unisanté
Centre universitaire
de médecine générale
et santé publique · Lausanne

Génomique au cabinet: futur proche

Dre Semira Gonseth Nusslé, cheffe de clinique, DESS, Unisanté

Jeudi Unisanté, 9 décembre 2021,

« Innovations qui changeront (peut-être) votre pratique »

*Déclaration: Co-fondatrice et Chief Medical Officer de Genknowme SA, laboratoire d'**épi**génétique (startup spinoff du CHUV)*

*"Un jour, il y aura une **application** sur votre smartphone qui saura **exactement quel médicament** sera le plus efficace pour vous. Elle vous **avertira de votre risque** de développer certaines maladies et vous proposera un **plan personnalisé** pour les prévenir. Elle sera même capable de déterminer votre probabilité de **transmettre certaines maladies à votre futur bébé**. En définitive, cela augmentera votre **durée de vie** et vous aidera à jouir d'une meilleure **qualité de vie**.«*

Alice Bell, 2021
Blogueuse pour Intermountain healthcare

Tests génétiques en Suisse, status quo

Loi actuelle LAGH

Laboratoires certifiés

Tests prescriptibles par la/le médecin spécialiste

BRCA1, BRCA2

Tests prescriptibles par la/le généraliste

Facteur 5 Leiden, intolerance au gluten/lactose

No man's land legal (pour le moment)

***Over the counter* sur internet**

Tests génétiques médicaux

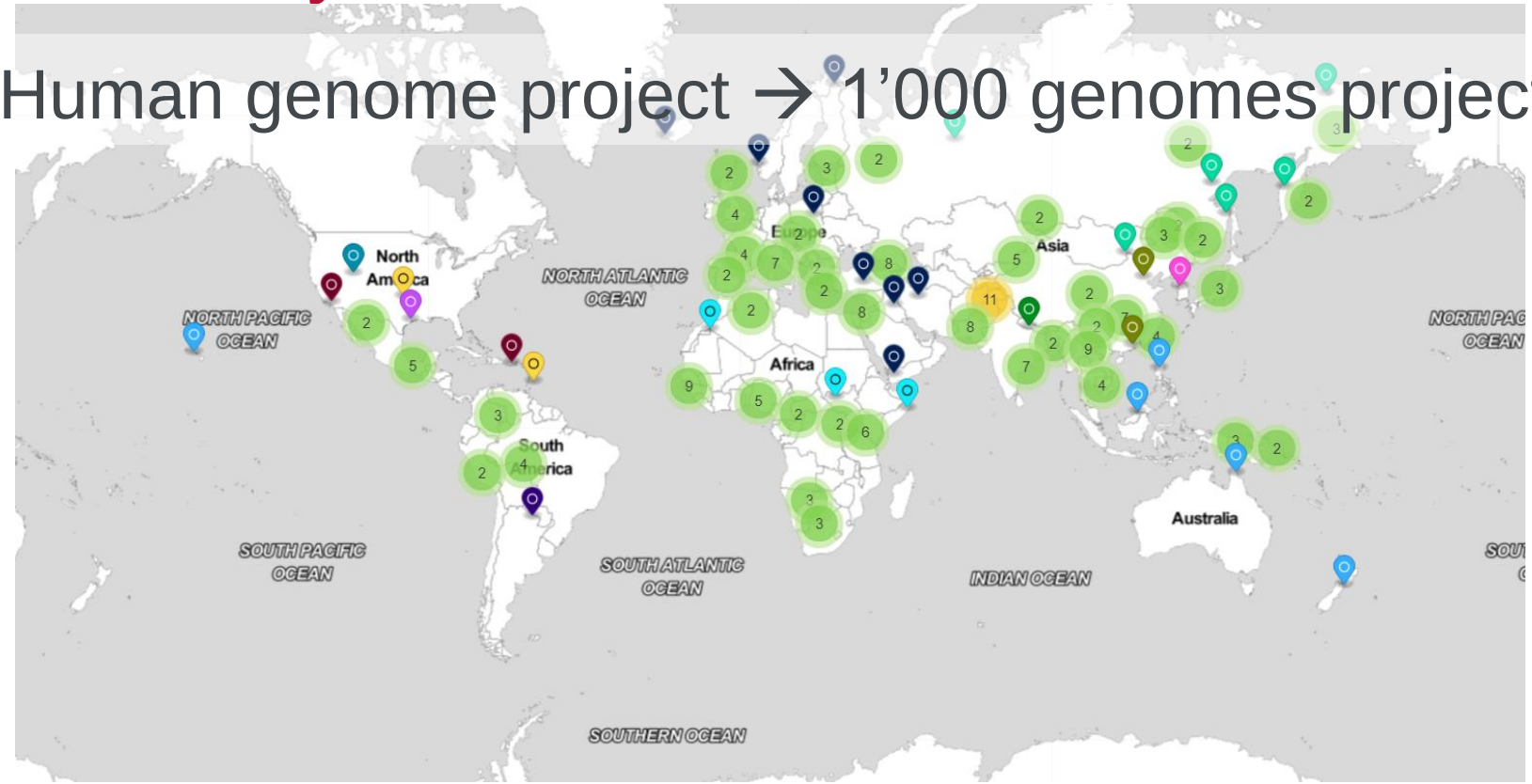
Facteur 5 Leiden, intolerance au gluten/lactose, BRCA1, variants Alzheimer

