Genen controleren hoe cellen werken. Genen maken proteïnen met specifieke functies die acteren als boodschapper. De boodschapper‘proteïne’ moet ieder gen correcte instructies of ‘code’ geven voor de productie van zijn proteïnen om de cel de correcte functie uit te laten voeren (genexpressie).

Alle vormen van kanker beginnen als een of meer genen zijn gemuteerd of veranderd. Dit veroorzaakt een abnormale proteïne of zelfs geen proteïne. Dit kan ervoor zorgen dat cellen oncontroleerbaar gaan delen wat kan leiden tot kanker.

Brontekst:
Genes control how your cells work by making proteins that have specific functions and act as messengers for the cell. Therefore, each gene must have the correct instructions or "code" for making its protein. This is so the protein can perform the correct function for the cell. All cancers begin when one or more genes in a cell are mutated, or changed. This creates an abnormal protein or no protein at all. An abnormal protein provides different information than a normal protein, which can cause cells to multiply uncontrollably and become cancerous.

Bronnen: http://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/genetics-cancer
www.genecards.org

Analyse wetenschappelijk onderzoek naar de impact (verandering) in genexpressie vrouwelijk gluteaal weefsel m.b.t. kanker:

In het onderzoek onderzochte methode verdubbeld natuurlijke vetverbranding van onderhuidse vetten.

Biopsies zijn afgenomen in gluteaal (bil)weefsel. Het is onbekend of de gebruikte methode effect heeft op verandering in genexpressie in andere weefsels/organen.

Dit is een informatieve analyse van veranderingen in expressie van genen die betrekking hebben op kanker. Er kunnen geen rechten aan worden ontleend en/of medische conclusies uit worden getrokken. De analyse is met grootst mogelijke zorg en nauwkeurigheid gemaakt, ondanks deze nauwkeurigheid kan Mevrouw de Vries niet verantwoordelijk worden gesteld voor de inhoud.

Eigenaar Mardan Massages

Nauwe Geldelozepad 15

2012 EV Haarlem

Tel.: 06-23324708

Website: www.mardanmassages.nl - www.antistress.solutions

Pagina 2 v.h. onderzoek:	Gene	Location	Fold change
	AADACL1	**plasma membrane**	**5.17**

Gene name: neutral cholesterol ester hydrolase 1

May be responsible for cholesterol ester hydrolysis in macrophages, thereby contributing to the development of atherosclerosis. Also involved in organ detoxification by hydrolyzing exogenous organophosphorus compounds. May contribute to cancer pathogenesis by promoting tumor cell migration.

	GPNMB	**plasma membrane**	**3.29**

Gene name: glycoprotein (transmembrane) nmb

May be involved in growth delay and reduction of metastatic potential (uitzaaiingen van kwaadaardige gezwellen (tumoren) elders in het lichaam (primaire tumor). Could be a melanogenic enzyme

	ALDH1A3	**cytoplasm**	**3.23**

Gene name: aldehyde dehydrogenase 1 family, member A3

Mutations in this gene have been associated with microphthalmia, isolated 8, and expression changes have also been detected in tumor cells. Seems to be the key enzyme in the formation of an RA gradient along the dorso-ventral axis during the early eye development and also in the development of the olfactory system (reukzintuig).

	IFI30	**cytoplasm**	**2.92**

Gene name interferon, gamma-inducible protein 30

Plays an important role in antigen processing. Facilitates also MHC class I-restricted recognition of exogenous antigens containing disulfide bonds by CD8+ T-cells or crosspresentation

	IL4I1	**cytoplasm**	**2.75**

Gene name: interleukin 4 induced 1

Protein Coding gene. Diseases associated with IL4I1 include Primary Mediastinal Large B-Cell Lymphoma and Posterior Myocardial Infarction.

	TYMS	**nucleus**	**2.56**

Gene name: thymidylate synthetase

This function maintains the dTMP (thymidine-5-prime monophosphate) pool critical for DNA replication and repair. The enzyme has been of interest as a

target for cancer chemotherapeutic agents. Among its related pathways are Purine metabolism and RB in Cancer.

BF373107/ASAH1 cytoplasm 2.02

Gene name: N-acylsphingosine amidohydrolase (acid ceramidase) 1

This enzyme is overexpressed in multiple human cancers and may play a role in cancer progression.

AADAC cytoplasm 1.96

Gene name: arylacetamide deacetylase (esterase)

Microsomal arylacetamide deacetylase competes against the activity of cytosolic arylamine N-acetyltransferase, which catalyzes one of the initial biotransformation pathways for arylamine and heterocyclic amine carcinogens

ST5 unknown 1.91

Gene name: suppression of tumorigenicity 5

This gene was identified by its ability to suppress the tumorigenicity (ontstaan van tumoren) of Hela cells in nude mice. The protein encoded by this gene contains a C-terminal region that shares similarity with the Rab 3 family of small GTP binding proteins. This protein preferentially binds to the SH3 domain of c-Abl kinase, and acts as a regulator of MAPK1/ERK2 kinase, which may contribute to its ability to reduce the tumorigenic phenotype in cells.

SDCBP plasma membrane 1.84

Gene name: syndecan binding protein (syntenin)

Multifunctional adapter protein involved in diverse array of functions including trafficking of transmembrane proteins, neuro and immunomodulation, exosome biogenesis, and tumorigenesis. In concert with SDC1/4 and PDCD6IP, regulates exosome biogenesis (PubMed:22660413). Regulates migration, growth, proliferation, and cell cycle progression in a variety of cancer types

BIRC3 cytoplasm 1.81

Gene name: baculoviral IAP repeat-containing 3

This gene encodes a member of the IAP family of proteins that inhibit (verhinderen) apoptosis by binding to tumor necrosis factor receptor-associated factors TRAF1 and TRAF2, probably by interfering with activation of ICE-like proteases. The encoded protein inhibits apoptosis induced by serum deprivation but does not affect apoptosis resulting from exposure to menadione, a potent inducer of free radicals. Multi-functional protein which

regulates not only caspases and apoptosis, but also modulates inflammatory signaling and immunity, mitogenic kinase signaling and cell proliferation, as well as cell invasion and metastasis.

GSTT2 **cytoplasm** **1.73**

Gene name: glutathione S-transferase theta 2

Human GSTs can be divided into five main classes: alpha, mu, pi, theta, and zeta. The theta class includes GSTT1, GSTT2, and GSTT2B. GSTT2 and GSTT2B are nearly identical to each other, and share 55% amino acid identity with GSTT1. All three genes may play a role in human carcinogenesis.

TPMT **cytoplasm** **1.65**

Gene name: thiopurine S-methyltransferase

This gene encodes the enzyme that metabolizes thiopurine drugs via S-adenosyl-L-methionine as the S-methyl donor and S-adenosyl-L-homocysteine as a byproduct. Thiopurine drugs such as 6-mercaptopurine are used as chemotherapeutic agents.

Pagina 3 v.h. onderzoek: **MSH2** **nucleus** **1.42**

Gene name: mutS homolog 2, colon cancer, nonpolyposis type 1 (E. coli)

This locus is frequently mutated in hereditary nonpolyposis colon cancer (HNPCC). When cloned, it was discovered to be a human homolog of the E. coli mismatch repair gene mutS, Component of the post-replicative DNA mismatch repair system (MMR). Forms two different heterodimers: MutS alpha (MSH2-MSH6 heterodimer) and MutS beta (MSH2-MSH3 heterodimer) which binds to DNA mismatches thereby initiating DNA repair. When bound, heterodimers bend the DNA helix and shields approximately 20 base pairs.

CBR1 **cytoplasm** **1.42**

Gene name: carbonyl reductase 1

The protein encoded by this gene belongs to the short-chain dehydrogenases/reductases (SDR) family. Catalyzes the reduction of the antitumor anthracyclines doxorubicin and daunorubicin to the cardiotoxic compounds doxorubicinol and daunorubicinol.

LOXL1 **extracellular space** **1.35**

Gene name: lysyl oxidase-like 1

This gene encodes a member of the lysyl oxidase family of proteins. The prototypic member of the family is essential to the biogenesis of connective tissue, encoding an extracellular copper-dependent amine oxidase that catalyzes the first step in the formation of crosslinks in collagen and elastin. The encoded preproprotein is proteolytically processed to generate the mature enzyme. A highly conserved amino acid sequence at the C-terminus

end appears to be sufficient for amine oxidase activity, suggesting that each family member may retain this function. The N-terminus is poorly conserved and may impart (het geven van) additional roles in developmental regulation, senescence, tumor suppression, cell growth control, and chemotaxis to each member of the family.

KRAS **cytoplasm** **1.32**

Gene name: v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog

This gene, a Kirsten ras oncogene homolog from the mammalian ras gene family, encodes a protein that is a member of the small GTPase superfamily. Ras proteins bind GDP/GTP and possess intrinsic GTPase activity. Plays an important role in the regulation of cell proliferation (PubMed:23698361, PubMed:22711838). Plays a role in promoting oncogenic events by inducing transcriptional silencing of tumor suppressor genes (TSGs) in colorectal cancer (CRC) cells in a ZNF304-dependent manner

LAMP2 **plasma membrane** **1.28**

Gene name: ysosomal-associated membrane protein 2

Implicated in tumor cell metastasis. May function in protection of the lysosomal membrane from autodigestion, maintenance of the acidic environment of the lysosome, adhesion when expressed on the cell surface (plasma membrane), and inter- and intracellular signal transduction. Protects cells from the toxic effects of methylating mutagens.

RAB21 **cytoplasm** **1.22**

Gene name: RAB21, member RAS oncogene family

This gene is downregulated by the tumor suppressor miR-200b, and miRNA-200b is itself downregulated in glioma tissues.

CHFR **nucleus** **–1.16**

Gene name: checkpoint with forkhead and ring finger domains

This gene encodes an E3 ubiquitin-protein ligase required for the maintenance of the antephase checkpoint that regulates cell cycle entry into mitosis and, therefore, may play a key role in cell cycle progression and tumorigenesis (ontstaan van tumoren).

Pagina 4 v.h. onderzoek: **NOS3** **cytoplasm** **–1.17**

Gene name: nitric oxide synthase 3 (endothelial cell)

Nitric oxide is a reactive free radical which acts as a biologic mediator in several processes, including neurotransmission and antimicrobial and antitumoral activities.

SEPT4 **cytoplasm** **–1.20**

Gene name: septin 4

This gene is highly expressed in brain and heart. Alternatively spliced transcript variants encoding different isoforms have been described for this gene. One of the isoforms (known as ARTS) is distinct; it is localized to the mitochondria, and has a role in apoptosis and cancer

MGAT4B unknown –1.20

Gene name: mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase,

The encoded protein may play a role in regulating the availability of serum glycoproteins, oncogenesis (ontstaan van (kanker) gezwellen), and differentiation

MRAS plasma membrane –1.21

Gene name: muscle RAS oncogene homolog

This gene encodes a member of the Ras family of small GTPases. These membrane-associated proteins function as signal transducers in multiple processes including cell growth and differentiation, and dysregulation of Ras signaling has been associated with many types of cancer. The encoded protein may play a role in the tumor necrosis factor-alpha and MAP kinase signaling pathways. (**Necrose** is vaak schadelijk voor het organisme aangezien de celinhoud niet meteen verwijderd wordt, en zo omliggende cellen kan aantasten).

