selectin, lymphocyte	0.378737018
AA028411	D7Ertd760e	DNA segment, Chr 7, ERATO Doi 760, expressed	0.377683276
W33982	HDAC7	histone deacetylase 7	0.375622229
AW544285	Gnai2	guanine nucleotide binding protein, alpha inhibiting 2	0.375530863
AW544580	Ero1l-pendin	ERO1-like (S. cerevisiae)	0.373517048
AI327378		ESTs, Highly similar to putative E1-E2 ATPase [M.musculus]	0.372692878
C79918		Mus musculus serine protease OMI (Omi) mRNA, complete cds	0.371971496
AA423584	Expi	extracellular proteinase inhibitor	0.371842492
C81309	Gata3	GATA-binding protein 3	0.371089436
AW553343	Lgals7	lectin, galactose binding, soluble 7	0.368788049
AA017742	Hdac5	histone deacetylase 5	0.368222326
AU021695		ESTs, Weakly similar to cDNA EST yk325c7.5 comes from this gene [C.elegans]	0.362313766
AI324651	Csk	C-src tyrosine kinase	0.361784019
AI323916	Hbb-bh3	Hemoglobin beta, pseudogene bh3	0.359390956
AA140511	Coro1a	coronin, actin binding protein 1A	0.348942089
AW550250		ESTs, Moderately similar to P53-BINDING PROTEIN 53BP2 [M.musculus]	0.348279234
W59402		Solute carrier family 2 (facilitated glucose transporter) member 1	0.347266069
AI323455		Mus musculus peptidylglycine alpha-amidating monooxygenase (PAM) mRNA, compl	0.342252509
AI324019		ESTs, Highly similar to PANCREATIC LIPASE RELATED PROTEIN 1 PRECURSOF	0.342094965
AI323613	Inpp5d	Inositol polyphosphate-5-phosphatase, 145 kDa	0.341842445
W48074		ESTs, Weakly similar to U82695_2 expressed-Xq28STS protein [H.sapiens]	0.341545463
AI449289		ESTs, Weakly similar to regulator of G protein signaling 12 [H.sapiens]	0.340525506
AW554421	C1qa	complement component 1, q subcomponent, alpha polypeptide	0.337939883

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AA286654	LOC54129	hypothetical protein	0.337264557
AW549905	Hba-a1	hemoglobin alpha, adult chain 1	0.330145717
AA008051		Mus musculus Dkc1 gene for dyskerin, exon 1 and join CDS	0.330043228
W41258		GT12 protein	0.325468276
AW549905	Hba-a1	hemoglobin alpha, adult chain 1	0.324856566
AA245029	Dlk1	Dlk1-like homolog (Drosophila)	0.321318128
C88087	Pbx3	pre B-cell leukemia transcription factor 3	0.320595592
AU041875	Apobec1	apolipoprotein B editing complex 1	0.315363153
AI451067		ESTs, Weakly similar to LIGATIN [M.musculus]	0.314553028
AA208883	Tln	talin	0.310653211
AI326839		Mus musculus high mobility group protein homolog HMG4 (Hmg4) mRNA, complete c	0.310482414
C79179		EST, Weakly similar to organic anion transporter OATP-C [H.sapiens]	0.302074885
AW552972		ESTs, Highly similar to ATP-DEPENDENT PROTEASE LA 2 [Myxococcus xanthus]	0.297372968
AA145212	Clpx	caseinolytic protease X (E.coli)	0.29513184
AI605734		VCF - V21 - Pnut	0.295081875
AW546106	Tyms	thymidylate synthase	0.295071229
C77182		ESTs, Weakly similar to glycogen debranching enzyme isoform 6 [H.sapiens]	0.294297238
AW556657		ESTs, Weakly similar to NY-REN-45 antigen [H.sapiens]	0.293288502
AA276003	Prlr-rs1	prolactin receptor related sequence 1	0.286620436
AU023528		Mus musculus tescalcin mRNA, complete cds	0.280511647
AI528713		Mus musculus predicted GTP binding protein (IRG-47) mRNA, complete cds	0.277481051
AW544018	Slc23a2	solute carrier family 23, (nucleobase transporters) member 2	0.274074155
AA098166	Pgf	Placental growth factor	0.265680649
AW551388		Mus musculus E2F-like transcriptional repressor protein mRNA, complete cds	0.25836127
AU045552	Lrp	low density lipoprotein receptor related protein	0.249126285
C78643		ESTs, Moderately similar to H-REV 107 PROTEIN [R.norvegicus]	0.246608761
AI323599		H-2 CLASS II HISTOCOMPATIBILITY ANTIGEN, I-A BETA CHAIN PRECURSOR	0.245441986
AW549905	Hba-a1	hemoglobin alpha, adult chain 1	0.243800073
AA413508	Serk1	SAPK/Erk/kinase 1	0.242356002
AA120574	Sod1	superoxide dismutase 1, soluble	0.235267761
AI528547	C2	Complement component 2 (within H-2S)	0.229074483
AW548291	Hbb-b2	hemoglobin, beta adult minor chain	0.227852807
AW552978		ESTs, Highly similar to ALPHA-ACTININ, SMOOTH MUSCLE ISOFORM [Gallus gall	0.213193615
AW545280	Tsn	translin	0.21028048
AA260985		ESTs, Weakly similar to ANX7_MOUSE ANNEXIN VII [M.musculus]	0.204873897
W89883	Col3a1	Procollagen, type III, alpha 1	0.196376754
C78503	Ask-pending	activator of S phase kinase	0.193218524
AU022963	Selp	selectin, platelet	0.192932242
C86607	Mat8	mammary tumor 8 kDa	0.190339745
AA434863		ESTs, Moderately similar to no similarities to reported gene products [H.sapiens]	0.189503955
AI464480		ESTs, Moderately similar to KIAA1014 protein [H.sapiens]	0.18862163
AA272807	H2-Aa	Histocompatibility 2, class II antigen A alpha	0.167760814
AA413764		ESTs, Weakly similar to P24_RAT COP-COATED VESICLE MEMBRANE PROTEIN	0.143346174
AI451475		ESTs, Highly similar to nucleolar protein Nopp140, hepatic [R.norvegicus]	0.121425101
AW553502	Cola2	procollagen, type I, alpha 2	0.121045883

Supplementary Table 5: Details of the number of genes up or down regulated in functional group and a comparison of their relative abundance compared to the spots printed on the microarrays.

Functional Groups	Cell Cycle	Apoptosis Tumor Suppressors and Oncogenes	Development and Differentiation	Metabolism	Protein Metabolism	Cytoskeletan and ECM	Membrane Associated	Signal Transduction	Nucleic acid chemistry	Others
Printed on microarrays	263	252	77	440	1102	698	468	1501	846	1134	1893
% of Sum of annotated	3.0	2.9	0.9	5.1	12.7	8.0	5.4	17.3	9.8	13.1	21.8
Regulated in the hyper-invasive cells											
Total	14	46	10	70	205	163	93	252	98	145	270
upregulated	11	39	8	59	172	137	78	211	82	121	225
downregulated	3	7	2	11	33	26	15	41	16	24	45
% of Sum of regulated	1.02	3.87	0.73	5.12	15.01	11.93	6.61	18.45	7.17	10.61	19.77

Difference between printed and regulated

Decrease

Increase

3B: Details of the functional category called "Cell Cycle"

Gene Symbol	Gene description	Fold change
	Suppression of cell proliferation	
Psmc5	protease (prosome, macropain) 26S subunit, ATPase 5	5.5
Rad9	cell cycle checkpoint control protein (Rad9) mRNA	4.0
Hmg1	high mobility group protein 1	3.5
CKS2	Cyclin-dependent kinases regulatory subunit 2	3.4
Cks1	cyclin-dependent kinase regulatory subunit 1	3.2
Fmo5	flavin containing monooxygenase 5	3.0
GAS6	GAS 6 mRNA associated with growth-arrest	2.8
Phb	prohibitin	2.8
Mad2	mitotic checkpoint component Mad2 mRNA	2.4
Madh3	MAD homolog 3	2.4
Hmg14	high mobility group protein 14	2.3
	Enhancement of cell proliferation	
CGMC	Carcinoembryonic antigen CGM6 precursor	0.5
CPR2	Cell cycle progression 2 protein (CPR2)	0.4
Ask	activator of S phase kinase	0.2

What is claimed is:

1. A method of isolating motile cells of interest from an animal tissue that comprises the motile cells of interest and other motile cells, the method comprising

obtaining a microneedle or capillary filled with a porous matrix comprising a chemotactic factor;

inserting the microneedle or capillary into the tissue for a time sufficient for the motile cells of interest to migrate into the porous matrix;

expelling the porous matrix with motile cells from the microneedle or capillary;

combining the porous matrix with microbeads, where the microbeads comprise a binding partner to a surface marker present on the other motile cells but not the motile cells of interest; and

removing the microbeads.