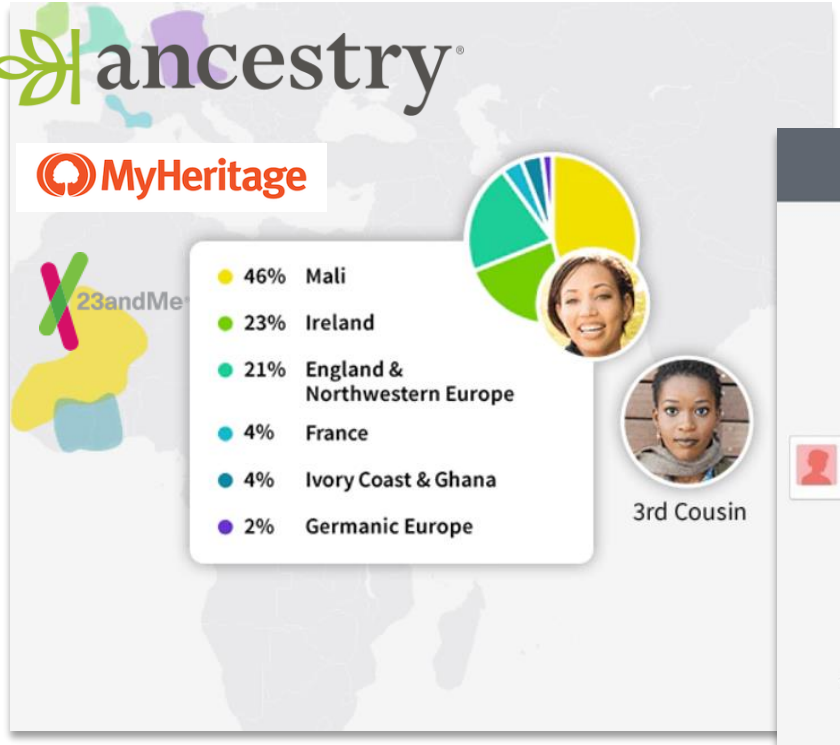
Tests génétiques non-médicaux

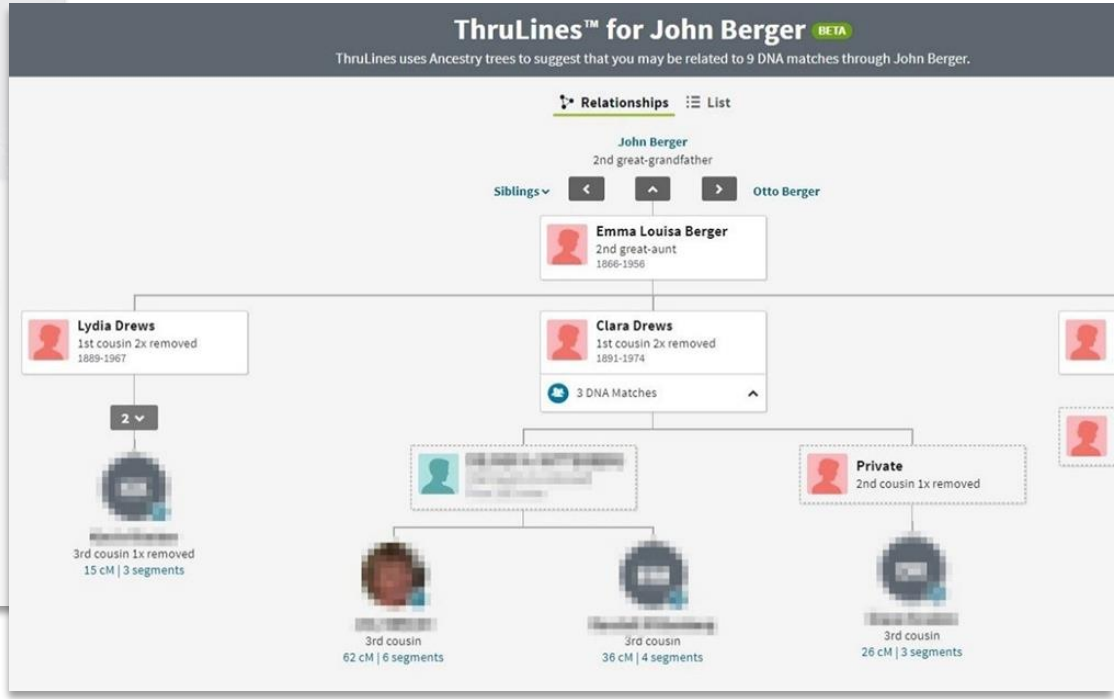
Ancestry, nutrigenomics, athleticomics

Ancestry

Human genome project → 1’000 genomes project

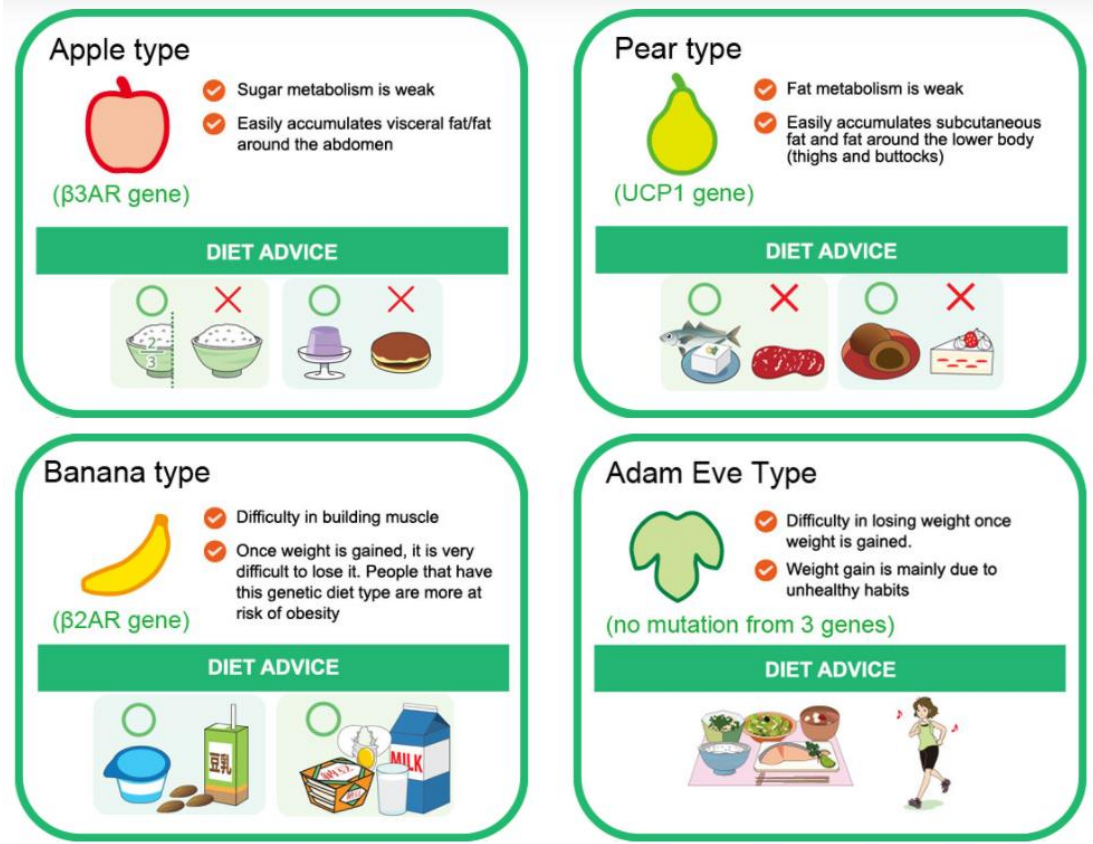



ancestry
MyHeritage
23andMe
46% Mali
23% Ireland
21% England & Northwestern Europe
4% France
4% Ivory Coast & Ghana
2% Germanic Europe
3rd Cousin


ThruLines™ for John Berger BETA
ThruLines uses Ancestry trees to suggest that you may be related to 9 DNA matches through John Berger.
Relationships
List
John Berger
2nd great-grandfather
Siblings
Otto Berger
Emma Louisa Berger
2nd great-aunt
1866-1956
Lydia Drews
1st cousin 2x removed
1889-1967
Clara Drews
1st cousin 2x removed
1891-1974
3 DNA Matches
2
Private
2nd cousin 1x removed
3rd cousin 1x removed
15 cM | 3 segments
3rd cousin
62 cM | 6 segments
3rd cousin
36 cM | 4 segments
3rd cousin
26 cM | 3 segments

GeneLife

Nutrigenomics



Imagene Labs

Your Results at A Glance

A quick summary of your DNA test results for your easy reference.