AKR7A2 cytoplasm –1.23

Gene name: aldo-keto reductase family 7, member A2 (aflatoxin aldehyde reductase)

May be involved in protection of liver against the toxic and carcinogenic effects of AFB1, a potent hepatocarcinogen.

GBP2 cytoplasm –1.23

Gene name: guanylate binding protein 2, interferon-inducible

This gene belongs to the guanine-binding protein (GBP) family, which includes interferon-induced proteins that can bind to guanine nucleotides. The protein may play a role as a **marker** of squamous cell carcinomas.

MGLL plasma membrane –1.24

Gene name: monoglyceride lipase

This gene encodes a serine hydrolase of the AB hydrolase superfamily that catalyzes the conversion of monoacylglycerides to free fatty acids and glycerol. Expression of this gene may play a role in cancer tumorigenesis (ontstaan van tumoren) and metastasis.

LEPREL1 unknown -1.24

Gene name: leprecan-like 1

This gene encodes a member of the prolyl 3-hydroxylase subfamily of 2-oxo-glutarate-dependent dioxygenases. These enzymes play a critical role in collagen chain assembly, stability and cross-linking by catalyzing post-translational 3-hydroxylation of proline residues. Downregulation of this gene may play a role in breast cancer. Alternatively spliced transcript variants encoding multiple isoforms have been observed for this gene.

NDUFA13 cytoplasm -1.25

Gene name: NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 13

This gene encodes a subunit of the mitochondrial membrane respiratory chain NADH dehydrogenase. The protein binds the signal transducers and activators of transcription 3 (STAT3) transcription factor, and can function as a tumor suppressor.

Pagina 5 v.h. onderzoek: **PHLPPL cytoplasm -1.26**

Gene name: PH domain and leucine rich repeat protein phosphatase 2

PHLPP2 (PH Domain And Leucine Rich Repeat Protein Phosphatase 2) is a Protein Coding gene. Inhibits cancer cell proliferation and may act as a tumor suppressor. (Remt proliferatie (verspreiding) van kankercellen en kan fungeren als een tumor suppressor.

AIFM2 cytoplasm -1.26

Gene name: apoptosis-inducing factor, mitochondrion-associated, 2

This gene encodes a flavoprotein oxidoreductase that binds single stranded DNA and is thought to contribute to apoptosis in the presence of bacterial and viral DNA. The expression of this gene is also found to be induced by tumor suppressor protein p53 in colon cancer cells.

AKR7A3 cytoplasm -1.26

Gene name: aldo-keto reductase family 7, member A3 (aflatoxin aldehyde reductase)

May be involved in protection of liver against the toxic and carcinogenic effects of AFB1, a potent hepatocarcinogen.

ANG extracellular space-1.27

Gene name: angiogenin, ribonuclease, RNase A family, 5

Binds to actin on the surface of endothelial cells; once bound, angiogenin is endocytosed and translocated to the nucleus. Stimulates ribosomal RNA

synthesis including that containing the initiation site sequences of 45S rRNA. Cleaves tRNA within anticodon loops to produce tRNA-derived stress-induced fragments (tiRNAs) which inhibit protein synthesis and triggers the assembly of stress granules (SGs). Angiogenin induces vascularization of normal and malignant tissues. (induceerd (op gang brengen van) doorbloeding van normale en kwaadaardige weefsels)

HSD17B1 cytoplasm -1.28

Gene name: hydroxysteroid (17-beta) dehydrogenase 1

HSD17B1 (Hydroxysteroid (17-Beta) Dehydrogenase 1) is a Protein Coding gene. Diseases associated with HSD17B1 include Acute T Cell Leukemia and Testicular Germ Cell Tumor. Among its related pathways are Prostate Cancer and Estrone metabolism.

TXN2 cytoplasm -1.34

Gene name: thioredoxin 2

This nuclear gene encodes a mitochondrial member of the thioredoxin family, a group of small multifunctional redox-active proteins. Could be involved in the resistance to anti-tumor agents. Possesses a dithiol-reducing activity.

PIN1 nucleus -1.39

Gene name: peptidylprolyl cis/trans isomerase, NIMA-interacting 1

Peptidyl-prolyl cis/trans isomerases (PPIases) catalyze the cis/trans isomerization of peptidyl-prolyl peptide bonds. This gene encodes one of the PPIases, which specifically binds to phosphorylated ser/thr-pro motifs to catalytically regulate the post-phosphorylation conformation of its substrates. The conformational regulation catalyzed by this PPIase has a profound impact on key proteins involved in the regulation of cell growth, genotoxic and other stress responses, the immune response, induction and maintenance of pluripotency, germ cell development, neuronal differentiation, and survival. This enzyme also plays a key role in the pathogenesis (het ontstaan van) of Alzheimer's disease and many cancers. Can transactivate multiple oncogenes and induce centrosome amplification, chromosome instability and cell transformation.

Pagina 6 v.h. onderzoek: **RAB23 cytoplasm -1.44**

Gene name: RAB23, member RAS oncogene family

This gene encodes a small GTPase of the Ras superfamily. Rab proteins are involved in the regulation of diverse cellular functions associated with intracellular membrane trafficking, including autophagy and immune response to bacterial infection. The encoded protein may play a role in central nervous system development by antagonizing sonic hedgehog signaling. Disruption of this gene has been implicated in Carpenter syndrome as well as cancer. Alternative splicing results in multiple transcript variants.

RHOB cytoplasm -1.44

Gene name: ras homolog gene family, member B

Plays a negative role in tumorigenesis as deletion causes tumor formation.

BRAF cytoplasm -1.46

Gene name: v-raf murine sarcoma viral oncogene homolog B1

This gene encodes a protein belonging to the raf/mil family of serine/threonine protein kinases. This protein plays a role in regulating the MAP kinase/ERKs signaling pathway, which affects cell division, differentiation, and secretion. Mutations in this gene are associated with cardiofaciocutaneous syndrome, a disease characterized by heart defects, mental retardation and a distinctive facial appearance. Mutations in this gene have also been associated with various cancers, including non-Hodgkin lymphoma, colorectal cancer, malignant melanoma, thyroid carcinoma, non-small cell lung carcinoma, and adenocarcinoma of lung. A pseudogene, which is located on chromosome X, has been identified for this gene. BRAF (B-Raf Proto-Oncogene, Serine/Threonine Kinase) is a Protein Coding gene. Diseases associated with BRAF include Cardiofaciocutaneous Syndrome and Lung Cancer.

ALDH1L1 cytoplasm -1.47

Gene name: aldehyde dehydrogenase 1 family, member L1

Loss of function or expression of this gene is associated with decreased apoptosis, increased cell motility, and cancer progression.

GPX1 cytoplasm -1.55

Gene name: glutathione peroxidase 1

This protein is characterized in a polyalanine sequence polymorphism in the N-terminal region, which includes three alleles with five, six or seven alanine (ALA) repeats in this sequence. The allele with five ALA repeats is significantly associated with breast cancer risk.

ST6GALNAC1 cytoplasm -1.58

Gene name: ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 1. The cancer-associated sialyl-Tn (sTn) antigen is formed by ST6GALNAC1-catalyzed sialylation of GalNAc residues on mucins

ALDH2 cytoplasm -1.80

Gene name: aldehyde dehydrogenase 2 family (mitochondrial)

This protein belongs to the aldehyde dehydrogenase family of proteins. Aldehyde dehydrogenase is the second enzyme of the major oxidative pathway of alcohol metabolism. The increased exposure to acetaldehyde in

individuals with the catalytically inactive form may also confer greater susceptibility to many types of cancer.

Impact op in gen-expressie: G-protein coupled receptor

Pagina 7 v.h. onderzoek: **EMR2** **plasma membrane 2.11**

Gene name: egf-like module containing, mucin-like, hormone receptor-like 2

The encoded protein is expressed mainly in myeloid cells (leukemie) where it promotes cell-cell adhesion through interaction with chondroitin sulfate chains.

MC1R **plasma membrane 1.58**

Gene name: melanocortin 1 receptor (alpha melanocyte stimulating hormone receptor)

This intronless gene encodes the receptor protein for melanocyte-stimulating hormone (MSH)

GPR68 **plasma membrane 1.48**

Gene name: G protein-coupled receptor 68

The receptor is almost silent at pH 7.8 but fully activated at pH 6.8. Function also as a metastasis suppressor gene in prostate cancer.

GPR125 **plasma membrane -1.41**

Gene name: G protein-coupled receptor 125

This membrane protein may play a role in tumor angiogenesis (vorming van nieuwe bloedvaten vanuit bestaande bloedvaten) through its interaction with the human homolog of the Drosophila disc large tumor suppressor gene.

CMTM7 **extracellular space 1.46**

Gene name: CKLF-like MARVEL transmembrane domain containing 7

This gene acts as a tumor suppressor that regulates G1/S transition in the cell cycle, and epidermal growth factor receptor/protein kinase B signaling during tumor pathogenesis.

GRN **extracellular space 1.34**

Gene name: granulin

Granulin family members are important in normal development, wound healing, and tumorigenesis.

Pagina 8 v.h. onderzoek: **HDGF** **extracellular space -1.26**

Gene name: hepatoma-derived growth factor

High levels of expression of this gene enhance the growth of many tumors.

FGF2 **extracellular space** **-1.31**

Gene name: fibroblast growth factor 2 (basic)

This protein has been implicated in diverse biological processes, such as limb and nervous system development, wound healing, and tumor growth.

GAS6 **extracellular space** **-1.39**

Gene name: growth arrest-specific 6

This gene is frequently overexpressed in many cancers and has been implicated as an adverse prognostic marker. Elevated protein levels are additionally associated with a variety of disease states, including venous thromboembolic disease, systemic lupus erythematosus, chronic renal failure, and preeclampsia.

KCTD12 **unknown** **-1,23**

Gene name: potassium channel tetramerisation domain containing 12

KCTD12 (Potassium Channel Tetramerization Domain Containing 12) is a Protein Coding gene. Diseases associated with KCTD12 include Gastrointestinal Stromal Tumor.

SYK **cytoplasm** **2.13**

Gene name:spleen tyrosine kinase

This protein is widely expressed in hematopoietic cells and is involved in coupling activated immunoreceptors to downstream signaling events that mediate diverse cellular responses, including proliferation, differentiation, and phagocytosis. It is thought to be a modulator of epithelial cell growth and a potential tumour suppressor in human breast carcinomas.

