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: DNA-repair

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	Loction	Fold change
Pagina 2 v.h. onderzoek:	**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.

ASCC3	**nucleus**	**+1.79**

Gene name: activating signal cointegrator 1 complex subunit 3

The encoded protein is the largest subunit of the activating signal cointegrator 1 complex that is involved in DNA repair and resistance to alkylation damage. Promotes DNA unwinding to generate single-stranded substrate needed for ALKHB3, enabling ALKHB3 to process alkylated N3-methylcytosine (3mC) within double-stranded regions. Enhances NF-kappa-B, SRF and AP1 transactivation.

ALKBH2	**nucleus**	**+1.76**

Gene name: alkB, alkylation repair homolog 2 (E. coli)

The Escherichia coli AlkB protein protects against the cytotoxicity of methylating agents by repair of the specific DNA lesions generated in single-stranded DNA. Dioxygenase that repairs alkylated DNA and RNA containing 1-methyladenine and 3-methylcytosine by oxidative demethylation. Can also repair alkylated DNA containing 1-ethenoadenine (in vitro). Has strong preference for double-stranded DNA.

TMEM23/SGMS1	**cytoplasm**	**+1.55**

Gene name: sphingomyelin synthase 1

May protect against cell death by reversing the stress-inducible increase in levels of proapoptotic ceramide.

GPX7	**cytoplasm**	**+1.54**

Gene name: glutathione peroxidase 7

GPX7 (Glutathione Peroxidase 7) is a Protein Coding gene. It suppresses acidic bile acid-induced reactive oxigen species (ROS) and protects against oxidative DNA damage and double-strand breaks.

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.

Pagina 3 v.h. onderzoek: **POLK** **nucleus** **+1.30**

Gene name: polymerase (DNA directed) kappa

External and internal DNA-damaging agents continually threaten the integrity of genetic material in cells. Although a variety of repair mechanisms exist to remove the resulting lesions, some lesions escape repair and block the replication machinery. Members of the Y family of DNA polymerases, such as POLK, permit the continuity of the replication fork by allowing replication through such DNA lesions. Each Y family polymerase has a unique DNA-damage bypass and fidelity profile. POLK is specialized for the extension step of lesion

TOP1MT **cytoplasm** **1.36**

Gene name: topoisomerase (DNA) I, mitochondrial

This gene encodes a DNA topoisomerase, an enzyme that controls and alters the topologic states of DNA during transcription. This enzyme catalyzes the transient breaking and rejoining of a single strand of DNA which allows the strands to pass through one another, thus altering the topology of DNA.

Releases the supercoiling and torsional tension of DNA introduced during the DNA replication and transcription by transiently cleaving and rejoining one strand of the DNA duplex.

Pagina 4 v.h. onderzoek: **RTEL1** **nucleus** **–1.18**

Gene name: regulator of telomere elongation helicase 1

ATP-dependent DNA helicase implicated in telomere-length regulation, DNA repair and the maintenance of genomic stability.

VCP **cytoplasm** **–1.21**

Gene name: valosin-containing protein

Also involved in DNA damage response: recruited to double-strand breaks (DSBs) sites in a RNF8- and RNF168-dependent manner and promotes the recruitment of TP53BP1 at DNA damage sites. Recruited to stalled replication forks by SPRTN: may act by mediating extraction of DNA polymerase eta (POLH) to prevent excessive translesion DNA synthesis and limit the incidence of mutations induced by DNA damage.

Pagina 6 v.h. onderzoek: **MAP1S** **cytoplasm** **-1.52**

Gen name: microtubule-associated protein 1S

Microtubule-associated protein that mediates aggregation of mitochondria resulting in cell death and genomic destruction (MAGD). Plays a role in anchoring the microtubule organizing center to the centrosomes. Binds to DNA. Plays a role in apoptosis. Involved in the formation of microtubule bundles

AK027610 **nucleus** **-1.79**

Gene name: ribonuclease H1

This gene encodes an endonuclease that specifically degrades the RNA of RNA-DNA hybrids and is necessary for DNA replication and repair.