	Traits	Percentile Score	Assessment
A	Vitamin A Deficiency	65	SLIGHTLY HIGH
B1	Vitamin B1 Deficiency	75	SLIGHTLY HIGH
B2	Vitamin B2 Deficiency	45	NORMAL
B3	Vitamin B3 Deficiency	75	NORMAL
B5	Vitamin B5 Deficiency	30	NORMAL
B6	Vitamin B6 Deficiency	45	SLIGHTLY HIGH
B7	Vitamin B7 Deficiency	70	SLIG
B9	Vitamin B9 Deficiency	60	SLIG
B12	Vitamin B12 Deficiency	40	N
C	Vitamin C Deficiency	90	
D	Vitamin D Deficiency	50	SLIG
E	Vitamin E Deficiency	25	N
K	Vitamin K Deficiency	35	N
	Calcium Deficiency	60	N

Vitamin A Deficiency

A

Vitamin A is essential for a healthy immune and reproductive system, healthy vision, maintenance of strong bones and teeth, red blood cell production, tissue repair and skin health.

RDA for retinol is 900 micrograms (3,000IU) and 700 micrograms (2,333IU) for males and females respectively. Your need for retinol increases in pregnancy, childbirth, infancy, and childhood growth.

Genes tested

BCO1, CYP26B1, TTR, RBP4-FFAR4

Your Percentile Score

65

Your score falls within the 65th percentile of the population.

Your Assessment

SLIGHTLY HIGH

You have a genetic predisposition for slight deficiency. You may not be efficient in converting carotenoids into retinol (active form of vitamin A).

y Recommendations

Vitamin A comes in two forms: retinol, the biologically active form, and carotenoids (vitamin A precursors, e.g. beta-carotene, lutein, lycopene), that are converted into retinol. Carotenoids come from plant foods, while animal sources provide retinol. Studies show that genetic variations may impair the conversion of carotenoids to retinol, affecting the levels of active vitamin A in your body. As you are likely to be less efficient in converting beta carotene to retinol, increase your vitamin A levels by eating foods such as liver, cod liver oil, egg yolk, and fish. If you are a vegetarian or vegan, you may can get your retinol from vitamin A fortified foods and beverages. Please refer to 'Nutrition Sources' at the end of this report for suggested calcium food sources.

Imagene Labs

Your Results at A Glance

A quick summary of your DNA test results for your easy reference

Traits	Percentile Score	Assessment
Aerobic Performance	40	NORMAL
Endurance	65	SLIGHTLY HIGH
Power	5	NORMAL
Lean Body Mass	35	NORMAL
Fitness Benefits	45	NORMAL
Reduced Heart Beat Response to Exercise	70	SLIGHTLY HIGH
Potential for Obesity	25	NORMAL
Difficulty in Losing Weight	85	SLIGHTLY HIGH
Exercise Aversion	15	NORMAL
Resting Metabolic Rate Impairment	90	HIGH
Stress Fracture	75	SLIGHTLY HIGH
Overall Injury Risk	5	NORMAL
Muscle Soreness	35	NORMAL
Muscle Damage Risk	75	SLIGHTLY HIGH
Muscle Repair Impairment	75	SLIGHTLY HIGH

Dietary Recommendations

Magnesium is useful under heavy aerobic training, as it improves energy utilization and reduces the stress of exercise, allowing quicker recovery. Food sources include nuts, dark leafy greens, lentils, and mackerel. Branch chain amino acids (BCAAs) have been shown to reduce fatigue during prolonged aerobic exercise, and are found in meat, chicken, fish, dairy products and eggs. These foods are also rich in beta-alanine, which helps increase the time to exhaustion during aerobic exercise. Creatine, found in meat, especially wild game, e.g. rabbit and venison, and wild fish, such as salmon and tuna, increases muscle strength and endurance.

Lifestyle Recommendations

If you are vegetarian, consider taking creatine as a supplement, as it is only found in animal products. Even meat eaters would benefit from supplementation, as the suggested dose for creatine is 5g per day. You may also benefit from supplementing with additional beta-alanine (2-3g for women, 4-6g for men).

Exercise Recommendations

Endurance exercise is one of the four types of exercise along with strength, balance and flexibility. Ideally, all four types of exercise should be included in a balanced fitness plan. Endurance exercises are particularly important for the heart. You will benefit from using lower weights and higher reps (8-10 reps). Your suggested weight is about 75% of your maximum effort lift. With specific training for the sport, you will be able to adapt to either strength sports or endurance sports. Some endurance activities you would do well in are brisk walking, running or jogging, swimming and cycling, soccer, tennis, and rowing. Climbing stairs and dancing are also good endurance exercises.