STK4 **cytoplasm** **1.60**

Gene name: serine/threonine kinase 4

Stress-activated, pro-apoptotic kinase which, following caspase-cleavage, enters the nucleus and induces chromatin condensation followed by internucleosomal DNA fragmentation. Key component of the Hippo signaling pathway which plays a pivotal role in organ size control and tumor suppression by restricting proliferation and promoting apoptosis. STK3/MST2 and STK4/MST1 are required to repress proliferation of mature hepatocytes, to prevent activation of facultative adult liver stem cells (oval cells), and to inhibit (verhinderen van) tumor formation.

PKM2 **cytoplasm** **1.52**

Gene name: pyruvate kinase, muscle

Plays a general role in caspase independent cell death of tumor cells.

DGKD **cytoplasm** **1.33**

Gene name: diacylglycerol kinase, delta 130kDa

May function as signaling molecule. Isoform 2 may be involved in cell growth and tumorigenesis. Involved in clathrin-dependent endocytosis.

LATS2 **nucleus** **-1.23**

Gene name: LATS, large tumor suppressor, homolog 2 (Drosophila)

This gene encodes a serine/threonine protein kinase belonging to the LATS tumor suppressor family.

HSPB8 **cytoplasm** **-1.24**

Gene name: heat shock 22kDa protein 8

The expression of this gene in induced (op gang gebracht) by estrogen in estrogen receptor-positive breast cancer cells.

ILK **plasma membrane** **-1.25**

Gene name: integrin-linked kinase

This gene encodes a protein with a kinase-like domain and four ankyrin-like repeats. Activity of this protein is important in the epithelial to mesenchymal transition, and over-expression of this gene is implicated in tumor growth and metastasis.

Pagina 9 v.h. onderzoek: **BCR** **cytoplasm** **-1,27**

Gene name: breakpoint cluster region

A reciprocal translocation between chromosomes 22 and 9 produces the Philadelphia chromosome, which is often found in patients with chronic myelogenous leukemia.

PRKAR1A **cytoplasm** **-1.27**

Gene name: protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1)

cAMP is a signaling molecule important for a variety of cellular functions.

This gene can fuse to the RET protooncogene by gene rearrangement and form the thyroid tumor-specific chimeric oncogene known as PTC2.

DDR2 plasma membrane -1.34

Gene name: discoidin domain receptor tyrosine kinase 2

Receptor tyrosine kinases (RTKs) play a key role in the communication of cells with their microenvironment.

Regulates remodeling of the extracellular matrix by up-regulation of the collagenases MMP1, MMP2 and MMP13, and thereby facilitates cell migration and tumor cell invasion.

PFKFB3 cytoplasm -1.37

Gene name: 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3

The protein encoded by this gene belongs to a family of bifunctional proteins that are involved in both the synthesis and degradation of fructose-2,6-bisphosphate, a regulatory molecule that controls glycolysis in eukaryotes. It functions as a regulator of cyclin-dependent kinase 1, linking glucose metabolism to cell proliferation and survival in tumor cells.

NUAK1 unknow -1.38

Gene name: NUAK family, SNF1-like kinase, 1

NUAK1 (NUAK Family Kinase 1) is a Protein Coding gene. Serine/threonine-protein kinase involved in various processes such as cell adhesion, regulation of cell ploidy and senescence, cell proliferation and tumor progression.

PKN2 cytoplasm -1.45

Gene name: protein kinase N2

PKN2 (Protein Kinase N2)/ Protein-Kinase C-Related Kinase 2 is a Protein Coding gene. PKC-related serine/threonine-protein kinase and Rho/Rac effector protein that participates in specific signal transduction responses in the cell. Plays a role in the regulation of cell cycle progression, actin cytoskeleton assembly, cell migration, cell adhesion, tumor cell invasion and transcription activation signaling processes.

MKNK2 cytoplasm -1.50

Gene name: MAP kinase interacting serine/threonine kinase 2

This gene encodes a member of the calcium/calmodulin-dependent protein kinases (CAMK) Ser/Thr protein kinase family, which belongs to the protein kinase superfamily.
This protein is one of the downstream kinases activated by mitogen-activated protein (MAP) kinases. It phosphorylates the eukaryotic initiation factor 4E

(eIF4E), thus playing important roles in the initiation of mRNA translation, oncogenic transformation and malignant cell proliferation.

STK36 cytoplasm -1.59

Gene name: serine/threonine kinase 36, fused homolog (Drosophila)

This gene encodes a member of the serine/threonine kinase family of enzymes. This family member is similar to a Drosophila protein that plays a key role in the Hedgehog signaling pathway. Because Hedgehog signaling is frequently activated in certain kinds of gastrointestinal cancers, it has been suggested that this gene is a target for the treatment of these cancers.

DDR1 plasma membrane -1.60

Gene name: discoidin domain receptor tyrosine kinase 1

Receptor tyrosine kinases play a key role in the communication of cells with their microenvironment. Expression of this protein is restricted to epithelial cells, particularly in the kidney, lung, gastrointestinal tract, and brain. In addition, it has been shown to be significantly overexpressed in several human tumors.

VDR nucleus 1.89

Gene name: vitamin D (1,25- dihydroxyvitamin D3) receptor

This gene encodes the nuclear hormone receptor for vitamin D3. Downstream targets of this nuclear hormone receptor are principally involved in mineral metabolism though the receptor regulates a variety of other metabolic pathways, such as those involved in the immune response and cancer.

PPARG nucleus -1.28

Gene name: peroxisome proliferator-activated receptor gamma

This gene encodes a member of the peroxisome proliferator-activated receptor (PPAR) subfamily of nuclear receptors. The protein encoded by this gene is PPAR-gamma and is a regulator of adipocyte differentiation. Additionally, PPAR-gamma has been implicated in the pathology of numerous diseases including obesity, diabetes, atherosclerosis and cancer.

ESR1 nucleus -1.31

Gene name: estrogen receptor 1

This gene encodes an estrogen receptor, a ligand-activated transcription factor composed of several domains important for hormone binding, DNA binding, and activation of transcription. Estrogen and its receptors are essential for sexual development and reproductive function, but also play a role in other tissues such as bone. Estrogen receptors are also involved in

pathological processes including breast cancer, endometrial cancer, and osteoporosis.

MMP9 extracellular space 4.22

Gene name: matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)

Proteins of the matrix metalloproteinase (MMP) family are involved in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis.

MMP19 extracellular space 3.15

Gene name: matrix metallopeptidase 19

This gene encodes a member of a family of proteins that are involved in the breakdown of extracellular matrix in normal physiological processes, such as embryonic development, reproduction, and tissue remodeling, as well as in disease processes, such as arthritis and metastasis.

ST14 plasma membrane 3.07

Gene name: suppression of tumorigenicity 14 (colon carcinoma)

The protein encoded by this gene is an epithelial-derived, integral membrane serine protease. This protease forms a complex with the Kunitz-type serine protease inhibitor, HAI-1, and is found to be activated by sphingosine 1-phosphate. This protease has been shown to cleave and activate hepatocyte growth factor/scattering factor, and urokinase plasminogen activator, which suggest the function of this protease as an epithelial membrane activator for other proteases and latent growth factors. The expression of this protease has been associated with breast, colon, prostate, and ovarian tumors, which implicates its role in cancer invasion, and metastasis Degrades extracellular matrix. Proposed to play a role in breast cancer invasion and metastasis.

FAP fcytoplasm 2.40

Gene name: ibroblast activation protein, alpha

The protein encoded by this gene is a homodimeric integral membrane gelatinase belonging to the serine protease family. It is selectively expressed in reactive stromal fibroblasts of epithelial cancers, granulation tissue of healing wounds, and malignant cells of bone and soft tissue sarcomas. Plays a role in tissue remodeling during development and wound healing. Participates in the cell invasiveness towards the ECM in malignant melanoma cancers. Enhances tumor growth progression by increasing angiogenesis, collagen fiber degradation and apoptosis and by reducing antitumor response of the immune system. Promotes glioma cell invasion through the brain parenchyma by degrading the proteoglycan brevican. Acts as a tumor suppressor in melanocytic cells through regulation of cell proliferation and survival in a serine protease activity-independent manner.

CTSB **cytoplasm** **2.13**

Gene name: cathepsin B

Overexpression of the encoded protein has been associated with esophageal adenocarcinoma and other tumors.

LGMN **cytoplasm** **2.05**

Gene name: legumain

Overexpression of this gene may be associated with the majority of solid tumor types.

Pagina 10 v.h. onderzoek: **MMP2** **extracellular space** **1.76**

Gene name: matrix metallopeptidase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase)

Ubiquitinous metalloproteinase that is involved in diverse functions such as remodeling of the vasculature, angiogenesis, tissue repair, tumor invasion, inflammation, and atherosclerotic plaque rupture.

CTSK **cytoplasm** **1.75**

Gene name: cathepsin K

The protein encoded by this gene is a lysosomal cysteine proteinase involved in bone remodeling and resorption. This protein, which is a member of the peptidase C1 protein family, is predominantly expressed in osteoclasts. However, the encoded protein is also expressed in a significant fraction of human breast cancers, where it could contribute to tumor invasiveness.

CTSH **cytoplasm** **1.65**

Gene name: cathepsin H

Increased expression of this gene has been correlated with malignant progression of prostate tumors.

USP6 **cytoplasm** **1.36**

Gene name: ubiquitin specific peptidase 6 (Tre-2 oncogene)

USP6 (Ubiquitin Specific Peptidase 6) is a Protein Coding gene. Is able to initiate tumorigenesis by inducing the production of matrix metalloproteinases following NF-kappa-B activation.

PRSS2 **extracellular space** **-1.11**

Gene name: protease, serine, 2 (trypsin 2)

This gene belongs to the trypsin family of serine proteases and encodes anionic trypsinogen. This protein has also been found to activate pro-urokinase in ovarian tumors, suggesting a function in tumor invasion.

EPS8 **plasma membrane** **-1.38**

Gene name: epidermal growth factor receptor pathway substrate 8

This gene encodes a member of the EPS8 family. Involved in the regulation of processes such as axonal filopodia growth, stereocilia length, dendritic cell migration and cancer cell migration and invasion.

BAP1 **nucleus** **-1.40**

Gene name: BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase)

This gene belongs to the ubiquitin C-terminal hydrolase subfamily of deubiquitinating enzymes that are involved in the removal of ubiquitin from proteins. The encoded enzyme binds to the breast cancer type 1 susceptibility protein (BRCA1) via the RING finger domain of the latter and acts as a tumor suppressor.

MMP28 **extracellular space** **-1,42**

Gene name: matrix metallopeptidase 28

Proteins of the matrix metalloproteinase (MMP) family are involved in the breakdown of extracellular matrix for both normal physiological processes, such as embryonic development, reproduction and tissue remodeling, and disease processes, such as asthma and metastasis.

PTPN6 **cytoplasm** **2.43**

Gene name: protein tyrosine phosphatase, non-receptor type 6

———

The protein encoded by this gene is a member of the protein tyrosine phosphatase (PTP) family. PTPs are known to be signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle, and oncogenic transformation.