2. The method of claim 1, wherein the animal is a mammal.

3. The method of claim 1, wherein the animal is a rodent.

4. The method of claim 1, wherein the animal is a human.

5. The method of claim 1, wherein the tissue is in a living mammal.

6. The method of claim 1, wherein the tissue is cancerous.

7. The method of claim 1, wherein the tissue is mammary tissue.

8. The method of claim 1, wherein the porous matrix comprises matrigel.

9. The method of claim 1, wherein the microneedle or capillary is a microneedle.

10. The method of claim 9, wherein the microneedle is 33-gauge.

11. The method of claim 1, wherein the binding partner is an antibody.

12. The method of claim 1, wherein the motile cells of interest are cancer cells.

13. The method of claim 12, wherein the chemotactic factor is an epidermal growth factor.

14. The method of claim 12, wherein the other motile cells are normal stromal cells.

15. The method of claim 12, wherein the other motile cells are substantially macrophages.

16. The method of claim 14, wherein the binding partner is an antibody is specific for CD11b.

17. The method of claim 1, wherein the motile cells of interest are macrophages.

18. The method of claim 14, wherein the macrophages are further analyzed.

19. The method of claim 18, wherein the macrophages are quantified.

20. The method of claim 18, wherein mRNA or protein expression of at least one gene in the macrophages is determined.

21. The method of claim 1, wherein the cells of interest are further analyzed.

22. The method of claim 21, wherein the cells of interest are quantified.

23. The method of claim 21, wherein mRNA or protein expression of at least one gene is determined in the cells of interest.

24. The method of claim 23, wherein the cells of interest are cancer cells.

25. The method of claim 24, wherein the cancer cells are motile carcinoma cells.

26. The method of claim 23, wherein the expression of the at least one gene is compared to expression of the at least one gene in a nonmotile cell from the same tissue.

27. The method of claim 23, wherein the at least one gene is selected from the group consisting of Arp2/3 p16 subunit, Arp2/3 p21 subunit, alpha subunit of capping protein, beta subunit of capping protein, cofilin, WAVE3, ROCK1, ROCK2, LIMK 1, PKCζ,, LIM-kinase PAK, type II alpha isoform of PI4, 5 kinase, mena, tropomyosin, calpain, gelsolin-like protein (CAPG), zyxin, vinculin, integrin β1, collagen type III α1, G-protein coupled receptor 26, fibroblast growth factor receptor 1, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor.

28. The method of claim 23, wherein the at least one gene is ZBP-1.

29. The method of claim 23, wherein mRNA or protein expression at least two genes are determined in the cells of interest, wherein the two genes are selected from the group consisting of collagen type III α1, G-protein coupled receptor 26, ZBP-1, fibroblast growth factor receptor 1, Arp2/3 p16 subunit, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor.

30. The method of claim 29, wherein mRNA expression of collagen type III α1, G-protein coupled receptor 26, ZBP-1, fibroblast growth factor receptor 1, Arp2/3 p16 subunit, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor are determined.

31. The method of claim 23, wherein the mRNA or protein expression is determined using a microarray.

32. The method of claim 23, wherein mRNA expression of the at least one gene is determined.

33. The method of claim 32, wherein the mRNA is amplified prior to determination of expression of the at least one gene.

34. The method of claim 33, wherein the mRNA is amplified by reverse transcription and cDNA amplification.

35. A method of determining mRNA or protein expression of a gene in motile cells of interest from an animal tissue, the method comprising isolating the motile cells of interest by the method of claim 1, extracting the mRNA or protein from the cells of interest, then determining mRNA or protein expression in the extraction of the cells of interest.

36. The method of claim 35, wherein mRNA expression of the gene is determined in the motile cells of interest.

37. The method of claim 36, wherein mRNA expression of a second gene is determined in the motile cells of interest.

38. The method of claim 36, wherein mRNA expression is determined by extracting and amplifying the mRNA from the motile cells of interest then determining the mRNA expression of the gene from the amplified mRNA.

39. The method of claim 38, wherein the mRNA is amplified by reverse transcription and cDNA amplification.

40. The method of claim 35, wherein the mRNA or protein expression is determined using a microarray.

41. The method of claim 35, wherein the animal is a mammal.

42. The method of claim 35, wherein the animal is a rodent.

43. The method of claim 35, wherein the animal is a human.

44. The method of claim 35, wherein the tissue is cancerous.

45. The method of claim 44, wherein the cancer is a carcinoma.

46. The method of claim 35, wherein the tissue is mammary tissue.

47. The method of claim 35, wherein the tissue is in a living animal.

48. The method of claim 35, wherein the gene is selected from the group consisting of Arp2/3 p16 subunit, Arp2/3 p21 subunit, alpha subunit of capping protein, beta subunit of capping protein, cofilin, WAVE3, ROCK1, ROCK2, LIMK 1, PKCζ,, LIM-kinase PAK, type II alpha isoform of PI4, 5 kinase, mena, tropomyosin, calpain, gelsolin-like protein (CAPG), zyxin, vinculin, integrin β1, collagen type III α1, G-protein coupled receptor 26, ZBP-1, fibroblast growth factor receptor 1, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor.

49. The method of claim 35, wherein mRNA or protein expression at least two genes are determined in the cells of interest, wherein the two genes are selected from the group consisting of collagen type III α1, G-protein coupled receptor 26, ZBP-1, fibroblast growth factor receptor 1, Arp2/3 p16 subunit, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor.

50. The method of claim 49, wherein mRNA expression of collagen type III α1, G-protein coupled receptor 26, ZBP-1, fibroblast growth factor receptor 1, Arp2/3 p16 subunit, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor are determined.

51. A method of determining whether a cancer in a tissue of a mammal is likely to metastasize, the method comprising

obtaining a microneedle or capillary filled with a porous matrix comprising a chemotactic factor;

inserting the microneedle into the cancer for a time sufficient for motile cells to migrate into the porous matrix;

expelling the porous matrix with motile cells from the microneedle or capillary;

combining the porous matrix with microbeads, where the microbeads comprise a binding partner to a surface marker present on macrophages from the tissue;

removing the microbeads; and

quantifying the motile cells,

wherein the presence of more motile cells than from the tissue when noncancerous or when comprising a non-metastatic cancer indicates that the cancer in the tissue of the mammal is likely to metastasize.

52. The method of claim 51, wherein the tissue is mammary tissue.

53. The method of claim 51, wherein the cancer is a carcinoma.

54. The method of claim 51, wherein the mammal is a rodent.

55. The method of claim 51, wherein the mammal is a human.

56. The method of claim 51, wherein the binding partner is an antibody is specific for CD11b.

57. The method of claim 51, wherein the chemotactic factor is an epidermal growth factor.

58. The method of claim 51, wherein the motile cells are quantified using a fluorescence-activated cell sorter.

59. The method of claim 51, wherein the motile cells are quantified by microscopic observation.

60. The method of claim 51, wherein the microneedle or capillary is a microneedle.

61. The method of claim 51, wherein the porous matrix comprises matrigel.

62. A method of inhibiting metastasis of a cancer in a tissue of a mammal, the method comprising enhancing collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 activity in the tissue.

63. The method of claim 62, wherein ZBP-1 activity is enhanced in the tissue.

64. The method of claim 62, wherein the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 activity is enhanced by transfecting the tissue with a vector comprising a collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 transgene, wherein the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 transgene is translated from the vector in the tissue.

65. The method of claim 62, wherein the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1activity is enhanced by adding a pharmaceutical composition of collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 protein to the tissue.

66. The method of claim 65, wherein the pharmaceutical composition comprises an agent to enhance penetration of the collagen type III α1, G-protein coupled receptor 26, ZBP-1, or fibroblast growth factor receptor 1 protein into the cell.

67. The method of claim 62, wherein the tissue is mammary tissue.

68. A method of inhibiting metastasis of a cancer in a tissue of a mammal, the method comprising reducing the presence or activity of a protein in the tissue, the protein selected from the group consisting of Arp2/3 p16 subunit, Arp2/3 p21 subunit, alpha subunit of capping protein, beta subunit of capping protein, cofilin, WAVE3, ROCK1, ROCK2, LIMK 1, PKCζ, LIM-kinase, PAK, type II alpha isoform of PI4, 5 kinase, mena, tropomyosin, calpain, gelsolin-like protein (CAPG), zyxin, vinculin, integrin β1, tight junction protein 2, member Ras oncogene family, and epidermal growth factor receptor.

69. The method of claim 68, wherein the presence or activity of the protein is reduced by addition of an antisense molecule, a ribozyme, or an RNAi molecule to the tissue, where the antisense molecule, ribozyme or RNAi molecule specifically inhibits expression of the protein.

70. The method of claim 69, wherein the antisense molecule, ribozyme or RNAi molecule is added to the tissue in a vector that transfects the tissue and expresses the antisense molecule, ribozyme or RNAi.

71. The method of claim 68, wherein the presence or activity of the protein is reduced by addition of an antibody or aptamer to the tissue, wherein the antibody or aptamer specifically binds and reduces the activity of the protein in the tissue.