Late-Onset Alzheimer's Disease

Alzheimer's disease is characterized by memory loss, cognitive decline, and personality changes.
Late-onset Alzheimer's disease is the most common form of Alzheimer's disease, developing after age 65.
Many factors, including genetics, can influence a person's chances of developing the condition.
This test includes the most common genetic variant associated with late-onset Alzheimer's disease.

Jamie, you have **one copy** of the ε4 variant we tested.

People with this variant have a slightly increased risk of developing late-onset Alzheimer's disease
Lifestyle, environment, and other factors can also affect your risk.

Test Interpretation

This report provides risk estimates for people of European, African American, East Asian, and South Asian descent. Estimates for other ethnicities are not currently available.

Health Risk Estimates

Risk estimates are based on clinical studies that identify an association between a genotype and a health condition.

Consider talking to a healthcare professional if you have any concerns about your results.

References [1, 9, 10, 17, 21]

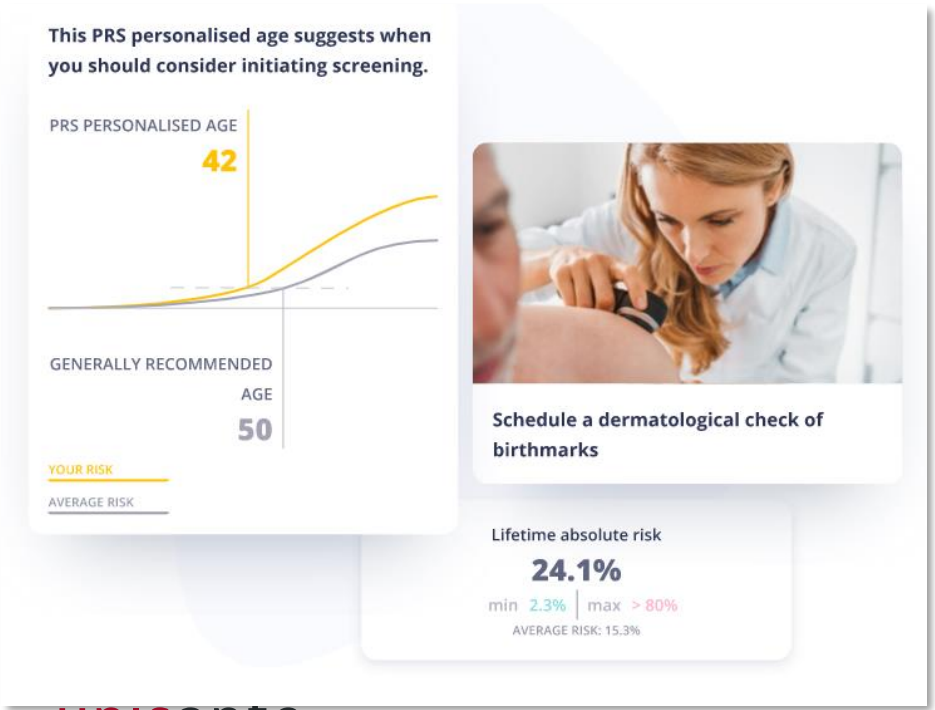
Lifetime risk | Likelihood ratios | Odds ratios

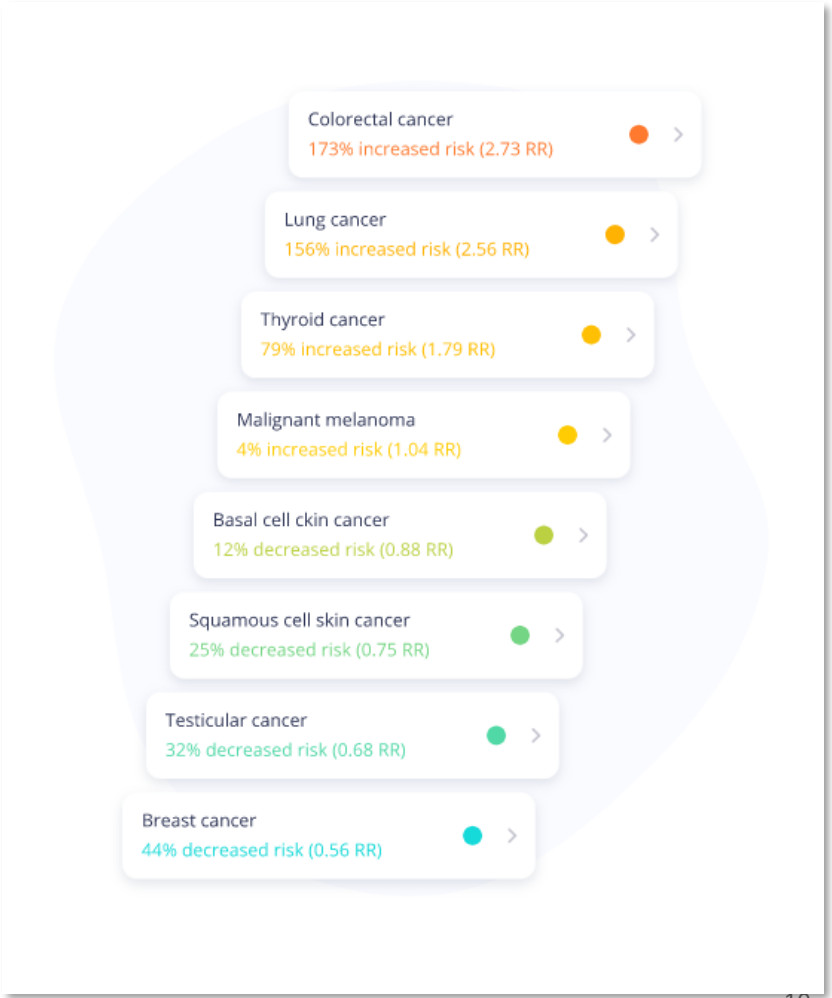
The lifetime risk estimates shown below represent the proportion of people expected to develop Alzheimer's disease by age 65, 75, and 85. These values are based on people of European descent. Lifetime risk estimates are not available for people of other ethnicities.

