Genom-sekventering – hvorfor, og hvad er problemet

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KONKLUSIONER

- God idé at satse på NGS i sundhedsvæsenet
- Vigtigt at overveje hvilke problemer der kan være (især uventede fund)
- NGS kan IKKE bruges til at spå om fremtiden
- Men i nogle tilfælde kan NGS bruges til at identificere hvilke personer der har RISIKO for at udvikle sygdomme
- NGS kan bruges til diagnostik
- Og måske i fremtiden til at give en bedre behandling
- Risiko for unødige tilbagemeldinger

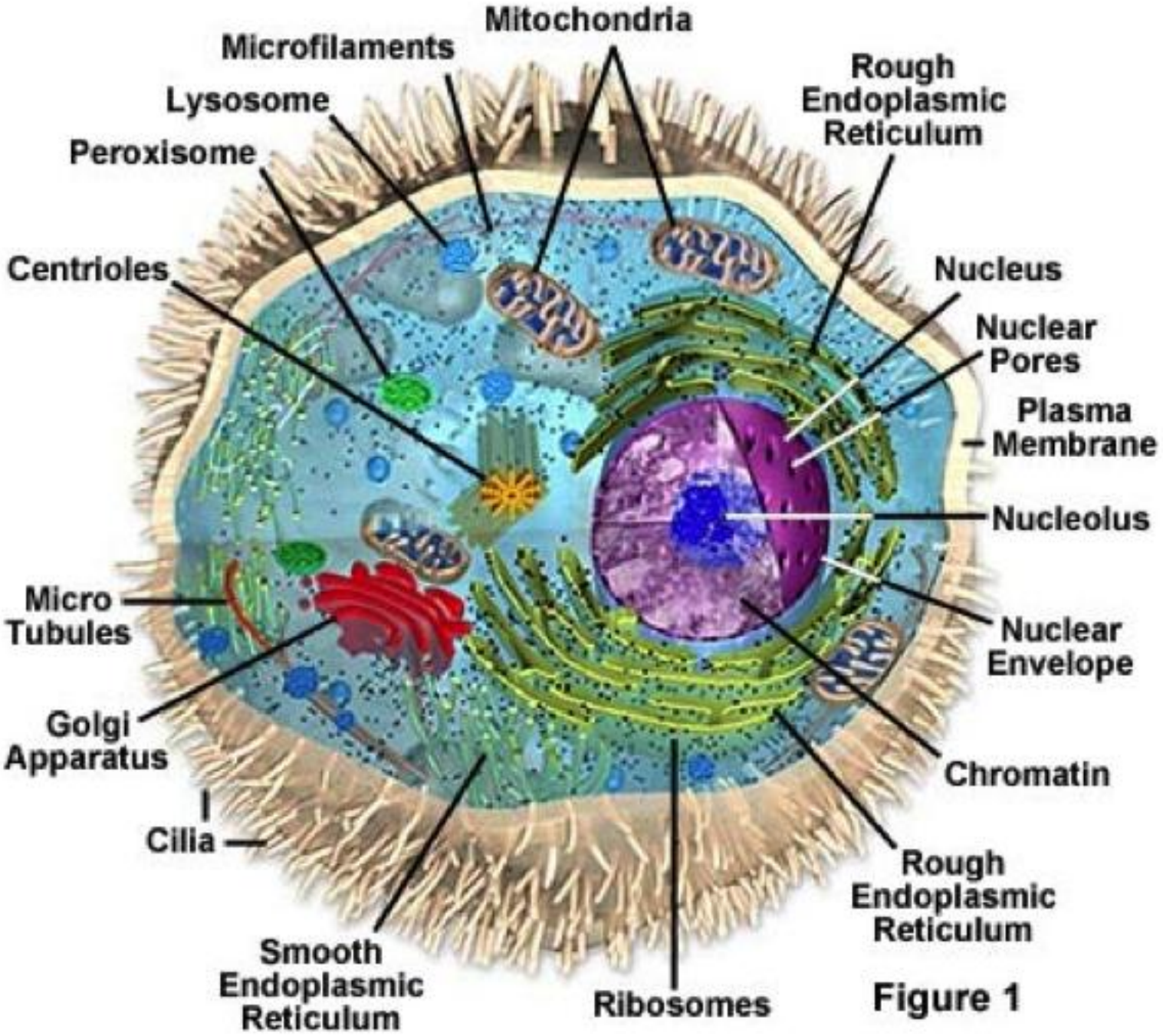
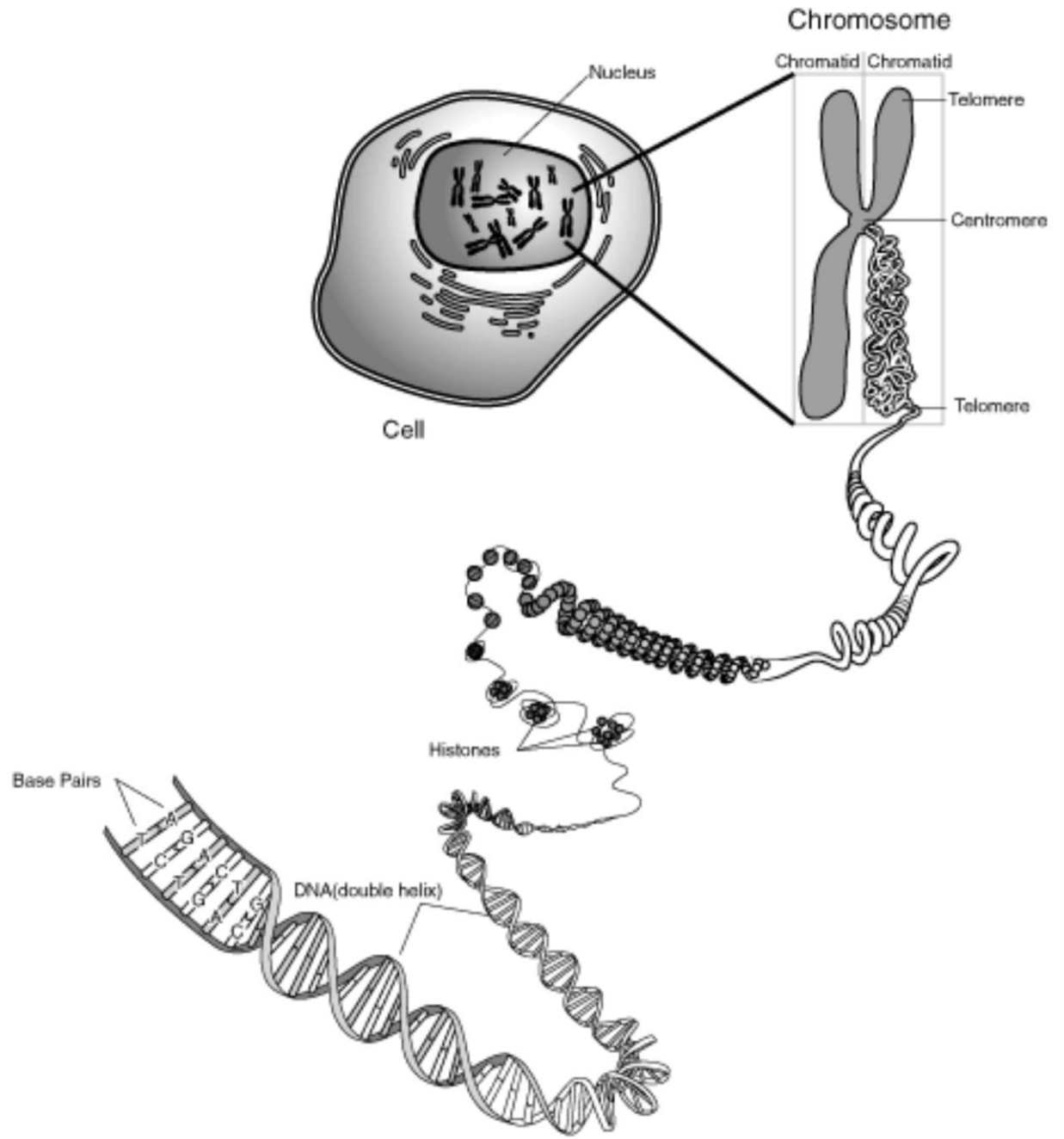

