

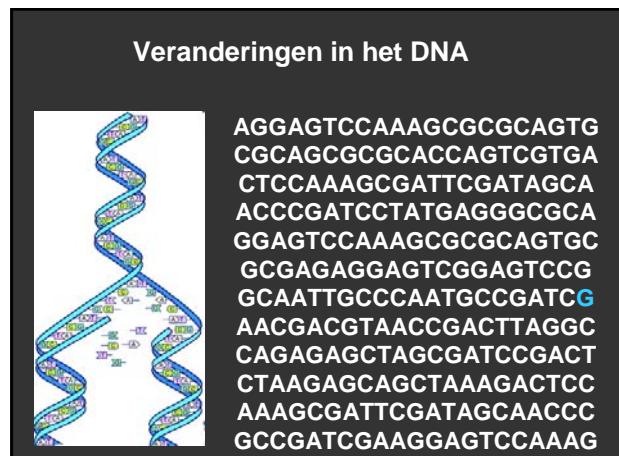
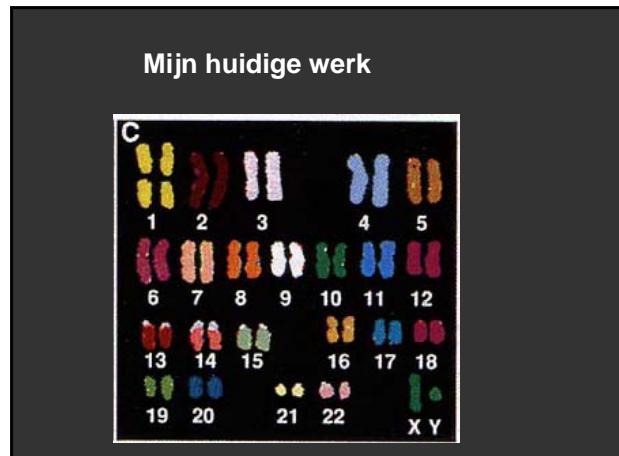


1e publicatie

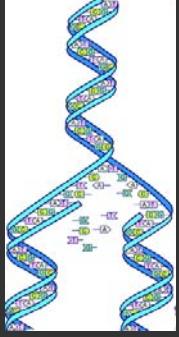
Micronutrients and the risk of lung cancer.

Kok FJ, van Duijn CM, Hofman A, Vermeeren R, de Bruijn AM, Valkenburg HA.

N Engl J Med. 1987;316(22):1416



Veranderingen in het DNA



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AGGAGTCCAAGCGCGCAGTG
CGCAGCGCGCACCAAGTCGTGA
CTCCAAAGCGATTGATAGCA
ACCCGATCCTATGAGGGCGCA
GGAGTCCAAGCGCGCAGTGC
GCGAGAGGAGTCGGAGTCCG
GCAATTGCCAATGCCGATCA
AACGACGTAACCGACTTAGGC
CAGAGAGCTAGCGATCCGACT
CTAAGAGCAGCTAAAGACTCC
AAAGCGATTGATAGCAACCC
GCCGATCGAAGGGAGTCAAAG

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Genen en kenmerken



Mijn huidige werk

Genetic variaties ⇒ Risico op ziekte



Beginsel 1: vind de niche

Science, Vol 261, Issue 5123, 921-923
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ARTICLES
Gene dose of apolipoprotein E type 4 allele associated with disease in late onset families
 EH Corades, AM Saunders, WJ Stittmeyer, DE Schmeichel, PC and MA Pericak-Vance

Department of Medicine, Joseph and Kathleen Bryan Alzheimer's Disease Center, Durham, NC 27710

The apolipoprotein E type 4 allele (APOE-epsilon 4) is genetically and sporadic forms of Alzheimer's disease (AD). Risk for AD increased from 84 to 68 years with increasing number of APOE-epi. Thus APOE-epsilon 4 gene dose is a major risk factor for late onset AD. APOE-epsilon 4 was virtually sufficient to cause AD by age 60.

Comella M, van Duijn P, Peerd de Kieff M, Cattaert A, Aissa Wahrman L, Louis M, Hervé L, Albert Hofman & Christine Van Broeckhoven C

Several studies have reported an association of the apolipoprotein E allele ε4 (APOE-ε4) to familial Alzheimer's disease (FAD) and late onset Alzheimer's disease (LOAD). We report the relationship between APOE-ε4 and early-onset Alzheimer's disease (EOAD) in a Dutch population-based study. The frequency of the APOE-ε4 allele was 2.2 times more common among EOAD cases compared to controls. Amongst carriers of the APOE-ε4 allele, the risk was 1.5 times higher in those with a positive family history than in those without. A significant increase in risk of EOAD was observed in individuals with two APOE-ε4 alleles. This increase in risk was independent of the presence of a family history of dementia. The association between the number of elements, but an increase in EOAD risk for APOE-ε4 heterozygotes could only be shown in subjects with a family history of dementia. This suggests that the genetic risk for the association between APOE-ε4 and EOAD which is modified by family history of dementia.