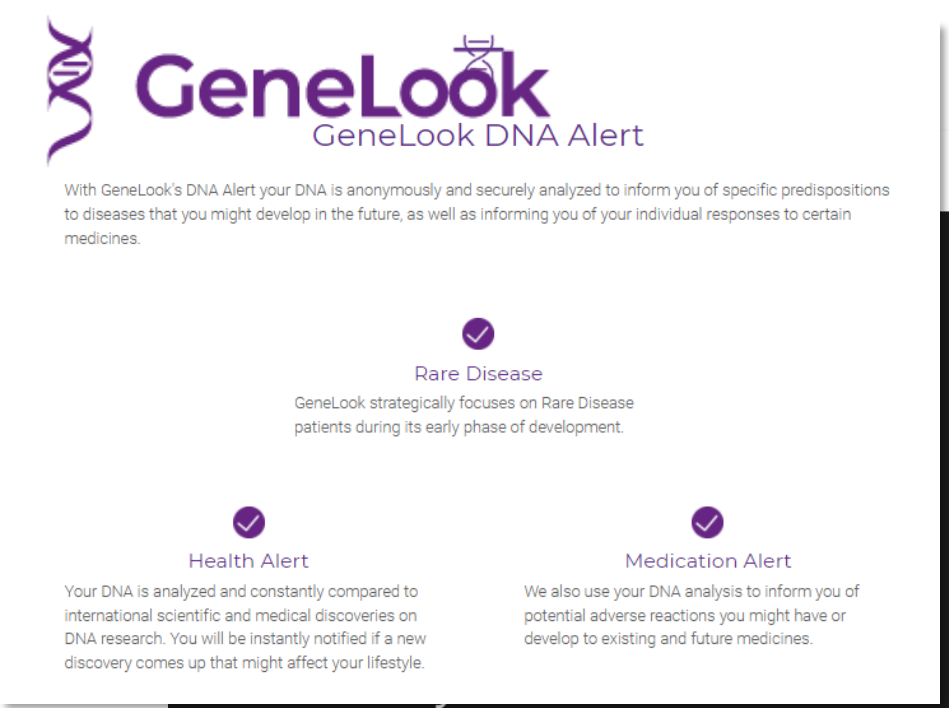
Genetic result	Sex	Age 65	Age 75	Age 85
General population	Men	<1%	3%	11%
General population	Women	<1%	3%	14%
No ε4 variants	Men	<1%	1-2%	5-8%
No ε4 variants	Women	<1%	1-2%	6-10%
One copy of ε4 variant	Men	1%	4-7%	20-23%
One copy of ε4 variant	Women	<1%	5-7%	27-30%
Two copies of ε4 variant	Men	4%	28%	51%
Two copies of ε4 variant	Women	2%	28%	60%

GENEPLANET

Risques de cancers







GenomSys

ABOUT US OUR SCIENCE OUR PRODUCTS NEWSROOM CONTACT

What was once matter of billions of dollars is now within everyone's reach. Discover how GenomSys is democratizing genomic analysis.

Your privacy is our commitment

DNA is truly unique. We empower you to fully control your genomic data instead of having it stored in someone else's server somewhere. If you lose your credit card or your home keys, they can be replaced. Your DNA cannot be changed or replaced, you are bond to it for life.