72. A method of determining resistance of a motile cancer cell population in an animal tissue to a chemotherapeutic agent, the method comprising

obtaining the motile cancer cell population by the method of claim 6;

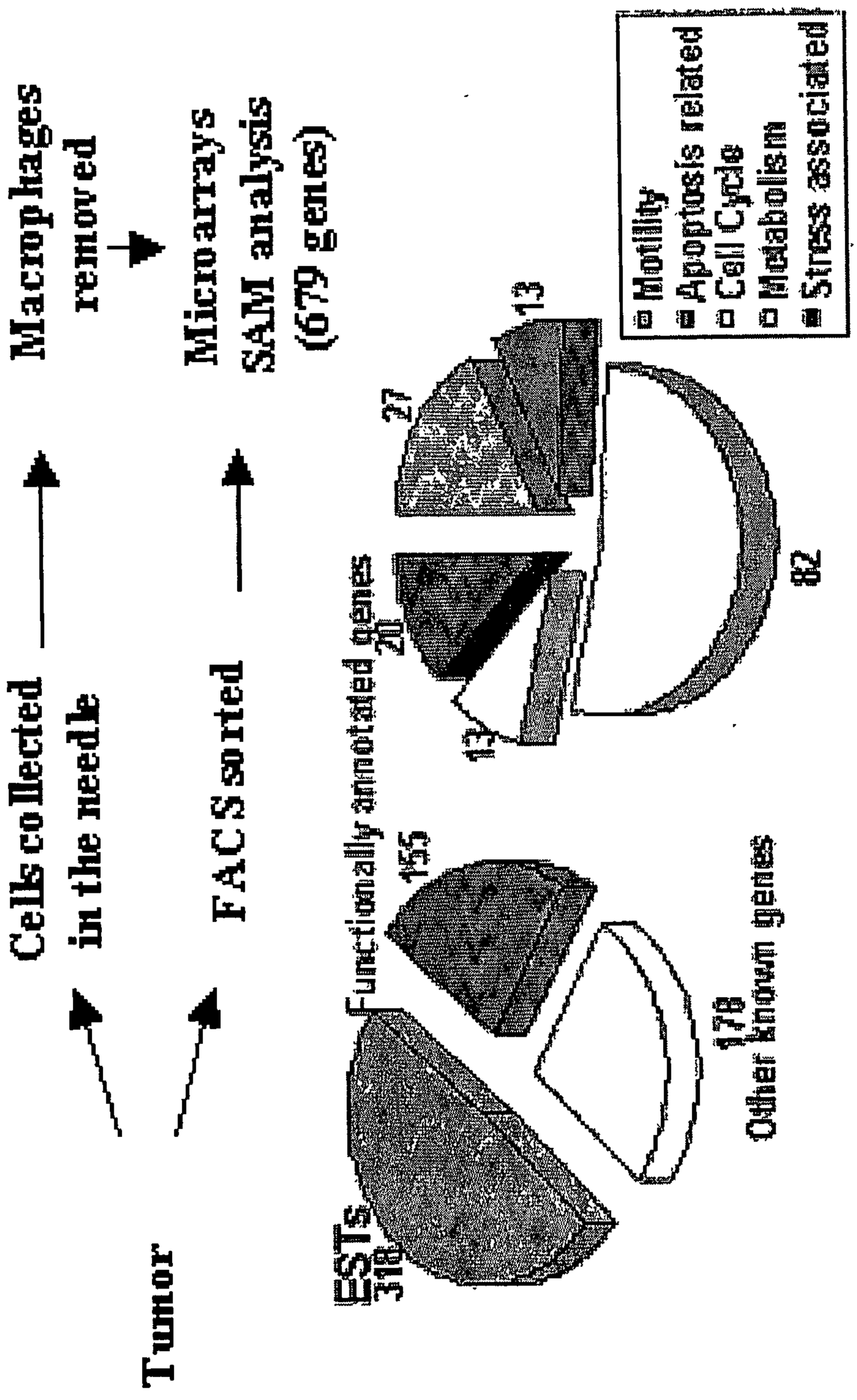
contacting the motile cancer cell population with the chemotherapeutic agent at a concentration and for a time sufficient to cause apoptosis in cancer cells susceptible to the chemotherapeutic agent; and

determining apoptosis in the motile cancer cell population,

wherein less apoptosis in the motile cancer cell population indicates that the motile cancer cell population is resistant to the chemotherapeutic agent.

73. The method of claim 72, wherein the chemotherapeutic agent is doxorobucin, cisplatin, or etoposide.

Replacement Sheet
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FIG. 1



Replacement Sheet

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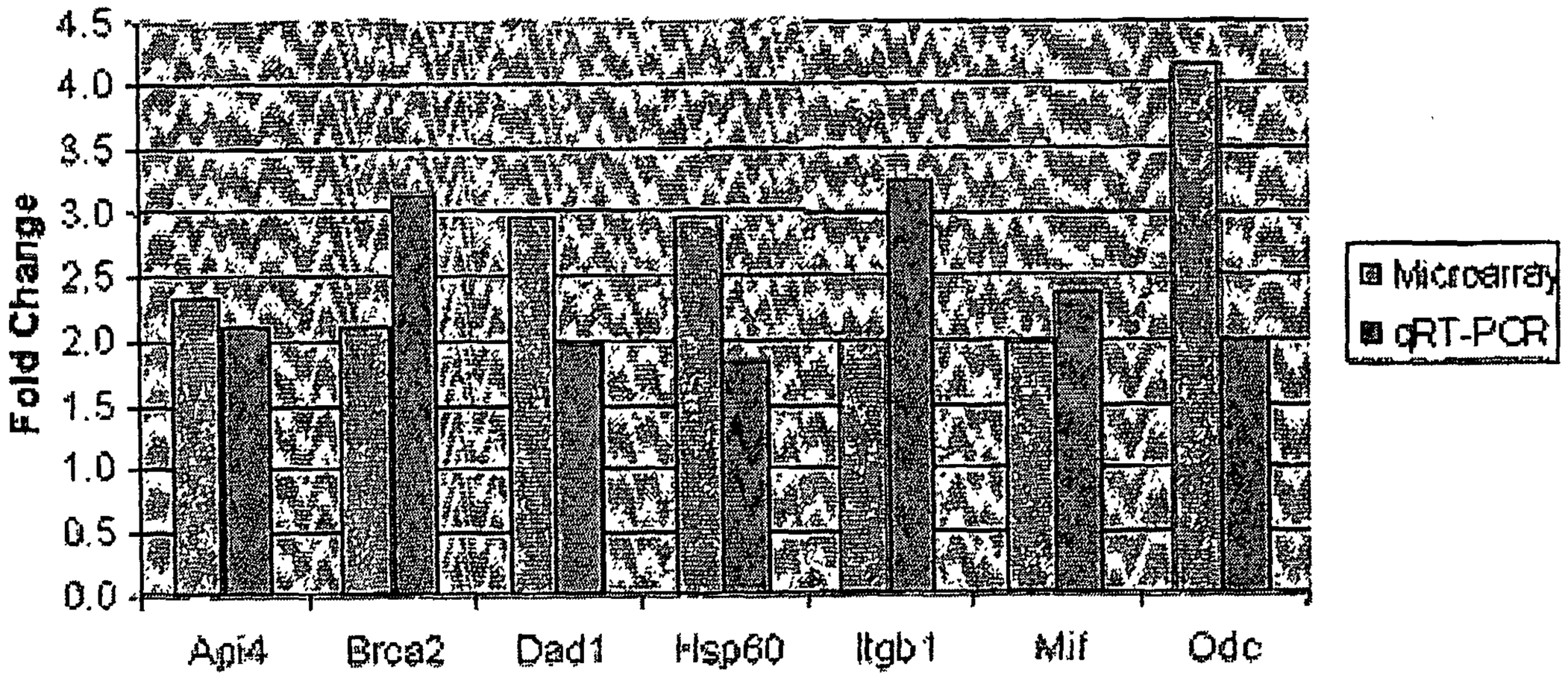
FIG. 2

A

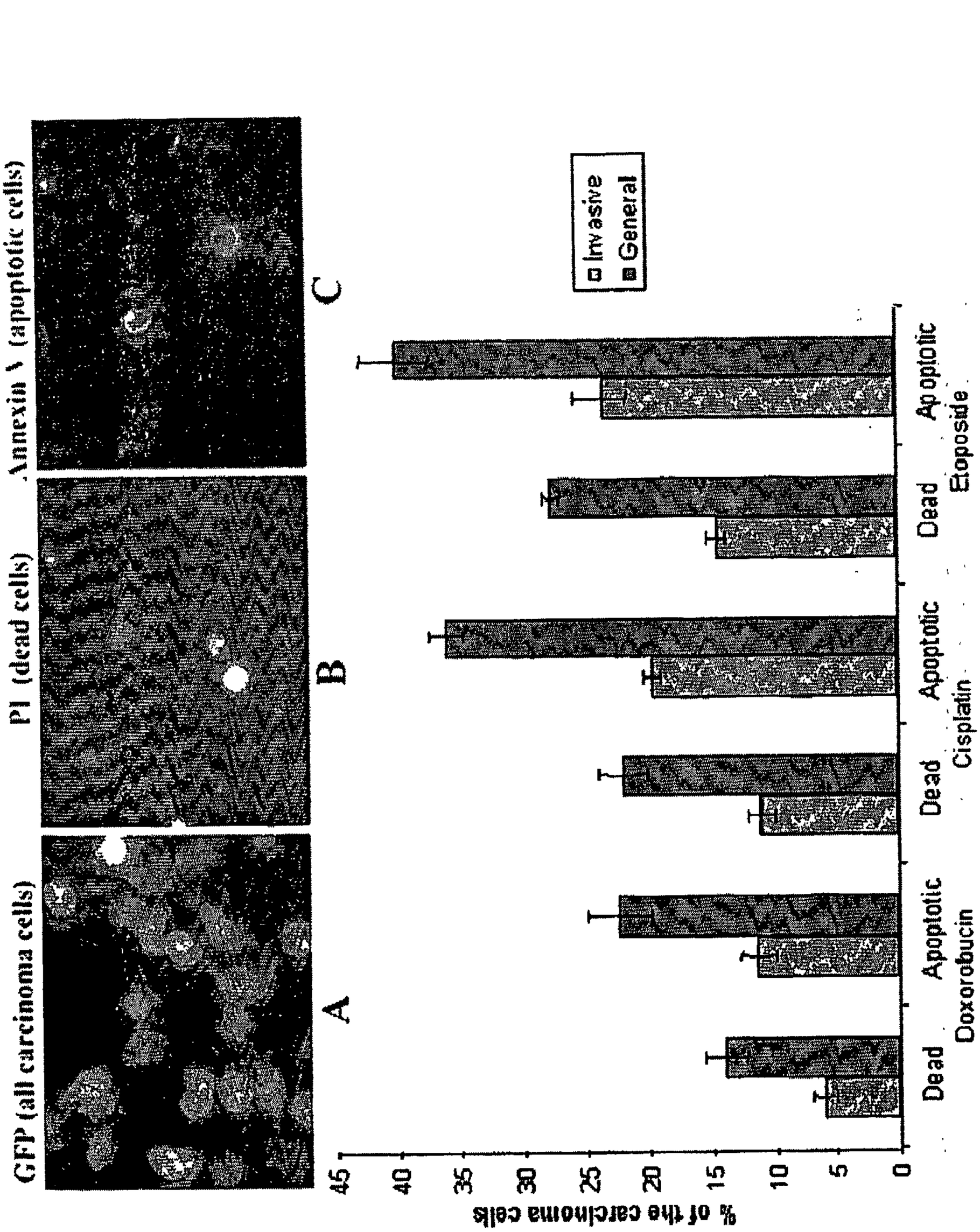
	Anti-apoptotic genes	
Gene	**Description**	**N/F**
ler3	immediate early response 3	4.9
Ubl1a2	ubiquitin-like 1 (sentrin) activating enzyme subunit 2	4.7
Txn	thioredoxin	3.7
Hsp105	heat shock protein, 105 kDa	3.5
Odc	ornithine decarboxylase, structural	3.0
Dad1	Defender against cell death 1	2.7
Trp53	transformation related protein 53	2.5
Hsp60	heat shock protein, 60 kDa	2.4
Api4	apoptosis inhibitor 4	2.3
Cldn3	claudin 3	2.3
Api5	apoptosis inhibitor 5	2.3
Hsp86-1	heat shock protein, 86 kDa 1	2.1
Api1	apoptosis inhibitor 1	2.0
Adam17	a disintegrin and metalloproteinase domain 17	2.0
	Pro-apoptotic genes	
Gene	**Description**	**N/F**
Pdcd4	programmed cell death 4	0.1
Fem1b	feminization 1 b homolog (C. elegans)	0.4
Apaf1	apoptotic protease activating factor 1	0.6
Pdcd8	programmed cell death 8 (apoptosis inducing factor)	0.8
	Cellular apoptosis susceptibility protein	1.1
	ESTs. Highly similar to apoptosis specific protein	1.1
	Apoptosis-associated spec-like protein containing CARD	1.2
AlF	Apoptosis-inducing factor AlF	1.3