Mitochondria
Microfilaments
Lysosome
Peroxisome
Rough Endoplasmic Reticulum
Centrioles
Nucleus
Nuclear Pores
Plasma Membrane
Nucleolus
Micro Tubules
Nuclear Envelope
Golgi Apparatus
Chromatin
Cilia
Rough Endoplasmic Reticulum
Smooth Endoplasmic Reticulum
Ribosomes

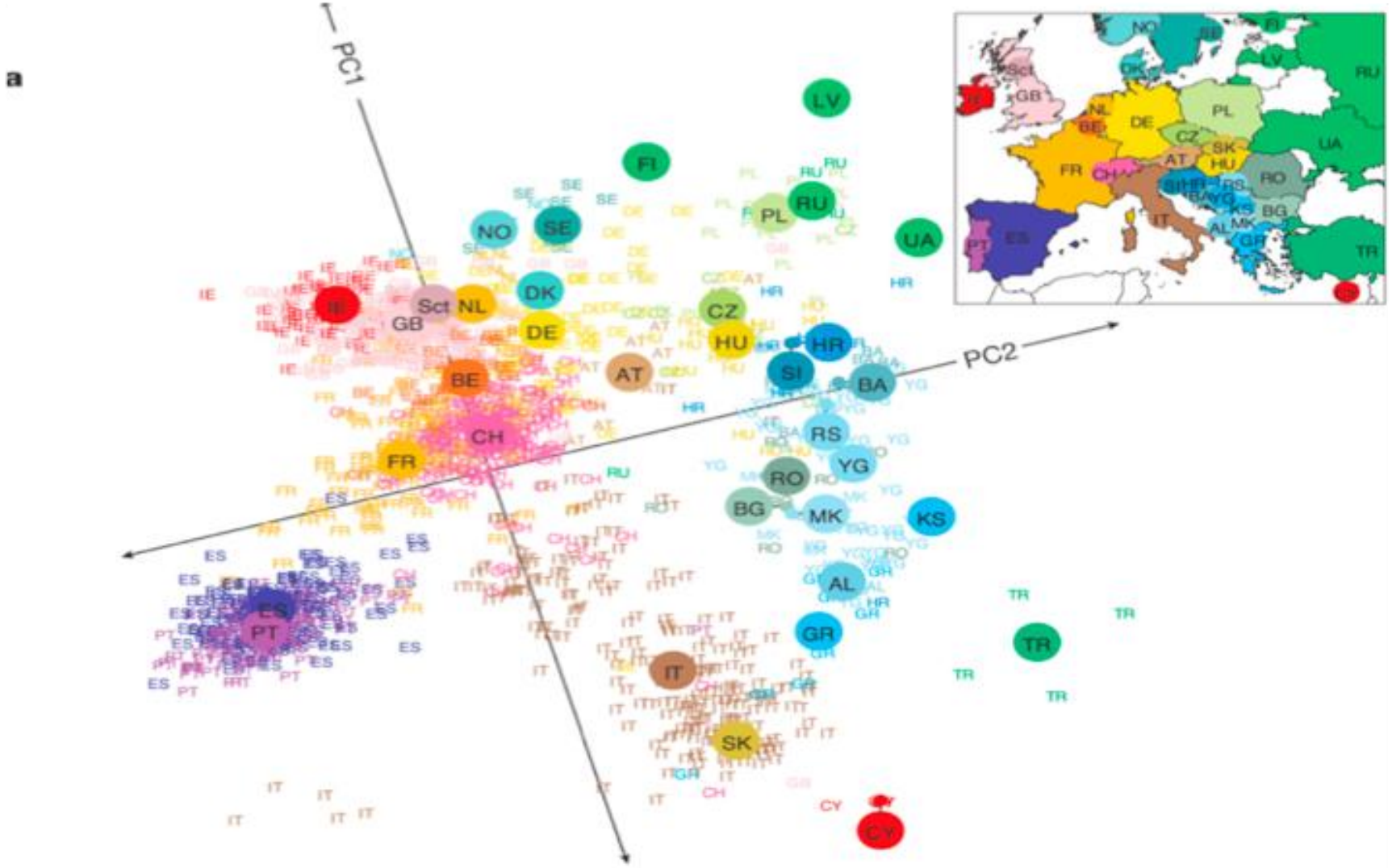
Figure 1


Chromosome
Chromatid
Chromatid