Analysis at a touch of button

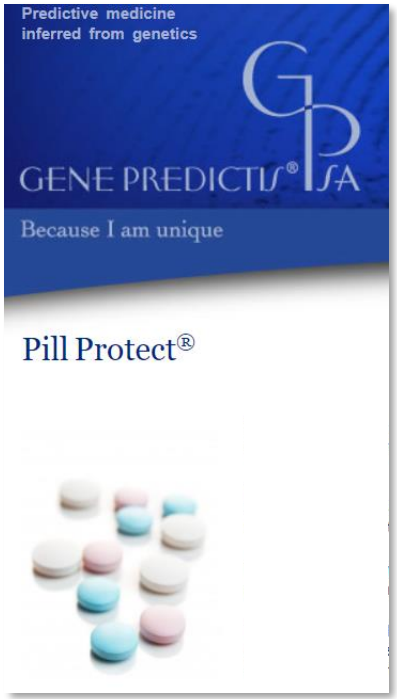
Thanks to our solutions based on a revolutionary ISO MPEG-G open standard and our native analysis tools, you can order and review results of genomic analyses on your smartphone, at any time. Need to check how a medicine truly works with you? Need to know if you carry any mutations potentially impacting your (future) children? Just ask in our app.

Direct line with doctors and labs

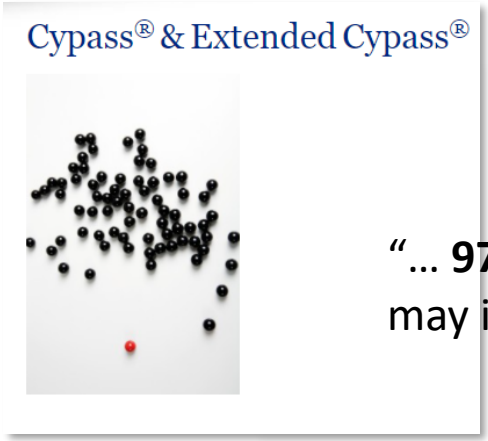
If you don't have it already, you can order your DNA to be sequenced directly from the genome app selecting where the analysis should be run (and you'll shortly get a kit at home to provide your sample) or you can securely share analysis reports with your caring physician directly from our app.

uni

Pharmacogenomics



"The test includes detection of specific genetic variations that can influence development of **thrombosis** (blood clots forming inside blood vessels). These genetic variations include known genetic changes such as **Factor V-Leiden and Factor II-G20210A**, but also **other genetic variations** associated with the **coagulation** and **hormone metabolism**."

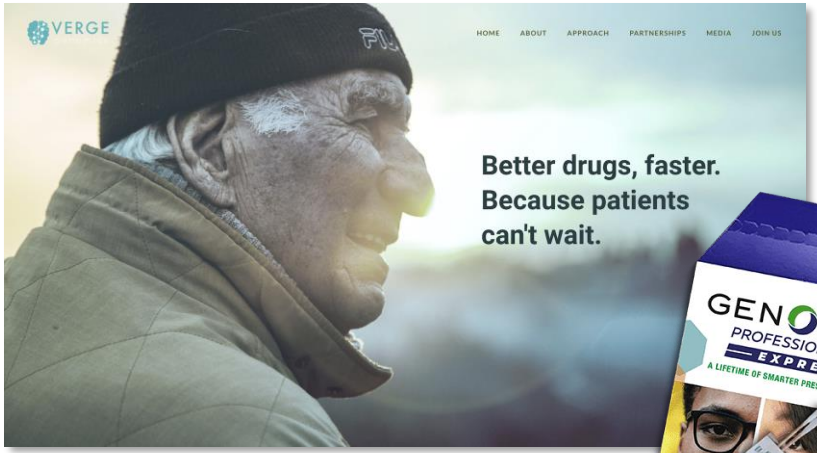


"… **97** clinically relevant genetic variants that may influence **drug metabolism**"

varsome

The human genetics search engine

Supported by the global community of geneticists



GeneDose Genetic Response Report

TruGenX

Pain

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
		Duloxetine Nortriptyline Protriptyline Venlafaxine Vortioxetine	
Antipsychotics	Olanzapine		
Beta Blockers	Nebivolol Propranolol		
Endocrine-Metabolic Agents		Eliglustat	
Immunosuppressants	Cyclosporine	Tacrolimus	
Muscle Relaxants	Carisoprodol		
Nonsteroidal Anti-Inflamatory Drugs (NSAIDs)	Celecoxib Diclofenac Flurbiprofen Ibuprofen Lornoxicam Meloxicam Piroxicam		
	Buprenorphine Fentanyl	Hydrocodone Oxycodone Oxycodone (CYP3A5)	Codeine Tramadol
lective Serotonin uptake Inhibitors RIs)	Citalopram Escitalopram Sertraline	Fluoxetine Fluvoxamine Paroxetine	

Enjeux présents et futurs

- **Données génétiques : résultats inattendus**
  - Sentences
  - «*Actionability*» ?
  - Contradiction avec histoire familiales, filiation
- **Protection des données, portée des données génétiques**
  - Vente des données
  - Membres de la famille
    - *Investigative genetic genealogy*

Enjeux présents et futurs

- **Médecine personnalisée** → hausse des coûts vs. allocation des ressources plus efficiente?