Alzheimer's Disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline, memory loss, and language difficulties. It is the most common form of dementia, with approximately 40 million people worldwide affected. The risk of developing AD increases with age, with approximately 5% of the population over 65 years old and 40% of those over 85 years old having some form of dementia. The exact cause of AD is unknown, but it is believed to be a complex interaction of genetic, environmental, and lifestyle factors. One of the most well-known genetic risk factors for AD is the APOE-ε4 allele. This allele is found in approximately 40% of the population and is associated with an increased risk of developing AD. Other genetic risk factors include the APP, PSEN1, and PSEN2 genes. Environmental factors such as head trauma, smoking, and exposure to certain chemicals have also been implicated in the development of AD. Lifestyle factors such as physical activity, diet, and cognitive stimulation may also play a role in preventing or delaying the onset of AD. Early diagnosis and treatment are important for managing the symptoms of AD and improving quality of life for patients and their caregivers. Research continues to explore the underlying mechanisms of AD and to develop more effective treatments for this devastating disease.



Grondbeginsel 2:

- Iedere paper is een mega effort (geld en tijd)
- Investeer maximaal (tijd, geld en menskracht) in belangrijke bevindigen
- Blijf niet "zoeken" naar een doorbraak in een doodlopende straat

Beginsel 3: je redt het niet alleen



Top publiceren is team work



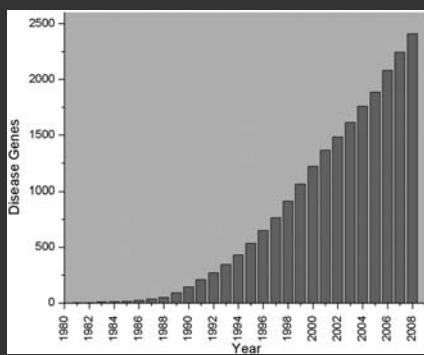
Beginsel 4: blijf je ontwikkelen



Genetische Epidemiologie

- Van familie onderzoek naar populatie onderzoek
- Van 3 patienten naar 120,000
- Van complexe statistiek tot simpele t-test

Genen en kenmerken



Nieuwe ontwikkelingen

- Publiceren met 100en auteurs
- Publicaties bij gen-ontdekkingen vrijwel altijd in toptijdschriften
- Belangrijk: waar sta je op de paper?

550ste publicatie

Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index.

Net Credit 2010 Nov

ARTICLES

Biological, clinical and population relevance of 95 loci for blood lipids

A list of authors and their affiliations appears at the end of the paper.

Plasma concentrations of total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides are among the most important risk factors for coronary artery disease (CAD) and are targets for therapeutic intervention. We screened the genome for common variants associated with plasma lipids in ~100,000 individuals of European ancestry. Herein we report 95 genome-wide associated variants ($P < 5 \times 10^{-8}$), with 59 showing genome-wide significant associations ($P < 10^{-8}$). These variants are enriched for being located near genes involved in lipid metabolism and/or SNPs near known lipid regulators. (For example, CYP27A1, NPC1L1 and SCARBB1) as well as in loci previously implicated in lipid regulation. The 95 loci contribute not only to nominal levels in plasma but also to extremes of lipid phenotypes and have an impact on lipid traits in non-European populations (East Asians, South Asians and African Americans). One SNP, rs10757272, located in the gene *PPBP1B*, was associated with all four lipid traits. When we validated these findings in three new genome-wide association studies (GWAS) in European populations (n=100,000) and meta-analyzed the results, we replicated 11 of the novel associations (GAIN27, PPBP1B and TTC26B) with expert validation in these samples. Taken together, our findings provide the foundation to develop a broader biological understanding of lipoprotein metabolism and to identify new therapeutic opportunities for the prevention of CAD.

Plasma concentrations of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) are heritable risk factors for cardiovascular disease and targets for therapeutic intervention¹. Genome-wide association studies (GWASs) involving up to 20,000 individuals of European ancestry have identified >30 genetic loci contributing to inter-individual variation in plasma lipid concentrations^{2–10}. In these loci harboured genes previously known to influence plasma lipid concentrations, establishing the technical validity of the

polymorphisms (SNPs) and phased chromosomes from the *MapPop* CEU (Utah residents with ancestry from northern and western Europe) sample to impute autosomal SNPs catalogued in the *MapPop*; SNPs with minor allele frequency (MAF) >1% and good imputation quality (see Methods in Supplementary Information) were analysed. A total of ~2.6 million directly genotyped or imputed SNPs were tested for association with each of the lipid traits in each study. For each SNP, evidence of association was combined across studies using a fixed effects meta-analysis.

Nieuwe ontwikkelingen

- Meepubliceren van belang voor toekomst: subsidies
 - Hoe stel je je rol veilig in grote consortia?
 - Hoe weeg je de verschillende belangen in de onderzoeksgroep?
 - Focus op de wetenschap en niet op de politiek!



A collage of four photographs illustrating glacial landscapes. The top-left image shows a large, smooth white iceberg floating in dark blue water under a cloudy sky. The top-right image features a smaller, more textured iceberg with blue meltwater pools at its base, set against a dramatic sky. The bottom-left image depicts a massive, multi-tiered iceberg with intricate internal structures and a bright white surface. The bottom-right image captures a wide view of a glacier's edge, where a thick wall of ice meets the ocean, with snow-covered mountains visible in the background.

Publiceren: grondbeginselen en nieuwe ontwikkelingen

Cock van Duijn