ATG7 **cytoplasm** **1.63**

Gene name: Autophagy related 7 homolog (S. cerevisiae)

This gene encodes an E1-like activating enzyme that is essential for autophagy and cytoplasmic to vacuole transport. The encoded protein is also thought to modulate p53-dependent cell cycle pathways during prolonged metabolic stress. It has been associated with multiple functions, including axon membrane trafficking, axonal homeostasis, mitophagy, adipose differentiation, and hematopoietic stem cell maintenance.

Pagina 9 v.h. onderzoek: **CSNK1G3** **cytoplasm** **-1.32**

Gene name: casein kinase 1, gamma 3

Casein kinase I (CK1) is a monomeric serine-threonine protein kinase with 7 isoforms: alpha, beta, gamma1, gamma2, gamma3, delta and epsilon. CK1 is involved in many cellular processes including DNA repair, cell division, nuclear localization and membrane transport. Isoforms are also integral to development.

HUS1 **nucleus** **-1.48**

Gene name: HUS1 checkpoint homolog (S. pombe)

Component of the 9-1-1 cell-cycle checkpoint response complex that plays a major role in DNA repair.

Pagina 11 v.h. onderzoek: **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

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. May also play a role in DNA repair via its interaction with Ku, possibly by connecting DNA damage-response pathways with sister chromatid separation.

Pagina 12 v.h. onderzoek: **UBA52** **cytoplasm** **+1.23**

Gene name: ubiquitin A-52 residue ribosomal protein fusion product 1

Ubiquitin: Exists either covalently attached to another protein, or free (unanchored). When covalently bound, it is conjugated to target proteins via an isopeptide bond either as a monomer (monoubiquitin), a polymer linked via different Lys residues of the ubiquitin (polyubiquitin chains) or a linear polymer linked via the initiator Met of the ubiquitin (linear polyubiquitin chains). Polyubiquitin chains, when attached to a target protein, have different functions depending on the Lys residue of the ubiquitin that is linked: Lys-6-linked may be involved in DNA repair; Lys-11-linked is involved in ERAD (endoplasmic reticulum-associated degradation) and in cell-cycle regulation; Lys-29-linked is involved in lysosomal degradation; Lys-33-linked is involved in kinase modification; Lys-48-linked is involved in protein degradation via the proteasome; Lys-63-linked is involved in endocytosis, DNA-damage responses as well as in signaling processes leading to activation of the transcription factor NF-kappa-B. Linear polymer chains formed via attachment by the initiator Met lead to cell signaling. Ubiquitin is usually conjugated to Lys residues of target proteins, however, in rare cases, conjugation to Cys or Ser residues has been observed.

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. Through interaction with the MRN complex it may be involved in the regulation of telomeres lengthening.

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 proto-oncogene and shown to be involved in regulation of telomerase.

RFC1 **nucleus** **-1.23**

Gene name: replication factor C (activator 1) 1, 145kDa

This gene encodes the large subunit of replication factor C, a five subunit DNA polymerase accessory protein, which is a DNA-dependent ATPase required for eukaryotic DNA replication and repair.

This intronless gene encodes a transcription factor that contains a basic leucine zipper (bZIP) domain and recognizes the CCAAT motif in the promoters of target genes.

Pagina 18 v.h. onderzoek: **CDKN1A** **nucleus** **+1.65**

Gene name: cyclin-dependent kinase inhibitor 1A (p21, Cip1)

This protein can interact with proliferating cell nuclear antigen, a DNA polymerase accessory factor, and plays a regulatory role in S phase DNA replication and DNA damage repair.

OBFC2A **unknown** **+1.64**

Gene name: oligonucleotide/oligosaccharide-binding fold containing 2A

Single-stranded DNA (ssDNA)-binding proteins, such as OBFC2A, are ubiquitous and essential for a variety of DNA metabolic processes, including replication, recombination, and detection and repair of damage

FANCC **nucleus** **+1.63**

Gene name: Fanconi anemia, complementation group C

DNA repair protein that may operate in a postreplication repair or a cell cycle checkpoint function. May be implicated in interstrand DNA cross-link repair and in the maintenance of normal chromosome stability.

FANCG **nucleus** **+1.57**

Gene name: Fanconi anemia, complementation group G

The Fanconi anemia complementation group (FANC) currently includes FANCA, FANCB, FANCC, FANCD1 (also called BRCA2), FANCD2, FANCE, FANCF, FANCG, FANCI, FANCJ (also called BRIP1), FANCL, FANCM and FANCN (also called PALB2). The previously defined group FANCH is the same as FANCA. Fanconi anemia is a genetically heterogeneous recessive disorder characterized by cytogenetic instability, hypersensitivity to DNA crosslinking agents, increased chromosomal breakage, and defective DNA repair.