Nucleus
Telomere
Centromere
Telomere
Cell
Histones
Base Pairs
DNA(double helix)

Population structure within Europe.

nature

J Novembre *et al.* *Nature* **000**, 1-4 (2008) doi:10.1038/nature07331



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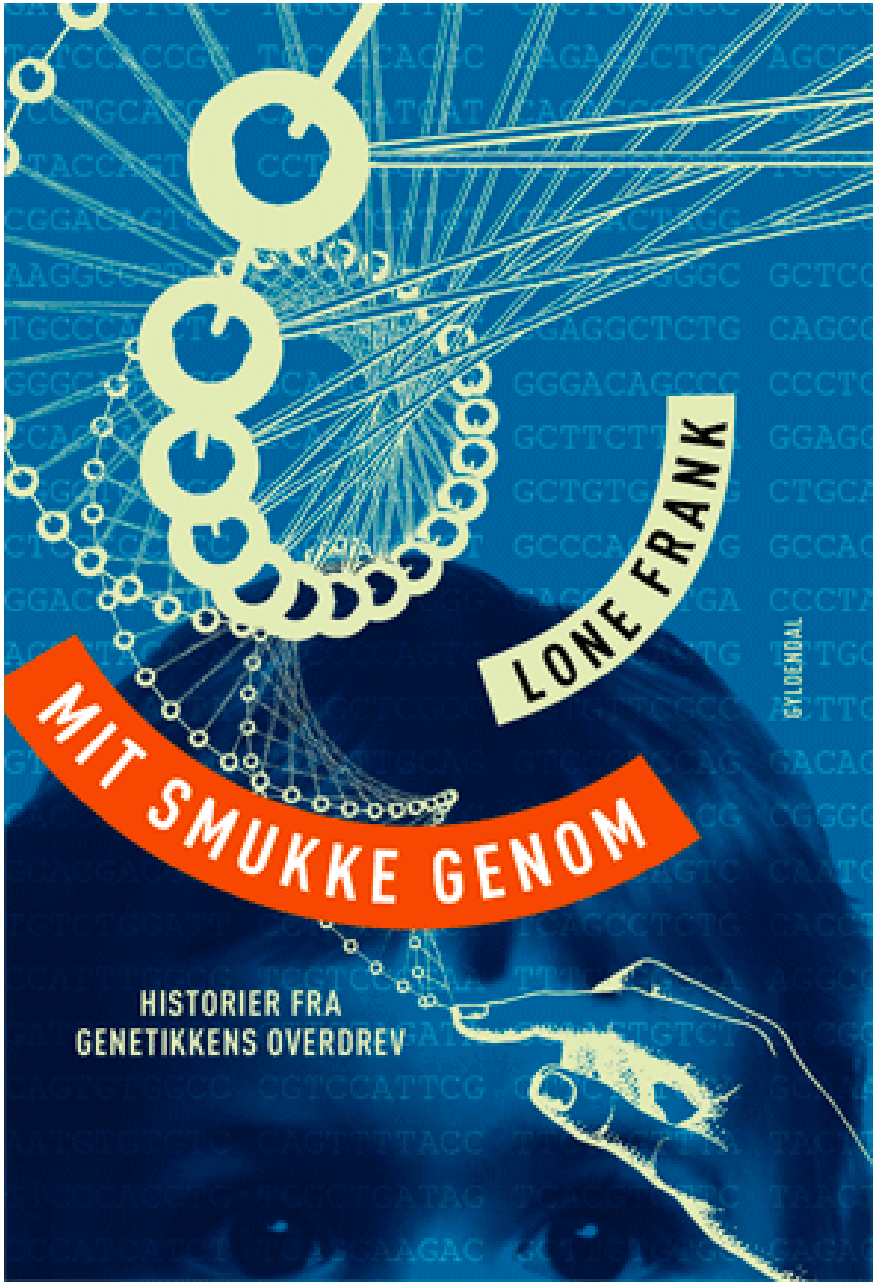
- Read our open letter to the scientific community

