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: tumor supressoren

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.

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	Gene	Location	Fold change
Pagina 2 v.h. onderzoek:	**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.

Pagina 3 v.h. onderzoek:	**LOXL1**	**extracellular spacev**	**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

	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.

Pagina 7 v.h. onderzoek: **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.

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.

Pagina 8 v.h. onderzoek: **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.

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 tumor suppressor in human breast carcinomas.

Pagina 9 v.h. onderzoek: **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.

Pagina 10 v.h. onderzoek: **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.

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.

Pagina 11 v.h. onderzoek: **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.

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.

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.

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.

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.

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.

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.

Pagina 16 v.h. onderzoek: **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*.

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: **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.

Pagina 18 v.h. onderzoek: **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.

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.

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.

Pagina 20 v.h. onderzoek: **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.

Pagina 21 v.h. onderzoek:

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.

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. <<<<

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

Gene name: 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.

Pagina 25 v.h. onderzoek: **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.

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.

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.

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.

Pagina 27 v.h. onderzoek:

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.

Pagina 29 v.h. onderzoek: **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.