Pagina 19 v.h. onderzoek: **PCNA** **nucleus** **+1.44**

Gene name: proliferating cell nuclear antigen

Plays a key role in DNA damage response (DDR) by being conveniently positioned at the replication fork to coordinate DNA replication with DNA repair and DNA damage tolerance pathways (PubMed:24939902).

Pagina 19 v.h. onderzoek: **TIPRL** **unknown** **+1.39**

Gene name: TIP41, TOR signaling pathway regulator-like (S. cerevisiae)

May play a role in the regulation of ATM/ATR signaling pathway controlling DNA replication and repair.

RINT1 **nucleus** **+1.35**

Gene name: RAD50 interactor 1

Essential for telomere length control (PubMed:16600870).

CUL4B **unknown** **+1.32**

Gene name: cullin 4B

Targeted to UV damaged chromatin by DDB2 and may be important for DNA repair and DNA replication.

Pagina 21 v.h. onderzoek: **DDB1** **nucleus** **+1.30**

Gene name: damage-specific DNA binding protein 1, 127kDa

The protein encoded by this gene is the large subunit (p127) of the heterodimeric DNA damage-binding (DDB) complex while another protein (p48) forms the small subunit.

Pagina 22 v.h. onderzoek: **PUM1** **cytoplasm** **+1.23**

Gene name: pumilio homolog 1 (Drosophila)

Represses a program of genes necessary to maintain genomic stability such as key mitotic, DNA repair and DNA replication factors.

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: **GADD45A** **nucleus** **-1.19**

Gene name: growth arrest and DNA-damage-inducible, alpha

This gene is a member of a group of genes whose transcript levels are increased following stressful growth arrest conditions and treatment with

DNA-damaging agents.

AA279208 nucleus -1.19

Gene name: RAD23 homolog B (S. cerevisiae)

This protein was also shown to interact with, and elevate the nucleotide excision activity of 3-methyladenine-DNA glycosylase (MPG), which suggested a role in DNA damage recognition in base excision repair. Cyclobutane pyrimidine dimers (CPDs) which are formed upon UV-induced DNA damage esacpe detection by the XPC complex due to a low degree of structural perurbation. Instead they are detected by the UV-DDB complex which in turn recruits and cooperates with the XPC complex in the respective DNA repair.

Pagina 29 v.h. onderzoek: **KIN nucleus -1.61**

Gene name: KIN, antigenic determinant of recA protein homolog (mouse)

The protein encoded by this gene is a nuclear protein that forms intranuclear foci during proliferation and is redistributed in the nucleoplasm during the cell cycle. Involved in DNA replication and the cellular response to DNA damage. May participate in DNA replication factories and create a bridge between DNA replication and repair mediated by high molecular weight complexes.

PRPF19 nucleus -1.70

PRP19/PSO4 pre-mRNA processing factor 19 homolog (S. cerevisiae)

Ubiquitin-protein ligase which is a core component of several complexes mainly involved pre-mRNA splicing and DNA repair. PSO4 (alias voor PRPF19) is the human homolog of yeast Pso4, a gene essential for cell survival and DNA repair.

Fold changes / veelvoud verandering. Rekenmethode 1 = 100%.
Getal achter de komma opgeteld = percentage van de verandering.
Groen - rood is percentage van de gemiddelde verandering in de genexpressie van DNA reparatie genen.

2.56	1.18
1.79	1.21
1.76	1.79
1.55	1.32
1.54	1.48
1.42	1.23
1.30	1.23
1.36	1.19
1.52	1.61
1.63	1.70
2.06	
1.23	
1.22	
1.20	
1.65	
1.64	
1.63	
1.57	
1.44	
1.39	
1.35	
1.32	
1.30	
1.23	
1.19	

394 vermindering genexpressie DNA reparatie genen

1285 verbetering in genexpressie DNA reparatiegenen

1285 verbetering -/- 394 vermindering = gemiddeld 891% = bijna 9-voudige verbetering in de genexpressie van reparatiegenen