Comparison between Microarray and Realtime RT-PCR

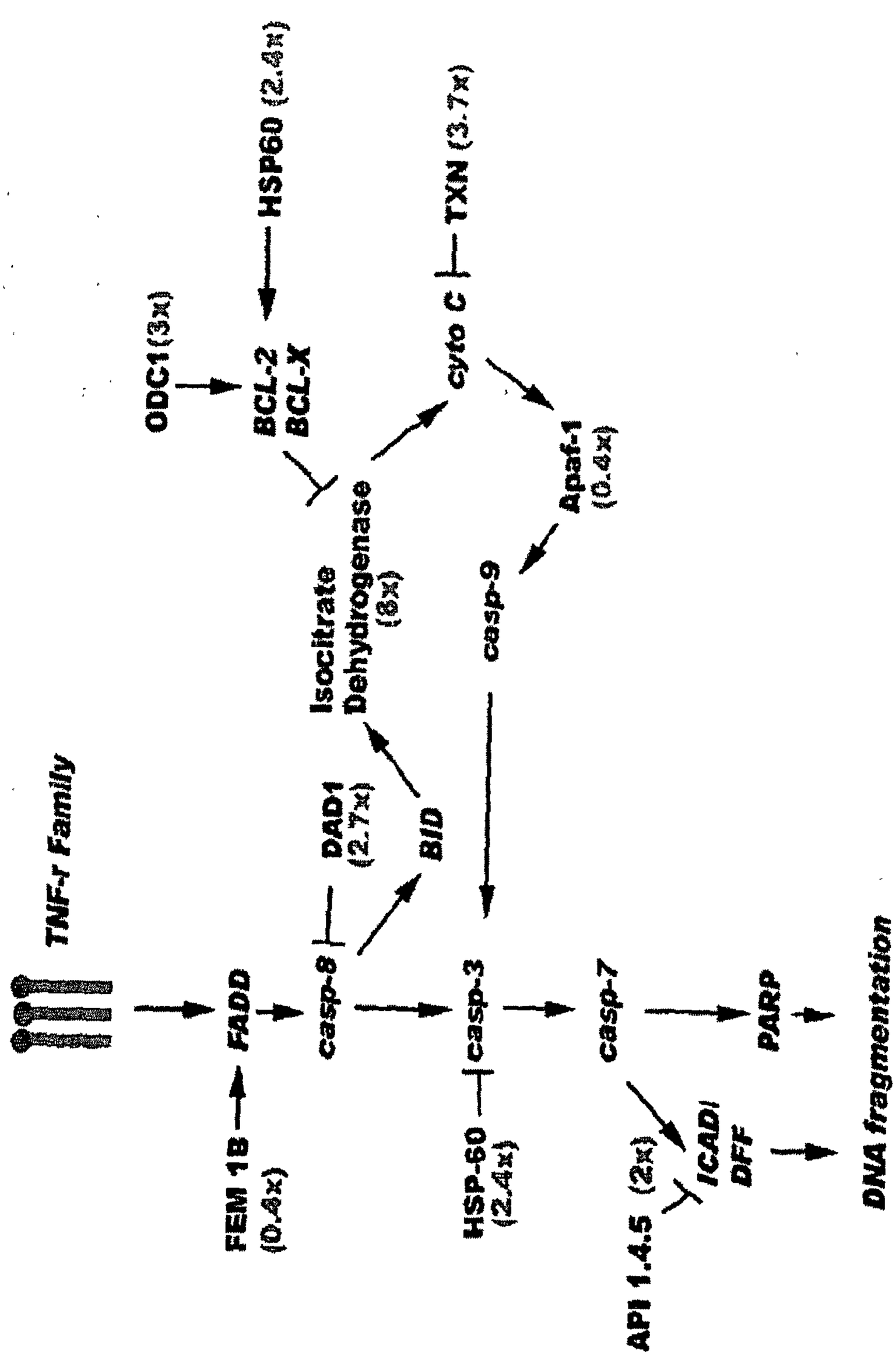
B



Replacement Sheet
3/11
FIG. 3

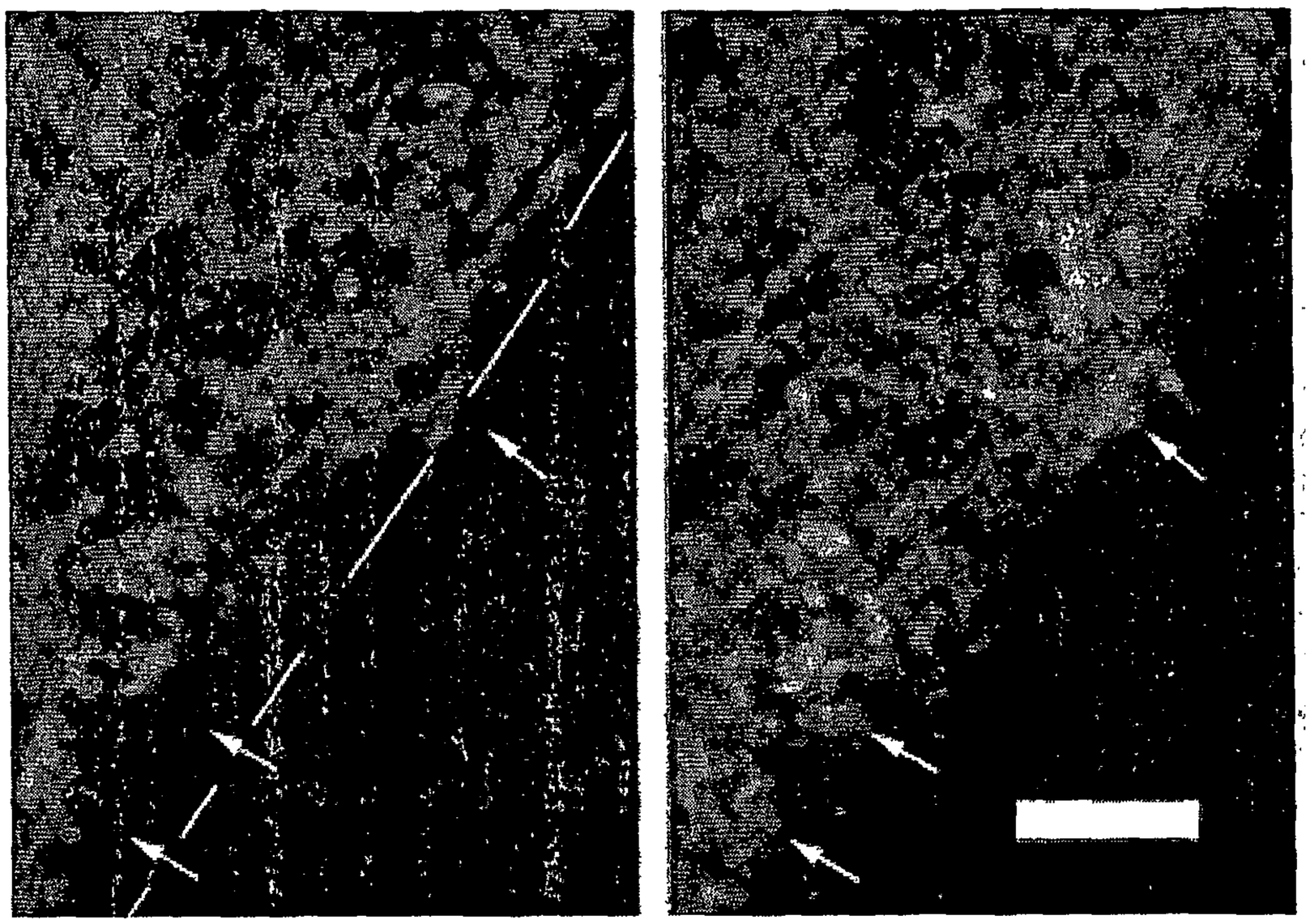