PTPRE **plasma membrane** **1.88**

Gene name: protein tyrosine phosphatase, receptor type, E

PTPN1 **cytoplasm** **1.81**

Gene name: protein tyrosine phosphatase, non-receptor type 1

PTPN18 **nucleus** **1.50**

Gene name: protein tyrosine phosphatase, non-receptor type 18 (brain-derived)

PTPN2 **cytoplasm** **1.42**

Gene name: protein tyrosine phosphatase, non-receptor type 2

BU618279 **cytoplasm** **1.32**

Gene name: protein phosphatase 3, catalytic subunit, alpha isozyme

Negatively regulates tumor necrosis factor-mediated signaling downstream via MAPK through SRC dephosphorylation.

PTEN **cytoplasm** **-1.19**

Gene name: phosphatase and tensin homolog

This gene was identified as a tumor suppressor that is mutated in a large number of cancers at high frequency. It negatively regulates intracellular levels of phosphatidylinositol-3,4,5-trisphosphate in cells and functions as a tumor suppressor by negatively regulating AKT/PKB signaling pathway.

The protein encoded by this gene is a member of the protein tyrosine phosphatase (PTP) family. PTPs are known to be signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, mitotic cycle, and oncogenic transformation.

PTPN11 **cyroplasm** **-1.23**

Gene name: protein tyrosine phosphatase, non-receptor type 11

PTPRS **plasma membrane** **-1.27**

Gene name: protein tyrosine phosphatase, receptor type, S

Pagina 11 v.h. onderzoek: **PTPN3** **cytoplasm** **-1.28**

Gene name: protein tyrosine phosphatase, non-receptor type 3

ATF3 **nucleus** **2.30**

Gene name: activating transcription factor 3

This gene encodes a member of the mammalian activation transcription factor/cAMP responsive element-binding (CREB) protein family of transcription factors. This gene is induced by a variety of signals, including many of those encountered by cancer cells, and is involved in the complex process of cellular stress response

LEF1 **nucleus** **2.27**

Gene name: lymphoid enhancer-binding factor 1

This gene encodes a transcription factor belonging to a family of proteins that share homology with the high mobility group protein-1. is involved in reducing cellular aggregation and increasing cell migration of pancreatic cancer cells. Isoform 1 transcriptionally activates MYC and CCND1 expression and enhances proliferation of pancreatic tumor cells.

PTTG1 nucleus 2.06

Gene name: pituitary tumor-transforming 1

The encoded protein is a homolog of yeast securin proteins, which prevent separins from promoting sister chromatid separation. The gene product has transforming activity in vitro and tumorigenic activity in vivo, and the gene is highly expressed in various tumors. The gene product contains 2 PXXP motifs, which are required for its transforming and tumorigenic activities, as well as for its stimulation of basic fibroblast growth factor expression.

BCL10 cytoplasm 1.99

Gene name: B-cell CLL/lymphoma 10

This gene was identified by its translocation in a case of mucosa-associated lymphoid tissue (MALT) lymphoma. This protein is found to form a complex with MALT1, a protein encoded by another gene known to be translocated in MALT lymphoma. MALT1 and this protein are thought to synergize in the activation of NF-kappaB, and the deregulation of either of them may contribute to the same pathogenetic process that leads to the malignancy.

RUNX3 nucleus 1.89

Gene name: runt-related transcription factor 3

This gene encodes a member of the runt domain-containing family of transcription factors. can either activate or suppress transcription. It also interacts with other transcription factors. It functions as a tumor suppressor,

NKX3 nucleus 1.82

Gene name: 1 NK3 homeobox 1

This gene encodes a homeobox-containing transcription factor. Acts as a tumor suppressor controlling prostate carcinogenesis, as shown by the ability to inhibit proliferation and invasion activities of PC-3 prostate cancer cells.

HMGA1 nucleus 1.45

Gene name: high mobility group AT-hook 1

This gene encodes a chromatin-associated protein involved in the regulation of gene transcription, integration of retroviruses into chromosomes, and the metastatic progression of cancer cells.

BMI1 nucleus 1.45

Gene name: BMI1 polycomb ring finger oncogene

This gene is an oncogene and aberrant expression is associated with numerous cancers and is associated with resistance to certain chemotherapies.

RUNX1 nucleus 1.44

Gene name: runt-related transcription factor 1

Core binding factor (CBF) is a heterodimeric transcription factor that binds to the core element of many enhancers and promoters. The protein encoded by this gene represents the alpha subunit of CBF and is thought to be involved in the development of normal hematopoiesis. CBF binds to the core site, 5-PYGPYGGT-3, of a number of enhancers and promoters, including murine leukemia virus, polyomavirus enhancer, T-cell receptor enhancers, LCK, IL-3 and GM-CSF promoters.

CREBL2 nucleus 1.41

Gene name: cAMP responsive element binding protein-like 2

cAMP response element (CRE)-binding protein-like-2 (CREBL2) was identified in a search to find genes in a commonly deleted region on chromosome 12p13 flanked by ETV6 and CDKN1B genes, frequently associated with hematopoietic malignancies, as well as breast, non-small-cell lung and ovarian cancers. The occurance of CREBL2 deletion in malignancy suggests that CREBL2 may act as a tumor suppressor gene. May also play a regulatory role in the cell cycle. Identification in a chromosomal region frequently deleted in various cancers suggests that it might act as a tumor suppressor.

SMAD3 nucleus 1.36

Gene name: SMAD family member 3

This protein functions as a transcriptional modulator activated by transforming growth factor-beta and is thought to play a role in the regulation of carcinogenesis.

Pagina 12 v.h. onderzoek: **C19orf2 nucleus 1.32**

Gene name: chromosome 19 open reading frame 2

This gene encodes member of the prefoldin family of molecular chaperones. May act as a tumor suppressor to repress AR-mediated gene transcription and to inhibit anchorage-independent growth in prostate cancer cells. Required for cell survival in ovarian cancer cells.

NOTCH2 plasma membrane 1.28

Gene name: Notch homolog 2 (Drosophila)

This gene encodes a member of the Notch family. Members of this Type 1 transmembrane protein family share structural characteristics including an extracellular domain consisting of multiple epidermal growth factor-like (EGF) repeats, and an intracellular domain consisting of multiple, different domain types. Positively regulates self-renewal of liver cancer cells

YBX1 **nucleus** **1.27**

Gene name: Y box binding protein 1

This gene encodes a highly conserved cold shock domain protein that has broad nucleic acid binding properties. Aberrant expression of the gene is associated with cancer proliferation in numerous tissues. This gene may be a prognostic marker for poor outcome and drug resistance in certain cancers.

CTNNB1 **nucleus** **1.26**

Gene name: catenin (cadherin-associated protein), beta 1, 88kDa

The protein encoded by this gene is part of a complex of proteins that constitute adherens junctions (AJs). AJs are necessary for the creation and maintenance of epithelial cell layers by regulating cell growth and adhesion between cells. Mutations in this gene are a cause of colorectal cancer (CRC), pilomatrixoma (PTR), medulloblastoma (MDB), and ovarian cancer.

NCOR2 **nucleus** **1.24**

Gene name: nuclear receptor co-repressor 2

This gene encodes a nuclear receptor co-repressor that mediates transcriptional silencing of certain target genes. This protein acts as part of a multisubunit complex which includes histone deacetylases to modify chromatin structure that prevents basal transcriptional activity of target genes. Aberrant expression of this gene is associated with certain cancers.

SP100 **nucleus** **1.22**

Gene name: SP100 nuclear antigen

This gene encodes a subnuclear organelle and major component of the PML (promyelocytic leukemia)-SP100 nuclear bodies. Together with PML, this tumor suppressor is a major constituent of the PML bodies, a subnuclear organelle involved in a large number of physiological processes including cell growth, differentiation and apoptosis. Through interaction with the MRN complex it may be involved in the regulation of telomeres lengthening.

PFDN5 **nucleus** **1.22**

Gene name: L prefoldin subunit 5

This gene encodes a member of the prefoldin alpha subunit family. The complex, consisting of two alpha and four beta subunits, forms a double beta barrel assembly with six protruding coiled-coils. The encoded protein may

also repress (onderdrukken) the transcriptional activity of the proto-oncogene c-Myc.

SRA1 **nucleus** **-1.06**

Gene name: steroid receptor RNA activator 1

Both long non-coding and protein-coding RNAs are transcribed from this gene, and they represent alternatively spliced transcript variants. Enhances cellular proliferation and differentiation and promotes apoptosis in vivo. May play a role in tumorigenesis.

TSC22D1 **nucleus** **-1.14**

Gene name: TSC22 domain family, member 1

This gene encodes a member of the TSC22 domain family of leucine zipper transcription factors. The encoded protein may play a critical role in tumor suppression through the induction of cancer cell apoptosis (in gang zetten celdood kankercellen),

TOB1 **nucleus** **-1.16**

Gene name: transducer of ERBB2, 1

This gene encodes a member of the transducer of erbB-2 /B-cell translocation gene protein family. Members of this family are anti-proliferative factors that have the potential to regulate cell growth. The encoded protein may function as a tumor suppressor.

PRKCBP1 **nucleus** **-1.20**

Gene name: zinc finger, MYND-type containing 8

The protein encoded by this gene is a receptor for activated C-kinase (RACK) protein. The encoded protein has been shown to bind in vitro to activated protein kinase C beta I. In addition, this protein is a cutaneous T-cell lymphoma-associated antigen.

ETS2 **nucleus** **-1.20**

Gene name: ets erythroblastosis virus E26 oncogene homolog 2 (avian)

This gene encodes a transcription factor which regulates genes involved in development and apoptosis. The encoded protein is also a protooncogene and shown to be involved in regulation of telomerase.

SP1 **nucleus** **-1.22**

Gene name: Sp1 transcription factor

The protein encoded by this gene is a zinc finger transcription factor that binds to GC-rich motifs of many promoters. Plays an essential role in the

regulation of FE65 gene expression. In complex with ATF7IP, maintains telomerase activity in cancer cells by inducing TERT and TERC gene expression.

RB1 **nucleus** **-1.23**

Gene name: retinoblastoma 1

The protein encoded by this gene is a negative regulator of the cell cycle and was the first tumor suppressor gene found. Key regulator of entry into cell division that acts as a tumor suppressor.

In case of viral infections, interactions with SV40 large T antigen, HPV E7 protein or adenovirus E1A protein induce the disassembly (de-assemblage in gang zetten) of RB1-E2F1 complex thereby disrupting RB1s activity.

(The E2F family plays a crucial role in the control of cell cycle and action of tumor suppressor proteins and is also a target of the transforming proteins of small DNA tumor viruses.)

KLF6 **nucleus** **-1.25**

Gene name: Kruppel-like factor 6

This gene encodes a member of the Kruppel-like family of transcription factors. The zinc finger protein is a transcriptional activator, and functions as a tumor suppressor.