Insurance, Privacy and Genetic Discrimination

- Learn how the Genetic Non-Discrimination Act protects your genetic privacy


LONE FRANK
MIT SMUKKE GENOM
HISTORIER FRA
GENETIKKENS OVERDREV
GYLDENDAL

Ingen er perfekt

ARTICLE

doi:10.1038/nature09534

A map of human genome variation from population-scale sequencing

The 1000 Genomes Project Consortium*

The 1000 Genomes Project aims to provide a deep characterization of human genome sequence variation as a foundation for investigating the relationship between genotype and phenotype. Here we present results of the pilot phase of the project, designed to develop and compare different strategies for genome-wide sequencing with high-throughput platforms. We undertook three projects: low-coverage whole-genome sequencing of 179 individuals from four populations; high-coverage sequencing of two mother–father–child trios; and exon-targeted sequencing of 697 individuals from seven populations. We describe the location, allele frequency and local haplotype structure of approximately 15 million single nucleotide polymorphisms, 1 million short insertions and deletions, and 20,000 structural variants, most of which were previously undescribed. We show that, because we have catalogued the vast majority of common variation, over 95% of the currently accessible variants found in any individual are present in this data set. On average, each person is found to carry approximately 250 to 300 loss-of-function variants in annotated genes and 50 to 100 variants previously implicated in inherited disorders. We demonstrate how these results can be used to inform association and functional studies. From the two trios, we directly estimate the rate of *de novo* germline base substitution mutations to be approximately 10^{-8} per base pair per generation. We explore the data with regard to signatures of natural selection, and identify a marked reduction of genetic variation in the neighbourhood of genes, due to selection at linked sites. These methods and public data will support the next phase of human genetic research.

Nature 2010 Oct 28

“Alle sygdomme er genetiske”

Monogene
Polygene
Multifaktorielle/komplekse

Monogene sygdomme/egenskaber

Autosomerne:	ca 15000
X-kromosomet:	ca 1100
Y-kromosomet:	56

OMIM 2005

Arv/miljø ved monogene sygdomme

Selv monogent arvelige sygdomme kan påvirkes af miljøet.

Eksempel PKU: Kan behandles med diæt.

Fremtidens fosterdiagnostik

—

Det Etiske Råd

DNVKs retningslinier for NGS

- Diagnostik skal ikke anmeldes til DNVK
- Biobanker skal ikke anmeldes til DNVK
- Forskning skal anmeldes
- Tilbagemelding (hvis man ikke frabeder sig) hvis: en væsentlig sygdom kan forebygges eller behandles
- Mulighed for rådgivning før samtykke og efter analysen
- Der skal være retningslinier for håndtering af tilfældighedsfund

Uventede fund VIL ses

Secondary variants in individuals undergoing exome sequencing: screening of 572 individuals identifies high-penetrance mutations in cancer-susceptibility genes

We piloted secondary variant detection by analyzing exomes for mutations in cancer-susceptibility syndromes in subjects ascertained for atherosclerosis phenotypes.

Seven participants, four of whom were of Ashkenazi Jewish descent and three of whom did not meet family-history-based referral criteria, had deleterious BRCA1 or BRCA2 mutations.

Johnston et al, Am J Hum Genet. 2012 13; 91: 97-108

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- Risiko for unødige tilbagemeldinger

Tak for opmærksomheden