Replacement Sheet
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FIG. 4

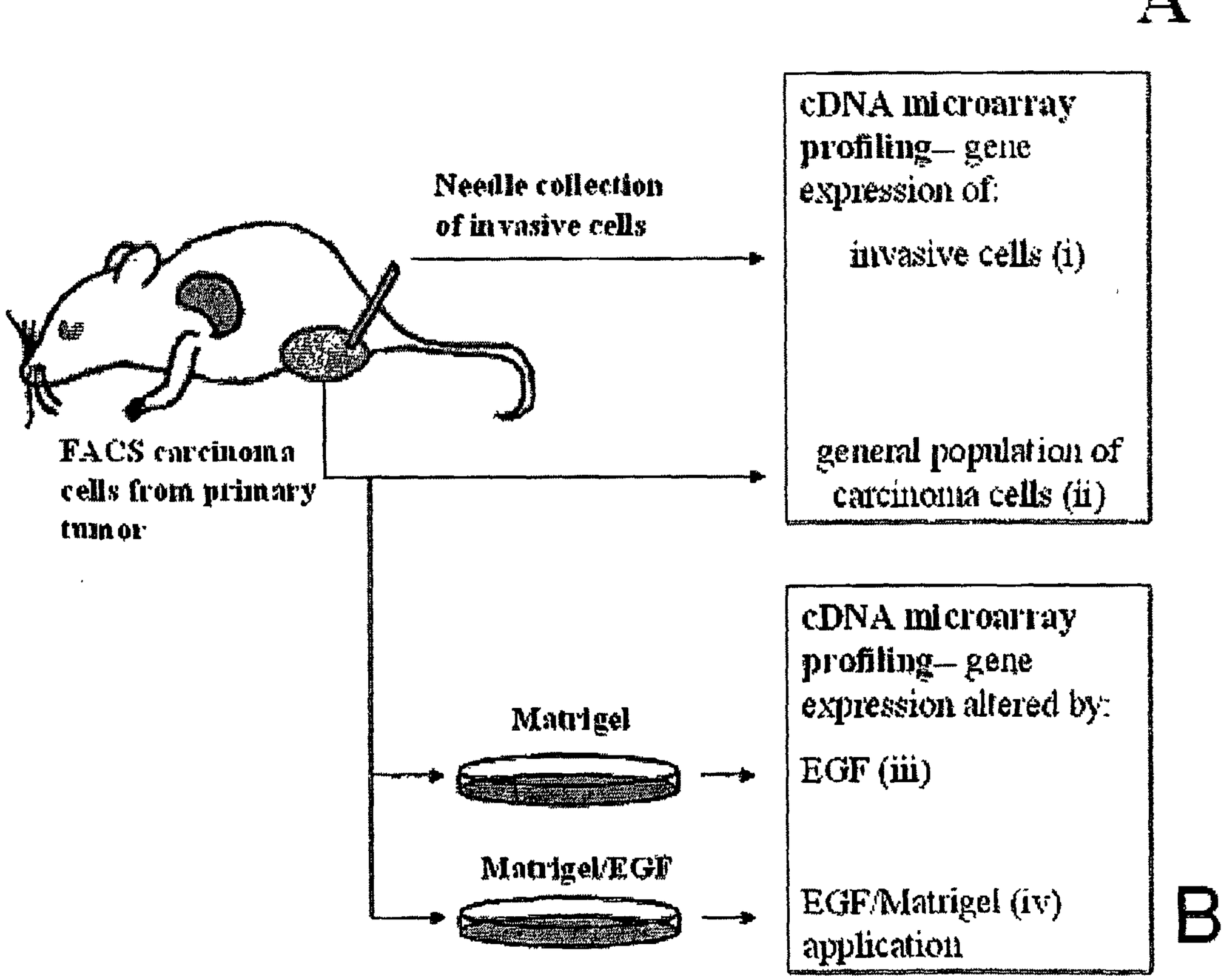


Replacement Sheet 5/11

FIG. 5

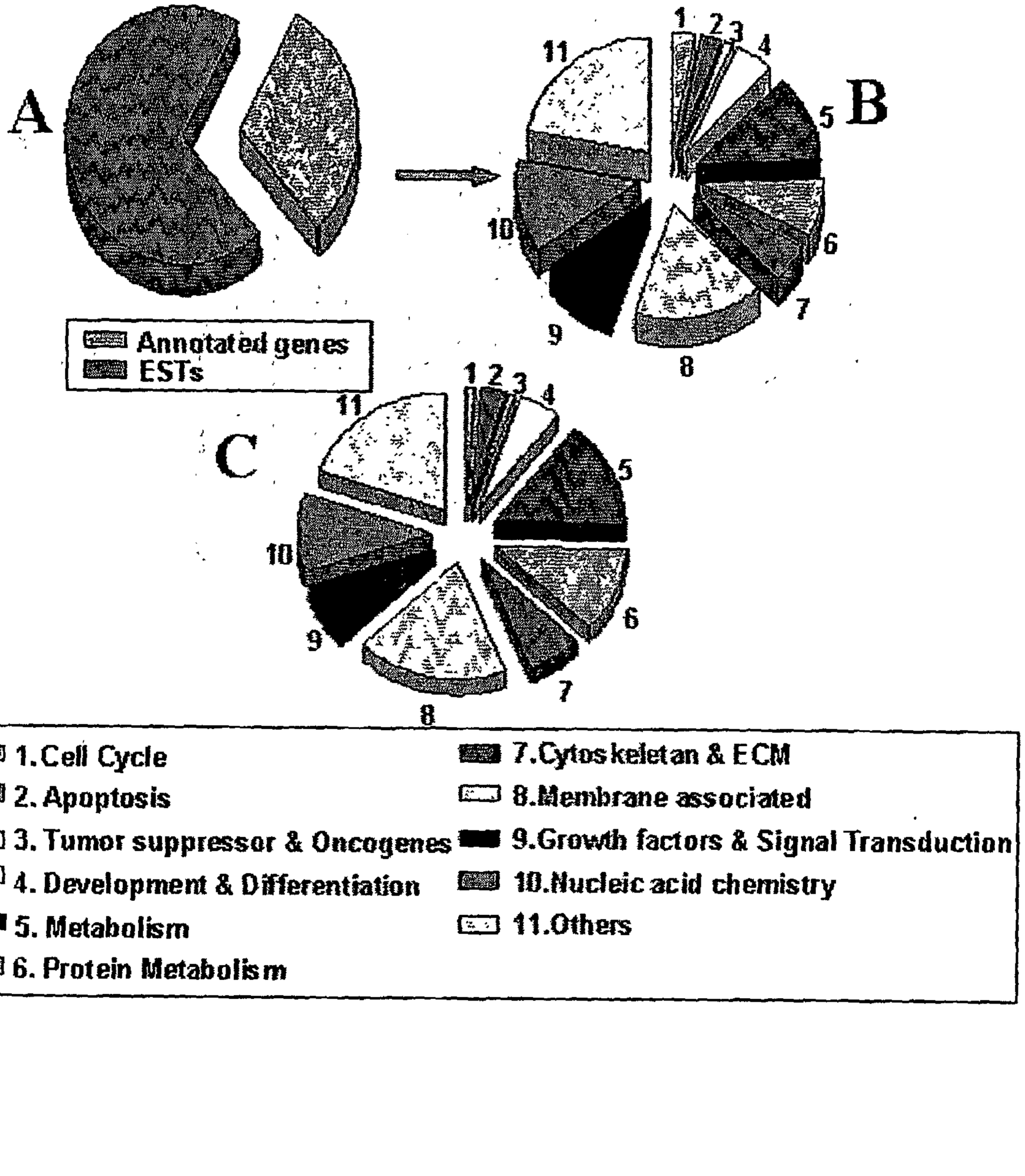