ENO1 **cytoplasm** **-1.25**

Gene name: enolase 1, (alpha)

This gene encodes alpha-enolase, one of three enolase isoenzymes found in mammals. Alternative splicing of this gene results in a shorter isoform that has been shown to bind to the c-myc promoter and function as a tumor suppressor. May be a tumor suppressor.

AFF1 **nucleus** **-1.28**

Gene name: AF4/FMR2 family, member 1

This gene encodes a member of the AF4/ lymphoid nuclear protein related to AF4/Fragile X E mental retardation syndrome family of proteins, which have been implicated in childhood lymphoblastic leukemia, Fragile X E site mental retardation, and ataxia. Through RNA interference screens, this gene has been shown to promote the expression of CD133, a plasma membrane glycoprotein required for leukemia cell survival.

Pagina 13 v.h. onderzoek: **AK130514** **nucleus** **-1.32**

Gene name: WW domain containing transcription regulator 1

WWTR1 (WW Domain Containing Transcription Regulator 1) is a Protein Coding gene. Transcriptional coactivator which acts as a downstream regulatory target in the Hippo signaling pathway that plays a pivotal role in organ size control and tumor suppression by restricting proliferation and promoting apoptosis.

DMAP1 nucleus -1.33

Gene name: DNA methyltransferase 1 associated protein 1

This gene encodes a subunit of several, distinct complexes involved in the repression or activation of transcription.

transcriptional corepressor tumor susceptibility gene 101 and the pro-apoptotic death-associated protein 6, among others.

YAP1 nucleus -1.40

Gene name: Yes-associated protein 1

This gene encodes a downstream nuclear effector of the Hippo signaling pathway which is involved in development, growth, repair, and homeostasis. This gene is known to play a role in the development and progression of multiple cancers as a transcriptional regulator of this signaling pathway and may function as a potential target for cancer treatment.

TBX2 nucleus -1.42

Gene name: T-box 2

This gene is a member of a phylogenetically conserved family of genes that share a common DNA-binding domain, the T-box. T-box genes encode transcription factors involved in the regulation of developmental processes. Expression studies indicate that this gene may have a potential role in tumorigenesis as an immortalizing agent

MLLT10 nucleus -1.62

Gene name: myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 10

This gene encodes a transcription factor and has been identified as a partner gene involved in several chromosomal rearrangements resulting in various leukemias.

CRTC1 nucleus -1.69

Gene name: CREB regulated transcription coactivator 1

CRTC1 (CREB Regulated Transcription Coactivator 1) is a Protein Coding gene. Also coactivator for TAX activation of the human T-cell leukemia virus type 1 (HTLV-1) long terminal repeats (LTR).

EIF5A **cytoplasm** **-1.26**

Gene name: eukaryotic translation initiation factor 5A

EIF5A (Eukaryotic Translation Initiation Factor 5A) is a Protein Coding gene. Also described as a cellular cofactor of human T-cell leukemia virus type I (HTLV-1) Rex protein and of human immunodeficiency virus type 1 (HIV-1) Rev protein, essential for mRNA export of retroviral transcripts.

HAVCR2 **plasma membrane** **2.42**

Gene name: hepatitis A virus cellular receptor 2

The protein encoded by this gene belongs to the immunoglobulin superfamily, and TIM family of proteins.

Expressed on dendritic cells (DCs/uitloper zenuw(cellen)) positively regulates innate (aangeboren) immune response and in synergy with Toll-like receptors promotes secretion of TNF-alpha. In tumor-imfiltrating DCs suppresses (onderdrukken) nucleic acid-mediated innate immune repsonse by interaction with HMGB1 and interfering with nucleic acid-sensing and trafficking of nucleid acids to endosomes

Pagina 14 v.h. onderzoek: **IL10RA** **plasma membrane** **1.97**

Gene name: interleukin 10 receptor, alpha

The protein encoded by this gene is a receptor for interleukin 10. This receptor is reported to promote survival of progenitor (voorloper cellen van) myeloid cells through the insulin receptor

ITGB1 **plasma membrane** **-1.21**

Gene name: integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)

Integrins are heterodimeric proteins made up of alpha and beta subunits. Integrin family members are membrane receptors involved in cell adhesion and recognition in a variety of processes including embryogenesis, hemostasis, tissue repair, immune response and metastatic diffusion of tumor cells.

SFRP1 **plasma membrane** **-1.21**

Gene name: secreted frizzled-related protein 1

This gene encodes a member of the SFRP family that contains a cysteine-rich domain homologous to the putative Wnt-binding site of Frizzled proteins. Members of this family act as soluble modulators of Wnt signaling; epigenetic silencing of SFRP genes leads to deregulated activation of the Wnt-pathway which is associated with cancer.

TNFRSF10A plasma membrane -1.30

Gene name: tumor necrosis factor receptor superfamily, member 10a

The protein encoded by this gene is a member of the TNF-receptor superfamily. This receptor is activated by tumor necrosis factor-related apoptosis inducing ligand (TNFSF10/TRAIL), and thus transduces cell death signal and induces cell apoptosis.

BCAM plasma membrane -1.46

Gene name: basal cell adhesion molecule (Lutheran blood group)

This gene encodes Lutheran blood group glycoprotein, a member of the immunoglobulin superfamily and a receptor for the extracellular matrix protein, laminin. This protein may play a role in epithelial cell cancer and in vaso-occlusion of red blood cells in sickle cell disease

ABCG2 plasma membrane 5.46

Gene name: ATP-binding cassette, sub-family G (WHITE), member 2

The membrane-associated protein encoded by this gene is included in the superfamily of ATP-binding cassette (ABC) transporters. ABC proteins transport various molecules across extra- and intra-cellular membranes. ABC genes are divided into seven distinct subfamilies (ABC1, MDR/TAP, MRP, ALD, OABP, GCN20, White). This protein is a member of the White subfamily. Alternatively referred to as a breast cancer resistance protein, this protein functions as a xenobiotic transporter, which may play a major role in multi-drug resistance.

ECM1 extracellular space 2.86

Gene name: extracellular matrix protein 1

This gene encodes a soluble protein that is involved in endochondral bone formation, angiogenesis, and tumor biology.

ABCC5 plasma membrane 1.70

Gene name: ATP-binding cassette, sub-family C (CFTR/MRP), member 5

The protein encoded by this gene is a member of the superfamily of ATP-binding cassette (ABC) transporters. Studies show that this protein provides resistance to thiopurine anticancer drugs.

TMC6 cytoplasm 1.58

Gene name: transmembrane channel-like 6

Epidermodysplasia verruciformis (EV) is an autosomal recessive dermatosis characterized by abnormal susceptibility to human papillomaviruses (HPVs)

and a high rate of progression to squamous cell carcinoma on sun-exposed skin.

Pagina 14 v.h. onderzoek: **TRAF5** **cytoplasm** **1.44**

Gene name: TNF receptor-associated factor 5

The scaffold protein encoded by this gene is a member of the tumor necrosis factor receptor-associated factor (TRAF) protein family and contains a meprin and TRAF homology (MATH) domain, a RING-type zinc finger, and two TRAF-type zinc fingers. Adapter protein and signal transducer that links members of the tumor necrosis factor receptor family to different signaling pathways by association with the receptor cytoplasmic domain and kinases.

SNX5 **cytoplasm** **-1.21**

Gene name: sorting nexin 5

This gene encodes a member of the sorting nexin family.This gene may play a role in the tumorigenesis of papillary thyroid carcinoma.

VTI1A **plasma membrane** **-1.22**

Gene name: vesicle transport through interaction with t-SNAREs homolog 1A (yeast)

The protein encoded by this gene is a member of the family of soluble N-ethylmaleimide-sensitive fusion protein-attachment protein receptors (SNAREs) that function in intracellular trafficking. Polymorphisms in this gene have been associated with binocular function, and also with susceptibility to colorectal and lung cancers. A recurrent rearrangement has been found between this gene and the transcription factor 7-like 2 (TCF7L2) gene in colorectal cancers.

SLC35C2 **unknown** **-1.22**

Gene name: solute carrier family 35, member C2

This gene encodes a member of the triose-phosphate transporter protein family. This gene is regulated by oxygen tension, is induced in hypoxic trophoblast cells, and is overexpressed in ovarian cancer.

SLC2A1 plasma membrane **-1.23**

Gene name: solute carrier family 2 (facilitated glucose transporter), member 1

This gene encodes a major glucose transporter in the mammalian blood-brain barrier. The encoded protein is found primarily in the cell membrane and on the cell surface, where it can also function as a receptor for human T-cell leukemia virus (HTLV) I and II.

APOL3 **cytoplasm** **-1.23**

Gene name: apolipoprotein L, 3

This gene is a member of the apolipoprotein L gene family, and it is present in a cluster with other family members on chromosome 22. The encoded protein is found in the cytoplasm, where it may affect the movement of lipids, including cholesterol, and/or allow the binding of lipids to organelles. In addition, expression of this gene is up-regulated by tumor necrosis factor-alpha in endothelial cells lining the normal and atherosclerotic iliac artery and aorta.

NNAT **plasma membrane** **-1.28**

Gene name: neuronatin

The protein encoded by this gene is a proteolipid that may be involved in the regulation of ion channels during brain development. The encoded protein may also play a role in forming and maintaining the structure of the nervous system. This gene is found within an intron of another gene, bladder cancer associated protein, but on the opposite strand.

Pagina 16 v.h. onderzoek: **ZBP1** **unknown** **-1.90**

Gene name: Z-DNA binding protein

This gene encodes a Z-DNA binding protein. Participates in the detection by the hosts innate immune system of DNA from viral, bacterial or even host origin. Plays a role in host defense against tumors and pathogens.

RARRES1 **plasma membrane** **6.52**

Gene name: retinoic acid receptor responder (tazarotene induced) 1

This gene was identified as a retinoid acid (RA) receptor-responsive gene. It encodes a type 1 membrane protein. The expression of this gene is upregulated by tazarotene as well as by retinoic acid receptors. The expression of this gene is found to be downregulated in prostate cancer, which is caused by the methylation of its promoter and CpG island.

Tumor suppressor RARRES1 interacts with cytoplasmic carboxypeptidase AGBL2 to regulate the α-tubulin tyrosination cycle*.

Abstract

Even though it is among the most commonly methylated loci in multiple cancers, the retinoic acid-induced tumor suppressor retinoic acid receptor responder 1 (RARRES1) has no known function. We now show that RARRES1 is lost in many cancer cells, particularly those with a mesenchymal phenotype, and is a transmembrane carboxypeptidase inhibitor that interacts with ATP/GTP binding protein-like 2 (AGBL2), a cytoplasmic carboxypeptidase. Knockdown of AGBL2 results in a failure of the cell to detyrosinate the C-terminal EEY region of α-tubulin and indicates that it is a candidate for the long sought-after tubulin tyrosine carboxypeptidase important in the regulation of microtubule dynamics. In contrast, knockdown of

RARRES1 increases the level of detyrosinated α-tubulin consistent with a role as the cognate inhibitor of AGBL2. We conclude that RARRES1, its interacting partners AGBL2, Eg5/KIF11, another EEY-bearing protein (EB1), and the microtubule tyrosination cycle are important in tumorigenesis and identify a novel area for therapeutic intervention*.