A

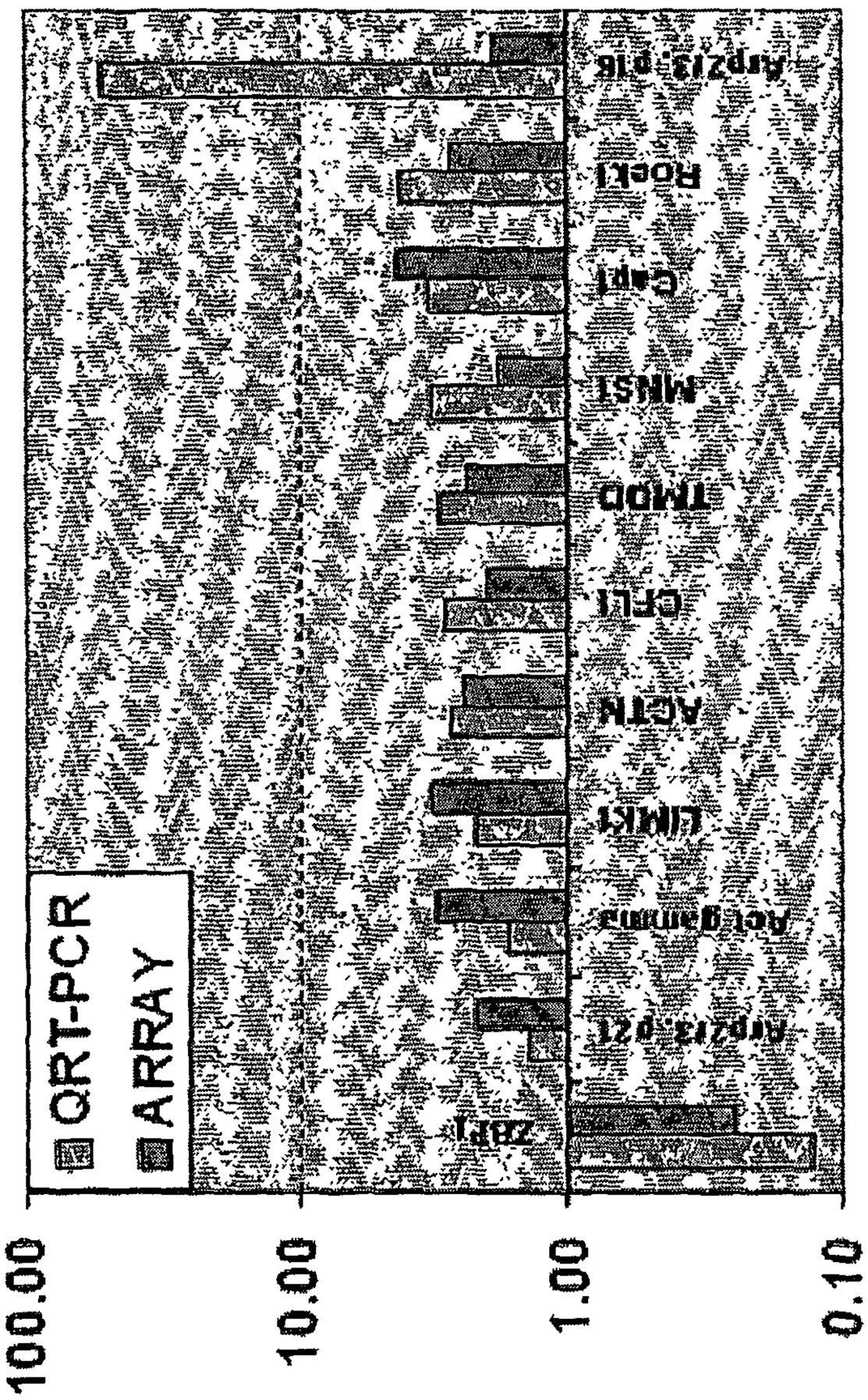


B

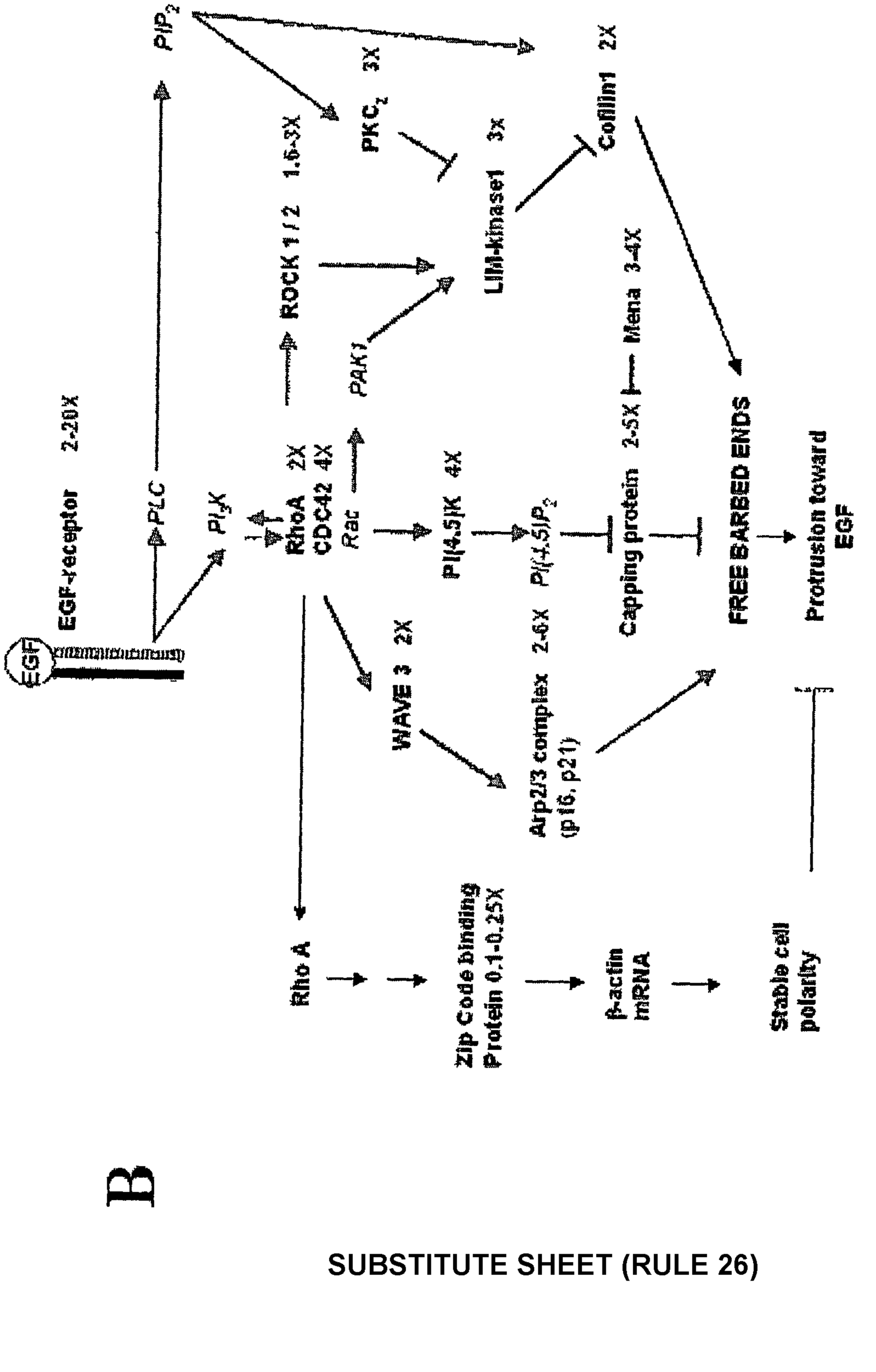
Replacement Sheet
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FIG. 6