Breast cancer subtype dictates DNA methylation and ALDH1A3-mediated expression of tumor suppressor RARRES1.

Abstract

Breast cancer subtyping, based on the expression of hormone receptors and other genes, can determine patient prognosis and potential options for targeted therapy. Among breast cancer subtypes, tumors of basal-like and claudin-low subtypes are typically associated with worse patient outcomes, are primarily classified as triple-negative breast cancers (TNBC), and cannot be treated with existing hormone-receptor-targeted therapies. Understanding the molecular basis of these subtypes will lead to the development of more effective treatment options for TNBC. In this study, we focus on retinoic acid receptor responder 1 (RARRES1) as a paradigm to determine if breast cancer subtype dictates protein function and gene expression regulation. Patient tumor dataset analysis and gene expression studies of a 26 cell-line panel, representing the five breast cancer subtypes, demonstrate that RARRES1 expression is greatest in basal-like TNBCs. Cell proliferation and tumor growth assays reveal that RARRES1 is a tumor suppressor in TNBC. Furthermore, gene expression studies, Illumina HumanMethylation450 arrays, and chromatin immunoprecipitation demonstrate that expression of RARRES1 is retained in basal-like breast cancers due to hypomethylation of the promoter. Additionally, expression of the cancer stem cell marker, aldehyde dehydrogenase 1A3, which provides the required ligand (retinoic acid) for RARRES1 transcription, is also specific to the basal-like subtype. We functionally demonstrate that the combination of promoter methylation and retinoic acid signaling dictates expression of tumor suppressor RARRES1 in a subtype-specific manner. These findings provide a precedent for a therapeutically-inducible tumor suppressor and suggest novel avenues of therapeutic intervention for patients with basal-like breast cancer*.Bron Pubmed.gov

GLIPR1 extracellular space 2.92

Gene name: GLI pathogenesis-related 1

This gene encodes a protein with similarity to both the pathogenesis-related protein (PR) superfamily and the cysteine-rich secretory protein (CRISP) family. Increased expression of this gene is associated with myelomocytic differentiation in macrophage and decreased expression of this gene through gene methylation is associated with prostate cancer. The protein has proapoptotic (geprogrammeerde celdood) activities in prostate and bladder cancer cells

LCP1 cytoplasm 2.47

Gene name: lymphocyte cytosolic protein 1 (L-plastin)

L-plastin has been found in many types of malignant human cells of non-hemopoietic origin suggesting that its expression is induced accompanying tumorigenesis in solid tissues.

CENPF nucleus 2.45

Gene name: centromere protein F, 350/400ka (mitosin)

This gene encodes a protein that associates with the centromere-kinetochore complex. Autoantibodies against this protein have been found in patients with cancer or graft versus host disease.

HCST plasma membrane 2.38

Gene name: hematopoietic cell signal transducer

Transmembrane adapter protein which associates with KLRK1 to form an activation receptor KLRK1-HCST in lymphoid and myeloid cells. In T-cells, it provides primarily costimulation for TCR-induced signals. KLRK1-HCST receptor plays a role in immune surveillance against tumors and is required for cytolysis of tumors cells; indeed, melanoma cells that do not express KLRK1 ligands escape from immune surveillance mediated by NK cells.

SPINT2 extracellular space 2.33

Gene name: serine peptidase inhibitor, Kunitz type, 2

This gene encodes a transmembrane protein with two extracellular Kunitz domains that inhibits a variety of serine proteases. The protein inhibits HGF activator which prevents the formation of active hepatocyte growth factor. This gene is a putative tumor suppressor, and mutations in this gene result in congenital sodium diarrhea.

Pagina 17 v.h. onderzoek: **TNFAIP6 extracellular space 2.23**

Gene name: tumor necrosis factor, alpha-induced protein 6

This protein has been shown to form a stable complex with inter-alpha-inhibitor (I alpha I), and thus enhance the serine protease inhibitory activity of I alpha I, which is important in the protease network associated with inflammation. This gene can be induced by proinflammatory cytokines such as tumor necrosis (afsterven van tumor cellen) factor alpha and interleukin-1.

ARMC9 unknown 2.19

Gene name: armadillo repeat containing 9

Aliases for ARMC9 Gene Armadillo Repeat Containing 9 Melanoma/ Melanocyte-Specific Tumor Antigen KU-MEL-1

KIAA1212 cytoplasm 2.01

Gene name: coiled-coil domain containing 88A

Increased expression of this gene and phosphorylation of the encoded protein may play a role in cancer metastasis.

BRWD2 unknown 1.91

Gene name: WD repeat domain 11

This gene encodes a member of the WD repeat protein family. WD repeats are minimally conserved regions of approximately 40 amino acids typically bracketed by gly-his and trp-asp (GH-WD), which may facilitate formation of heterotrimeric or multiprotein complexes. The gene location suggests that it is a candidate gene for the tumor suppressor locus.

TNFAIP2 extracellular space 1.84

Gene name: tumor necrosis factor, alpha-induced protein 2

This gene was identified as a gene whose expression can be induced by the tumor necrosis factor alpha (TNF) in umbilical vein endothelial cells. The expression of this gene was shown to be induced by retinoic acid in a cell line expressing a oncogenic version of the retinoic acid receptor alpha fusion protein, which suggested that this gene may be a retinoic acid target gene in acute promyelocytic leukemia.

THBS2 extracellular space 1.82

Gene name: thrombospondin 2

The protein encoded by this gene belongs to the thrombospondin family. It is a disulfide-linked homotrimeric glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. This protein has been shown to function as a potent inhibitor of tumor growth and angiogenesis.

TRIM37 cytoplasm 1.75

Gene name: tripartite motif-containing 37

This gene encodes a member of the tripartite motif (TRIM) family, whose members are involved in diverse cellular functions such as developmental patterning and oncogenesis.

CDCA7L nucleus 1.75

Gene name: cell division cycle associated 7-like

Plays a role in transcriptional regulation as a repressor that inhibits monoamine oxidase A (MAOA) activity and gene expression by binding to the promoter. Plays an important oncogenic role in mediating the full transforming effect of MYC in medulloblastoma cells.

Pagina 18 v.h. onderzoek: **CA421238 extracellular space 1.69**

Gene name: collagen, type VI, alpha 2

Plays a role in transcriptional regulation as a repressor that inhibits monoamine oxidase A (MAOA) activity and gene expression by binding to the promoter. Plays an important oncogenic role in mediating the full transforming effect of MYC in medulloblastoma cells. Involved in apoptotic signaling pathways; May act downstream of P38-kinase and BCL-2, but upstream of CASP3/caspase-3 as well as CCND1/cyclin D1 and E2F1.

MAFB **nucleus** **1.69**

Gene name: v-maf musculoaponeurotic fibrosarcoma oncogene homolog B (avian)

The protein encoded by this gene is a basic leucine zipper (bZIP) transcription factor that plays an important role in the regulation of lineage-specific hematopoiesis. Involved either as an oncogene or as a tumor suppressor, depending on the cell context.

VWCE **unknown** **1.67**

Gene name: von Willebrand factor C and EGF domains

May be a regulatory element in the beta-catenin signaling pathway and a target for chemoprevention of hapatocellular carcinoma.

CD9 **plasma membrane** **1.66**

Gene name: CD9 molecule

The encoded protein functions in many cellular processes including differentiation, adhesion, and signal transduction, and expression of this gene plays a critical role in the suppression of cancer cell motility and metastasis.

THBS1 **extracellular space** **1.63**

Gene name: thrombospondin 1

This protein has been shown to play roles in platelet aggregation, angiogenesis, and tumorigenesis.

THY1 **plasma membrane** **1.63**

Gene name: Thy-1 cell surface antigen

This gene may function as a tumor suppressor in nasopharyngeal carcinoma.

EMP3 **plasma membrane** **1.61**

Gene name: epithelial membrane protein 3

The protein encoded by this gene belongs to the PMP-22/EMP/MP20 family of proteins. The protein contains four transmembrane domains and two N-linked glycosylation sites. It is thought to be involved in cell proliferation, cell-cell interactions and function as a tumor suppressor.

TCL6 **unknown** **1.61**

Gene name: T-cell leukemia/lymphoma 6 (non-protein coding)

TCL6 (T-Cell Leukemia/Lymphoma 6 (Non-Protein Coding)) is an RNA Gene, and is affiliated with the non-coding RNA class. Diseases associated with TCL6 include T-Cell Leukemia.

FAM57A **plasma membrane** **1.58**

Gene name: family with sequence similarity 57, member A

The protein encoded by this gene is a membrane-associated protein that promotes lung carcinogenesis

Pagina 19 v.h. onderzoek: **ABI1** **cytoplasm** **1.52**

Gene name: abl-interactor 1

This gene may play a role in the progression of several malignancies including melanoma, colon cancer and breast cancer, and a t(10;11) chromosomal translocation involving this gene and the MLL gene has been associated with acute myeloid leukemia.

GNL3 **nucleus** **1.52**

Gene name: guanine nucleotide binding protein-like 3 (nucleolar)

The protein encoded by this gene may interact with p53 and may be involved in tumorigenesis.

PLEKHO1 **plasma membrane** **1.50**

Gene name: pleckstrin homology domain containing, family O member 1

PLEKHO1 (Pleckstrin Homology Domain Containing O1) is a Protein Coding gene. Appears to target ATM to the plasma membrane. Appears to also inhibit (verhinderen van) tumor cell growth by inhibiting AKT-mediated cell-survival. Also implicated in PI3K-regulated muscle differentiation, the regulation of AP-1 activity (plasma membrane bound AP-1 regulator that translocates to the nucleus) and the promotion of apoptosis induced by tumor necrosis factor TNF.

CD44 **plasma membrane** **1.47**

Gene name: CD44 molecule (Indian blood group)

The protein encoded by this gene is a cell-surface glycoprotein involved in cell-cell interactions, cell adhesion and migration. Alternative splicing is the basis for the structural and functional diversity of this protein, and may be related to tumor metastasis

Pagina 20 v.h. onderzoek: **TNXB** **extracellular space** **1.42**

Gene name: tenascin XB

May play a role in supporting the growth of epithelial tumors.

RPL6 **cytoplasm** **1.42**

Gene name: ribosomal protein L6

This gene encodes a protein component of the 60S ribosomal subunit. This protein can bind specifically to domain C of the tax-responsive enhancer element of human T-cell leukemia virus type 1, and may participate in tax-mediated transactivation of transcription.

DAZAP2 **nucleus** **1.40**

Gene name: DAZ associated protein 2

The encoded protein may function in various biological and pathological processes including spermatogenesis, cell signaling and transcription regulation, formation of stress granules during translation arrest, RNA splicing, and pathogenesis of multiple myeloma

RBMX **nucleus** **1.37**

Gene name: RNA binding motif protein, X-linked

RNA-binding protein that plays several role in the regulation of pre- and post-transcriptional processes. Implicated in tissue-specific regulation of gene transcription and alternative splicing of several pre-mRNAs. Binds to and stimulates transcription from the tumor suppressor TXNIP gene promoter; may thus be involved in tumor suppression.

S100A11 **cytoplasm** **1.34**

Gene name: S100 calcium binding protein A11

Chromosomal rearrangements and altered expression of this gene have been implicated in tumor metastasis.

Pagina 21 v.h. onderzoek: **ITGAV** **plasma membrane** **1.32**

Gene name: integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)

The product of this gene belongs to the integrin alpha chain family. Integrins are heterodimeric integral membrane proteins composed of an alpha subunit and a beta subunit that function in cell surface adhesion and signaling. The heterodimer consisting of alpha V and beta 3 subunits is also known as the vitronectin receptor. This integrin may regulate angiogenesis and cancer progression

RPL34 **cytoplasm** **1.31**

Gene name: ribosomal protein L34

This gene encodes a ribosomal protein that is a component of the 60S subunit. Overexpression of this gene has been observed in some cancer cells.

BCAS2 **nucleus** **1.30**

Gene name: breast carcinoma amplified sequence 2

BCAS2 (Breast Carcinoma Amplified Sequence 2) is a Protein Coding gene. Component of the PRP19-CDC5L complex that forms an integral part of the spliceosome and is required for activating pre-mRNA splicing. May have a scaffolding role in the spliceosome assembly as it contacts all other components of the core complex. The PRP19-CDC5L complex may also play a role in the response to DNA damage

CCAR1 **nucleus** **1.30**

Gene name: cell division cycle and apoptosis regulator 1

May play an important role in the growth and tumorigenesis of prostate cancer cells (PubMed:23887938).

TPR **nucleus** **1.30**

Gene name: translocated promoter region (to activated MET oncogene)

acts as a spatial regulator of the spindle-assembly checkpoint (SAC) response ensuring a timely and effective recruitment of spindle checkpoint proteins like MAD1L1 and MAD2L1 to unattached kinetochore during the metaphase-anaphase transition before chromosome congression. Its N-terminus is involved in activation of oncogenic kinases.

RBM5 **nucleus** **1.29**

Gene name: RNA binding motif protein 5

The encoded protein plays a role in the induction of cell cycle arrest and apoptosis through pre-mRNA splicing of multiple target genes including the tumor suppressor protein p53. This gene is located within the tumor suppressor region 3p21.3, and may play a role in the inhibition of tumor transformation and progression of several malignancies including lung cancer.

PROCR **plasma membrane** **1.29**

Gene name: protein C receptor, endothelial

The encoded protein may also play a role in malarial infection and has been associated with cancer.

FBLN1 **extracellular space** 1.28

Gene name: fibulin 1

Fibulin 1 is a secreted glycoprotein that becomes incorporated into a fibrillar extracellular matrix. Has been implicated in a role in cellular transformation and tumor invasion, it appears to be a tumor suppressor.

MLH1 **nucleus** 1.25

Gene name: mutL homolog 1, colon cancer, nonpolyposis type 2 (E. coli)

This gene was identified as a locus frequently mutated in hereditary nonpolyposis colon cancer (HNPCC). It is a human homolog of the E. coli DNA mismatch repair gene mutL, consistent with the characteristic alterations in microsatellite sequences (RER+phenotype) found in HNPCC.

RPL7A **cytoplasm** 1.25

Gene name: ribosomal protein L7a

This gene rearranges with the trk proto-oncogene to form the chimeric oncogene trk-2h, which encodes an oncoprotein consisting of the N terminus of ribosomal protein L7a fused to the receptor tyrosine kinase domain of trk.

Pagina 22 v.h. onderzoek: **MORF4L1** **nucleus** 1.23

Gene name: mortality factor 4 like 1

This complex may be required for the activation of transcriptional programs associated with oncogene and proto-oncogene mediated growth induction, tumor suppressor mediated growth arrest and replicative senescence, apoptosis, and DNA repair.

RPL15 **cytoplasm** 1.23

Gene name: ribosomal protein L15

This gene has been shown to be overexpressed in some esophageal tumors compared to normal matched tissues.

RUFY3 **unknown** -1.08

Gene name: RUN and FYVE domain containing 3

Promotes gastric cancer cell migration and invasion in a PAK1-dependent manner.

BRCC3 **unknown** -1.13

Gene name: BRCA1/BRCA2-containing complex, subunit 3

Component of the BRCA1-A complex, a complex that specifically recognizes Lys-63-linked ubiquitinated histones H2A and H2AX at DNA lesions sites,

leading to target the BRCA1-BARD1 heterodimer to sites of DNA damage at double-strand breaks (DSBs).

Pagina 23 v.h. onderzoek: **PHF17** **nucleus** **-1.21**

Gene name: PHD finger protein 17

Promotes apoptosis. May act as a renal tumor suppressor.

BNIP3L **cytoplasm** **-1.22**

BCL2/adenovirus E1B 19kDa interacting protein 3-like. May function as a tumor suppressor.

Pagina 24 v.h. onderzoek: **ST13** **cytoplasm** **-1.22**

Gene name: suppression of tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein)

The protein encoded by this gene is an adaptor protein that mediates the association of the heat shock proteins HSP70 and HSP90.The expression of this gene is reported to be downregulated in colorectal carcinoma tissue suggesting that it is a candidate tumor suppressor gene.

RASSF3 **unknown** **-1.24**

Gene name: Ras association (RalGDS/AF-6) domain family member 3

The RAS oncogene (MIM 190020) is mutated in nearly one-third of all human cancers.

NBPF3 **unknown** **-1.24**

Gene name: neuroblastoma breakpoint family, member 3

This gene is a member of the neuroblastoma breakpoint family (NBPF) which consists of dozens of recently duplicated genes primarily located in segmental duplications on human chromosome 1. This gene family has experienced its greatest expansion within the human lineage and has expanded, to a lesser extent, among primates in general. Members of this gene family are characterized by tandemly repeated copies of DUF1220 protein domains. DUF1220 copy number variations in human chromosomal region 1q21.1, where most DUF1220 domains are located, have been implicated in a number of developmental and neurogenetic diseases such as microcephaly, macrocephaly, autism, schizophrenia, mental retardation, congenital heart disease (aangeboren hartafwijkingen) , neuroblastoma, and congenital kidney and urinary tract anomalies. Altered expression of some gene family members is associated with several types of cancer.

TANK **cytoplasm** **-1,24**

Gene name: TRAF family member-associated NFKB activator

The TRAF (tumor necrosis factor receptor-associated factor) family of proteins associate with and transduce signals from members of the tumor necrosis factor receptor superfamily. the protein encoded by this gene can block TRAF2 binding to LMP1, the Epstein-Barr virus transforming protein, and inhibit LMP1-mediated NF-kappa-B activation.

CABLES1 nucleus -1.25

Gene name: Cdk5 and Abl enzyme substrate 1

This gene encodes a protein involved in regulation of the cell cycle through interactions with several cyclin-dependent kinases. One study (PMID: 16177568) reported aberrant splicing of transcripts from this gene which results in removal of the cyclin binding domain only in human cancer cells, and reduction in gene expression was shown in colorectal cancers

C2orf4 unknown -1.25

Gene name: mediator of cell motility 1

MEMO1 (Mediator Of Cell Motility 1/alias for C2orf4) is a Protein Coding gene. Is required for breast carcinoma cell migration.

MCF2L cytoplasm -1.25

Gene name: MCF.2 cell line derived transforming sequence-like

This gene encodes a guanine nucleotide exchange factor that interacts specifically with the GTP-bound Rac1 and plays a role in the Rho/Rac signaling pathways. Becomes activated and highly tumorigenic by truncation of the N-terminus

KIAA1109 unknown -1.25

Gene name: KIAA1109

This gene is located on the long arm of chromosome 4 in a region that is associated with susceptibility to celiac disease. this protein is thought to function in the regulation of epithelial growth and differentiation, and in tumor development.

MINA nucleus -1.26

Gene name: MYC induced nuclear antigen

MINA is a c-Myc (MYC; MIM 190080) target gene that may play a role in cell proliferation or regulation of cell growth. Diseases associated with MINA include lung cancer.

NPDC1 extracellular space -1.26

Gene name: neural proliferation, differentiation and control, 1

NPDC1 (Neural Proliferation, Differentiation And Control, 1) is a Protein Coding gene. Suppresses oncogenic transformation in neural and non-neural cells and down-regulates neural cell proliferation.

PRX **nucleus** **-1.26**

Gene name: periaxin

This gene encodes a protein involved in peripheral nerve myelin upkeep. The encoded protein contains 2 PDZ domains which were named after PSD95 (post synaptic density protein), DlgA (Drosophila disc large tumor suppressor), and ZO1 (a mammalian tight junction protein).

SNIP1 **nucleus** **-1,26**

Gene name: Smad nuclear interacting protein 1

This gene encodes a protein that contains a coiled-coil motif and C-terminal forkhead-associated (FHA) domain. The encoded protein also regulates the stability of cyclin D1 mRNA, and may play a role in cell proliferation and cancer progression.

NUMA1 **nucleus** **-1.26**

Gene name: nuclear mitotic apparatus protein 1

This gene encodes a large protein that forms a structural component of the nuclear matrix. Chromosomal translocation of this gene with the RARA (retinoic acid receptor, alpha) gene on chromosome 17 have been detected in patients with acute promyelocytic leukemia.

Pagina 25 v.h. onderzoek: **CALB2** **cytoplasm** **-1.26**

Gene name: calbindin 2

This gene encodes an intracellular calcium-binding protein belonging to the troponin C superfamily. It also functions as a modulator of neuronal excitability, and is a diagnostic marker for some human diseases, including Hirschsprung disease and some cancers.

MAGED2 **plasma membrane** **-1.27**

Gene name: melanoma antigen family D, 2

This gene is a member of the MAGED gene family. The MAGED genes are clustered on chromosome Xp11. This gene is located in Xp11.2, a hot spot for X-linked mental retardation (XLMR). This gene may also be involved in several types of cancer, including breast cancer and melanoma.

TUSC1 **unknown** **-1.28**

Gene name: tumor suppressor candidate 1

This gene is located within the region of chromosome 9p *that harbors tumor suppressor genes critical in carcinogenesis.* It is an intronless gene which is downregulated in non-small-cell lung cancer and small-cell lung cancer cell lines, suggesting that it may play a role in lung tumorigenesis. (het ontstaan van tumoren in de longen)

TSC1 **cytoplasm** **-1.28**

Gene name: tuberous sclerosis 1

This gene encodes a growth inhibitory protein thought to play a role in the stabilization of tuberin. Implicated as a tumor suppressor.