Replacement Sheet
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FIG. 7A

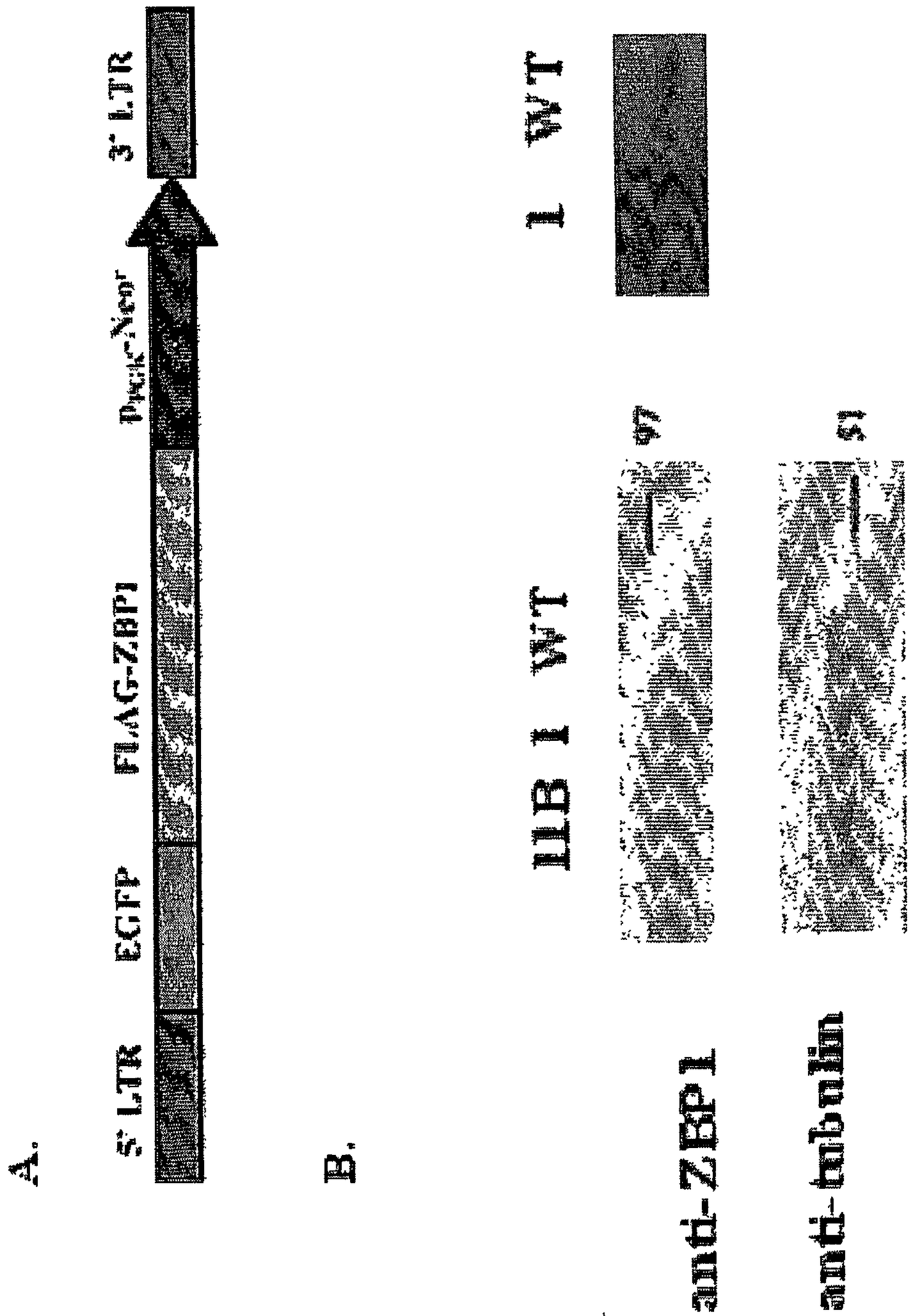


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FIG. 7B



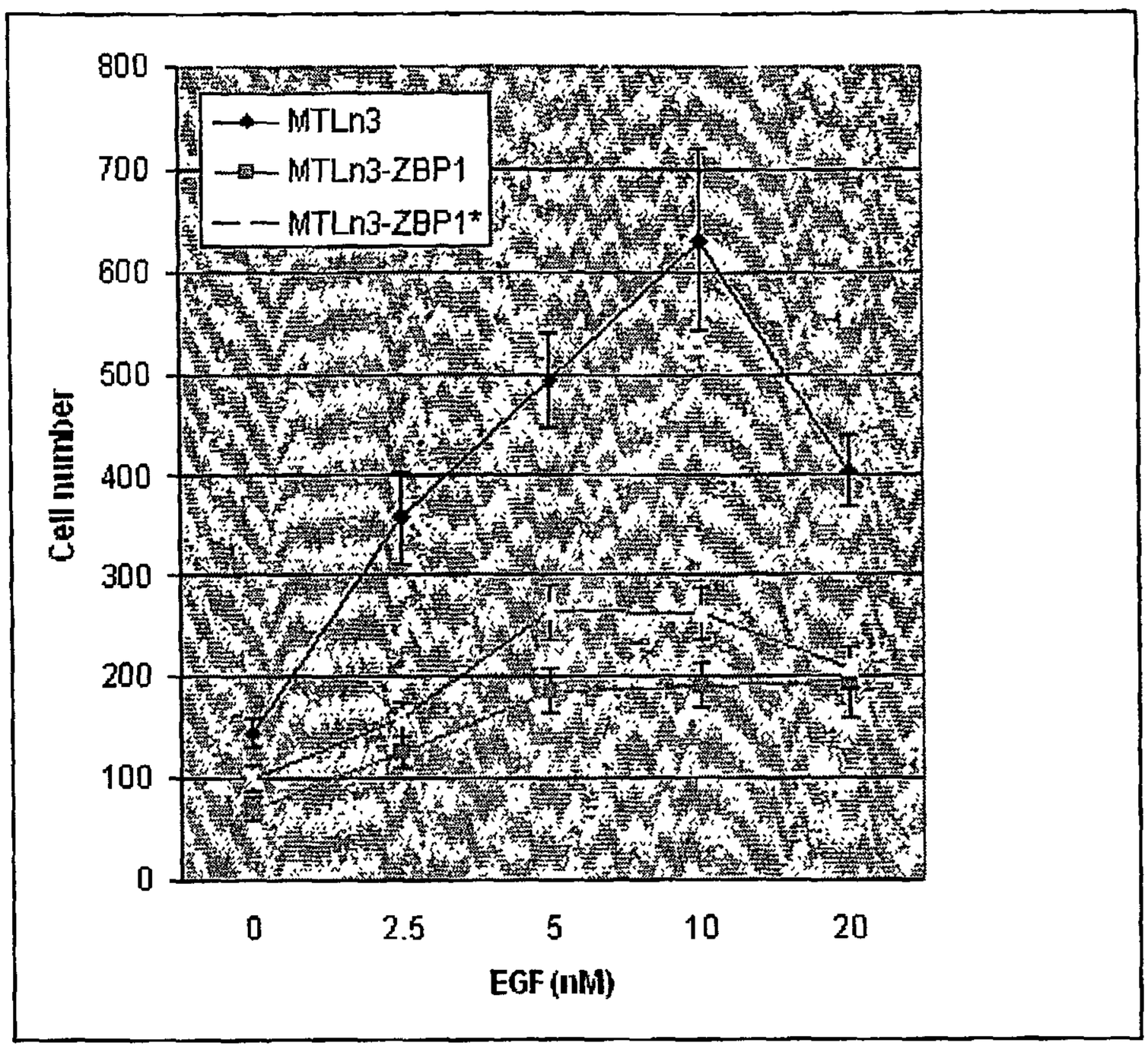
B

Replacement Sheet
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FIG. 8

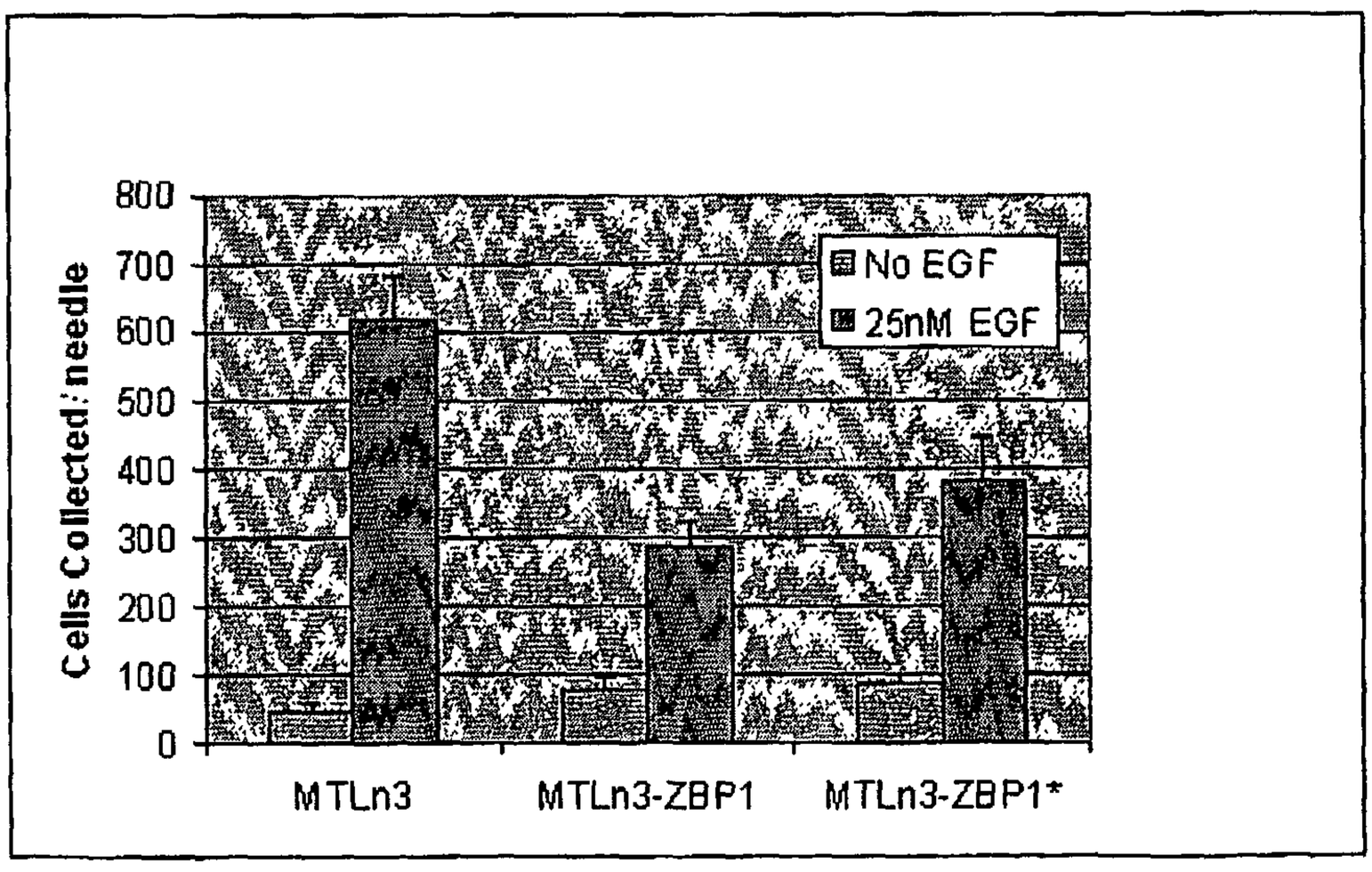