CSPG4 **plasma membrane** **-1.28**

Gene name: chondroitin sulfate proteoglycan 4

A human melanoma-associated chondroitin sulfate proteoglycan plays a role in stabilizing cell-substratum interactions during early events of melanoma cell spreading on endothelial basement membranes.

RNF20 **nucleus** **-1.28**

Gene name: ring finger protein 20

The protein encoded by this gene shares similarity with BRE1 of S. cerevisiae. The protein encoded by this human gene is an E3 ubiquitin ligase that regulates chromosome structure by monoubiquitinating histone H2B. This protein acts as a putative tumor suppressor and positively regulates the p53 tumor suppressor as well as numerous histone H2A and H2B genes. In contrast, this protein also suppresses the expression of several protooncogenes and growth-related genes, including many genes that are induced by epidermal growth factor.

BCAS3 **nucleus** **-1.28**

Gene name: breast carcinoma amplified sequence 3

BCAS3 (Breast Carcinoma Amplified Sequence 3) is a Protein Coding gene. Diseases associated with BCAS3 include breast cancer.

TUSC5 **unknown** **-1.28**

Gene name: tumor suppressor candidate 5

TUSC5 (Tumor Suppressor Candidate 5) is a Protein Coding gene. Diseases associated with TUSC5 include Accommodative Esotropia and Chiasmal Syndrome.

Pagina 26 v.h. onderzoek: **RBL2** **nucleus** **-1.29**

Gene name: retinoblastoma-like 2 (p130)

RBL2 (Retinoblastoma-Like 2) is a Protein Coding gene. Probably acts as a transcription repressor by recruiting chromatin-modifying enzymes to promoters. Potent inhibitor of E2F-mediated trans-activation, associates preferentially with E2F5. Binds to cyclins A and E. Binds to and may be involved in the transforming capacity of the adenovirus E1A protein. May act as a tumor suppressor.

BAK1 **cytoplasm** **-1.30**

Gene name: BCL2-antagonist/killer 1

The protein encoded by this gene belongs to the BCL2 protein family. This protein also interacts with the tumor suppressor P53 after exposure to cell stress.

GAS8 **cytoplasm** **-1.30**

Gene name: growth arrest-specific 8

This gene includes 11 exons spanning 25 kb and maps to a region of chromosome 16 that is sometimes deleted in breast and prostrate cancer. This gene is a putative (vermeend) tumor suppressor gene.

TRAF3IP2 **unknown** **-1.30**

Gene name: TRAF3 interacting protein 2

This gene encodes a protein involved in regulating responses to cytokines by members of the Rel/NF-kappaB transcription factor family. This gene product interacts with TRAF proteins (tumor necrosis factor receptor-associated factors) and either I-kappaB kinase or MAP kinase to activate either NF-kappaB or Jun kinase.

BATF2 **unknown** **-1.32**

Gene name: basic leucine zipper transcription factor, ATF-like 2

BATF2 (Basic Leucine Zipper ATF-Like Transcription Factor 2) is a Protein Coding gene. inhibits CYR61-induced anchorage-independent growth and invasion in several cancer types, such as breast cancer, malignant glioma and metastatic melanoma.

C1QTNF9 **unknown** **--1.32**

Gene name: C1q and tumor necrosis factor related protein 9

C1QTNF9 (C1q And Tumor Necrosis Factor Related Protein 9) is a Protein Coding gene.

Pagina 26 v.h. onderzoek: **ACTN4** **cytoplasm** **-1.35**

Gene name: actinin, alpha 4

Alpha actinins belong to the spectrin gene superfamily which represents a diverse group of cytoskeletal proteins, including the alpha and beta spectrins and dystrophins. thought to be involved in metastatic processes.

NET1 nucleus -1.35

Gene name: neuroepithelial cell transforming 1

This gene is part of the family of Rho guanine nucleotide exchange factors. Stimulates genotoxic stress-induced RHOB activity in breast cancer cells leading to their cell death.

MCAM plasma membrane -1.36

Gene name: melanoma cell adhesion molecule

MCAM (Melanoma Cell Adhesion Molecule) is a Protein Coding gene. Its expression may allow melanoma cells to interact with cellular elements of the vascular system, thereby enhancing hematogeneous tumor spread.

IER3IP1 unknown -1.37

Gene name: immediate early response 3 interacting protein 1

This gene encodes a small protein that is localized to the endoplasmic reticulum (ER) and may play a role in the ER stress response by mediating cell differentiation and apoptosis. Transcription of this gene is regulated by tumor necrosis factor alpha and specificity protein 1 (Sp1).

CD151 plasma membrane -1.37

Gene name: CD151 molecule (Raph blood group)

The protein encoded by this gene is a member of the transmembrane 4 superfamily, also known as the tetraspanin family. It is involved in cellular processes including cell adhesion and may regulate integrin trafficking and/or function. This protein enhances cell motility, invasion and metastasis of cancer cells.

BBC3 cytoplasm -1.38

Gene name: BCL2 binding component 3

This gene encodes a member of the BCL-2 family of proteins. Because of its pro-apoptotic role, this gene is a potential drug target for cancer therapy and for tissue injury.

CCND1 nucleus -1.40

Gene name: cyclin D1

The protein encoded by this gene belongs to the highly conserved cyclin family, whose members are characterized by a dramatic periodicity in protein

abundance throughout the cell cycle. This protein has been shown to interact with tumor suppressor protein Rb and the expression of this gene is regulated positively by Rb. Mutations, amplification and overexpression of this gene, which alters cell cycle progression, are observed frequently in a variety of tumors and may contribute to tumorigenesis (ontstaan van tumoren) .

SPARC **extracellular space** -1.43

Gene name: secreted protein, acidic, cysteine-rich (osteonectin)

The gene product has been associated with tumor suppression but has also been correlated with metastasis based on changes to cell shape which can promote tumor cell invasion.This gene encodes a cysteine-rich acidic matrix-associated protein.

VHL **nucleus** **-1.44**

Gene name: von Hippel-Lindau tumor suppressor

Von Hippel-Lindau syndrome (VHL) is a dominantly inherited familial cancer syndrome predisposing to a variety of malignant and benign tumors.

PHLDA3 **unknown** **-1.47**

Gene name: pleckstrin homology-like domain, family A, member 3

PHLDA3 (Pleckstrin Homology Like Domain Family A Member 3) is a Protein Coding gene. May act as a tumor suppressor.

ITGA7 **plasma membrane** **-1.48**

Gene name: integrin, alpha 7

The protein encoded by this gene belongs to the integrin alpha chain family. They mediate a wide spectrum of cell-cell and cell-matrix interactions, and thus play a role in cell migration, morphologic development, differentiation, and metastasis.

SELENBP1 **cytoplasm** **-1.52**

Gene name: selenium binding protein 1

This gene encodes a member of the selenium-binding protein family. Selenium is an essential nutrient that exhibits potent anticarcinogenic properties, and deficiency of selenium may cause certain neurologic diseases. The effects of selenium in preventing cancer and neurologic diseases may be mediated by selenium-binding proteins, and decreased expression of this gene may be associated with several types of cancer.

RPL7A **cytoplasm** **-1.53**

Gene name: ribosomal protein L7a

This gene rearranges with the trk proto-oncogene to form the chimeric oncogene trk-2h, which encodes an oncoprotein consisting of the N terminus of ribosomal protein L7a fused to the receptor tyrosine kinase domain of trk.

DVL1 **cytoplasm** **-1.56**

Gene name: dishevelled, dsh homolog 1 (Drosophila)

DVL1, the human homolog of the Drosophila dishevelled gene (dsh) encodes a cytoplasmic phosphoprotein that regulates cell proliferation, acting as a transducer molecule for developmental processes, including segmentation and neuroblast specification. DVL1 is a candidate gene for neuroblastomatous transformation. The Schwartz-Jampel syndrome and Charcot-Marie-Tooth disease type 2A have been mapped to the same region as DVL1. The phenotypes of these diseases may be consistent with defects which might be expected from aberrant expression of a DVL gene during development.

NOL8 **nucleus** **-1.56**

Gene name: nucleolar protein 8

NOL8 binds Ras-related GTP-binding proteins (see MIM 608267) and plays a role in cell growth Plays an essential role in the survival of diffuse-type gastric cancer cells. Acts as a nucleolar anchoring protein for DDX47. May be involved in regulation of gene expression at the post-transcriptional level or in ribosome biogenesis in cancer cells.

Pagina 29 v.h. onderzoek: **TXNIP** **cytoplasm** **-1.62**

Gene name: thioredoxin interacting protein

This gene encodes a thioredoxin-binding protein that is a member of the alpha arrestin protein family. Required for the maturation of natural killer cells. Acts as a suppressor of tumor cell growth.

THRSP **nucleus** **-1.64**

Gene name: thyroid hormone responsive (SPOT14 homolog, rat)

The protein encoded by this gene is similar to the gene product of S14, a rat gene whose expression is limited to liver and adipose tissue and is controlled by nutritional and hormonal factors. This gene has been shown to be expressed in liver and adipocytes, particularly in lipomatous modules. It is also found to be expressed in lipogenic breast cancers, which suggests a role in controlling tumor lipid metabolism.

NDRG2 **cytoplasm** **-1.66**

Gene name: NDRG family member 2

This gene is a member of the N-myc downregulated gene family which belongs to the alpha/beta hydrolase superfamily. This gene is a member of

the N-myc downregulated gene family which belongs to the alpha/beta hydrolase superfamily. This gene may be involved in glioblastoma carcinogenesis (ontstaan van tumoren). Down-regulates CTNNB1-mediated transcriptional activation of target genes, such as CCND1, and may thereby act as tumor suppressor.

MALAT1 unknown -1.94

Gene name: metastasis associated lung adenocarcinoma transcript 1 (non-protein coding)

This gene produces a precursor transcript from which a long non-coding RNA is derived by RNase P cleavage of a tRNA-like small ncRNA (known as mascRNA) from its 3' end. It may act as a transcriptional regulator for numerous genes, including some genes involved in cancer metastasis and cell migration, and it is involved in cell cycle regulation. Its upregulation in multiple cancerous tissues has been associated with the proliferation and metastasis of tumor cells.

CD63 plasma membrane -2.05

Gene name: CD63 molecule

The protein encoded by this gene is a member of the transmembrane 4 superfamily, also known as the tetraspanin family. The encoded protein is a cell surface glycoprotein that is known to complex with integrins. It may function as a blood platelet activation marker. Deficiency of this protein is associated with Hermansky-Pudlak syndrome. Also this gene has been associated with tumor progression

C10orf116 unknown -2.19

Gene name: chromosome 10 open reading frame 116

APM2 gene is exclusively expressed in adipose tissue. Its overexpression confers resistance to the anticancer chemotherapeutic drug cisplatin.