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FIG. 9

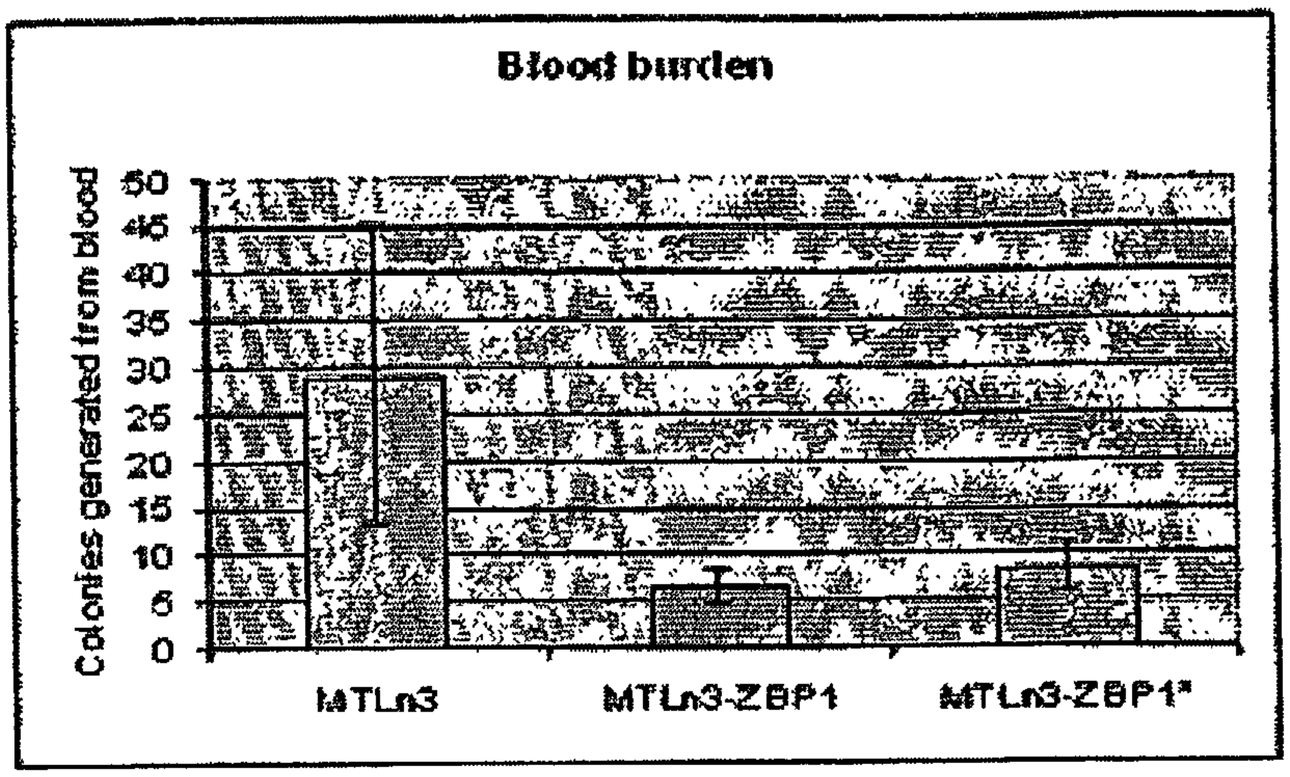
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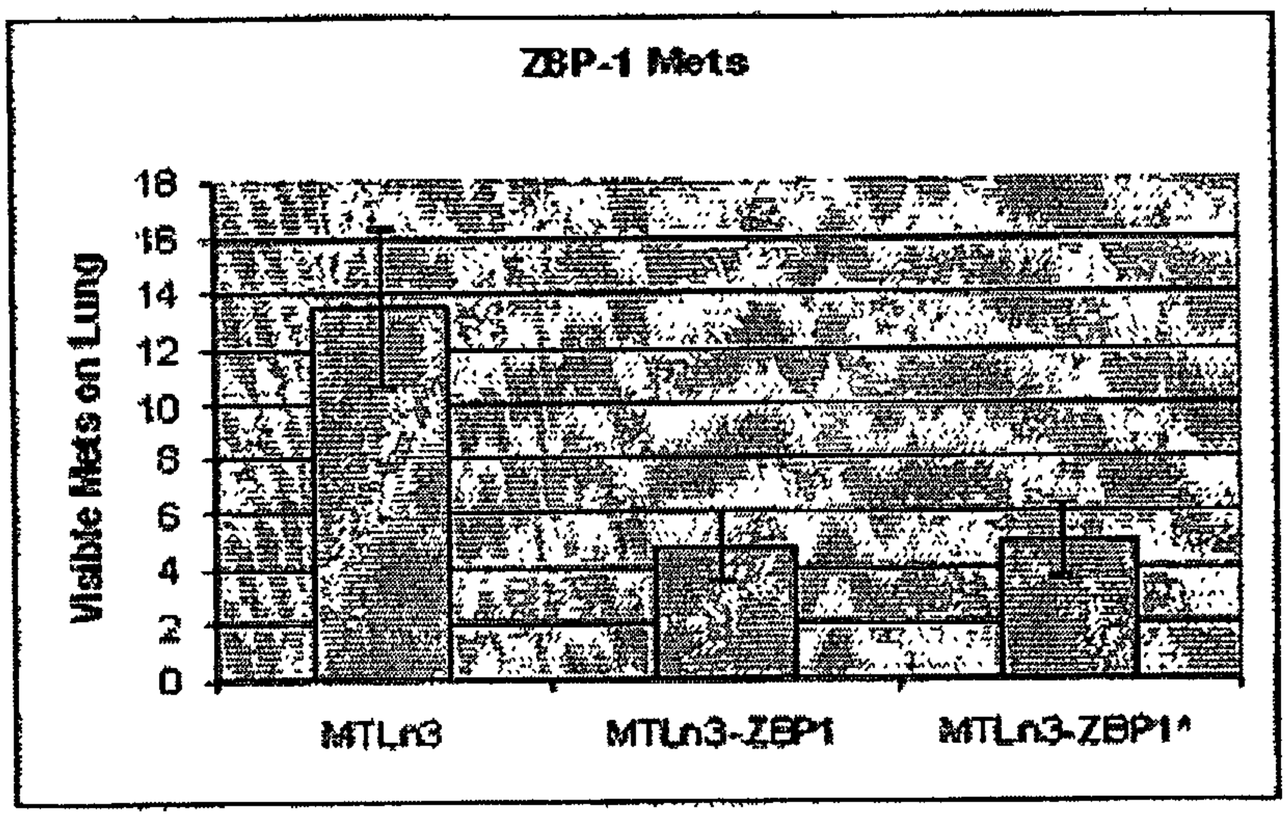
B.



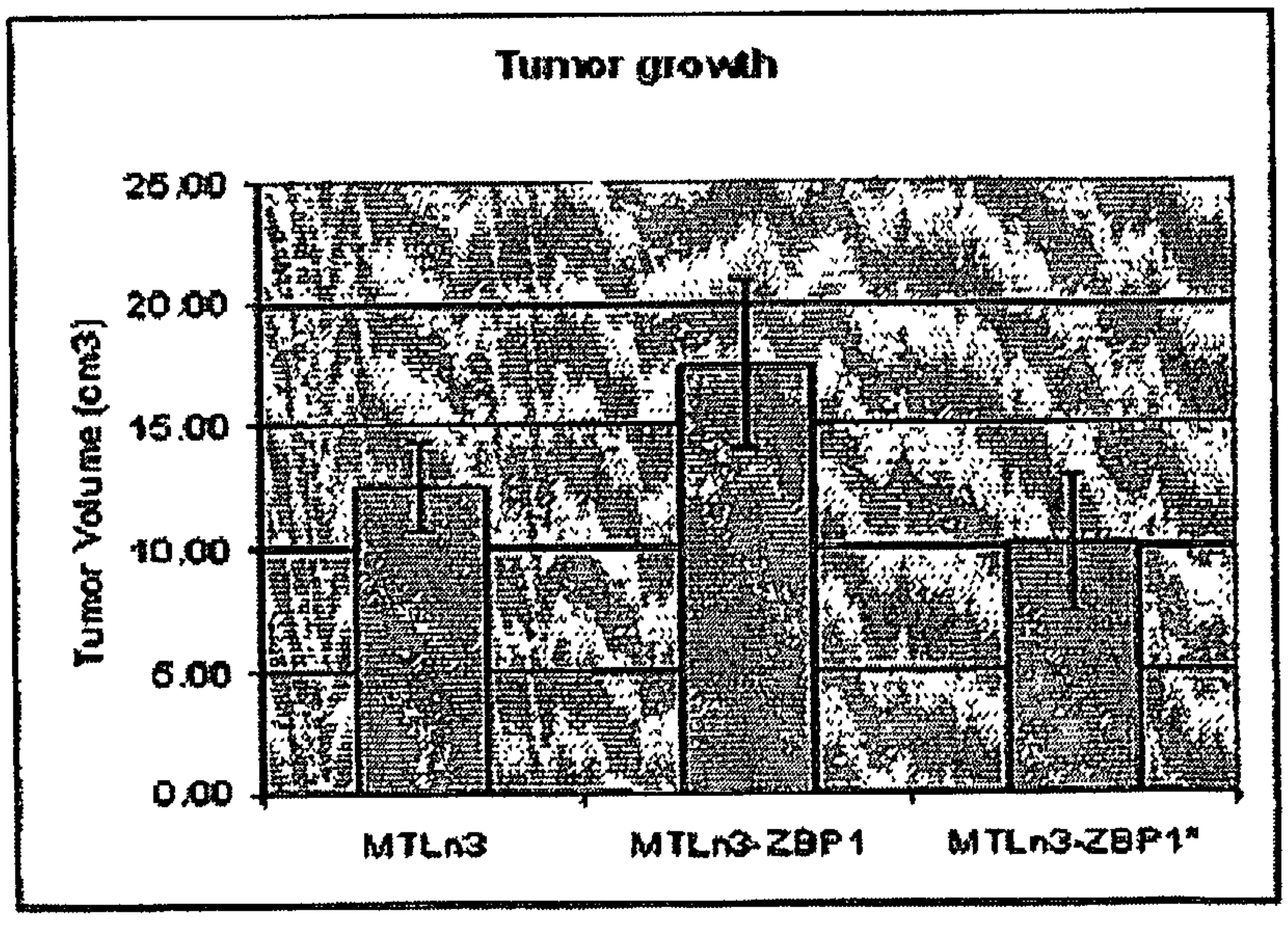
Replacement Sheet
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FIG. 10



A



B



C