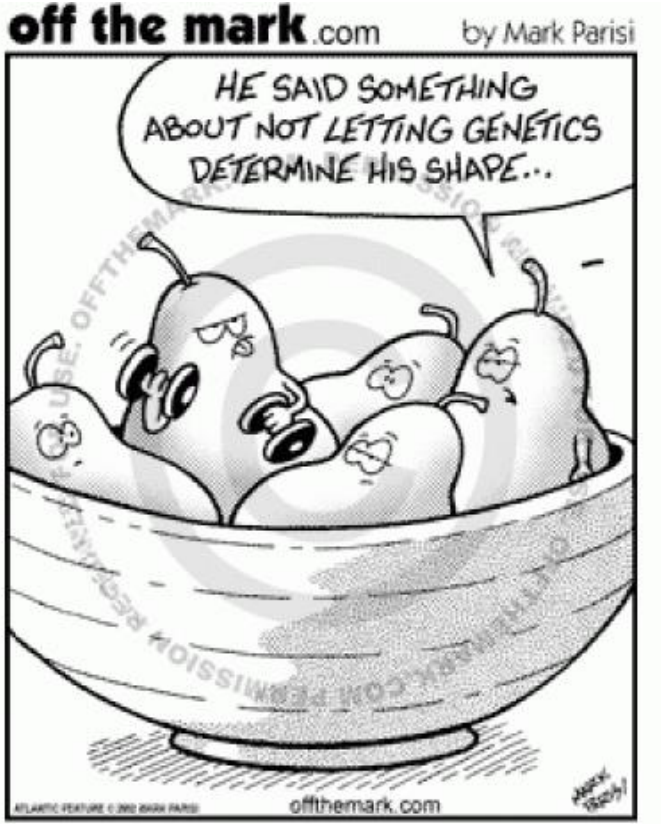
- **Cadre légal → nLAGH (2022)**
  - Information et consentement de la personne concernée
  - Toutes les analyses génétiques (incl. hors-médical)
  - Différents niveaux de la règlementation
  - Pas d'accès pour assurances/employeurs (sauf excp)

Donc dans le futur… *no more one-size-fits-all*

- Prévention guidée par la génétique:
  - Programme personnalisé de dépistage cancers, autres maladies chroniques: quels examens, à quel âge et à quelle fréquence
- Diagnostics:
  - Basé sur risques génétiques, classification plus précise, détection automatique selon avancée science (push notifications)
- Traitements:
  - Plus de prescription de médicament sans vérifier au préalable correspondance génétique pour molécule et dosage

… mais la génétique n'est pas tout! Estimé 15-20% des maladies sont d'origine génétique

Remerciements:
- *Dr. J.-M. Good, généticien CHUV*
- *Pierre-Jean Wipff, InnoVaud*
- *Séverine Trouillod, sociologue UNIL*
- *Prof. J. Marti, Unisanté*



Merci pour votre attention

unisanté
Centre universitaire
de médecine générale
et santé publique · Lausanne

Back up slides

Futur (proche)

1. Patients → whole genome seq → push notifications avancées médicales les concernant
2. Profil pharmaco-génétique complet utilisable pour *tous* les produits thérapeutiques
    1. No more 1-fits-all
3. Mode de vie
    1. Nutrigenomic
    2. Sport

MEDICALES *(LAGH)*

- Facteur 5 Leiden
- Facteur 2 (Prothrombine)
- MTHFR
- Intolérance au gluten (HLA-DQ2 et HLA-DQ8
- Intolérance au lactose (LCT)
- HLAB27
- Hémochromatose (HFE 2 mutations)
- Syndrome de Gilbert (UGT1A1*28)
- Thalassémie (HBA et HBB)

- ***Tests spécifiques prescrits par spécialistes***

natera — Santé de la femme et Diagnostic prénatal non-invasif

GENEPLANET

gene predictis — BECAUSE I AM UNIQUE

Unilabs

- Pharmacogénétique (variants dans les gènes des cytochromes)
- Polygénique risk score risque thrombo-embolique avec contraception hormonale
- Nutrigénomique:
  - l'intolérance au lactose et au gluten
  - cholesterol
  - réponse aux statines
  - métabolisme de l'homocysteine
  - vitamine D
  - gain de poids
  - métabolisme de l'alcool, du café et du thé

NON-MEDICALES

ancestry

MyHeritage

23andMe — Ancestry & médical

Imagene Labs

GeneLife

iGENEA

Et beaucoup d'autres…

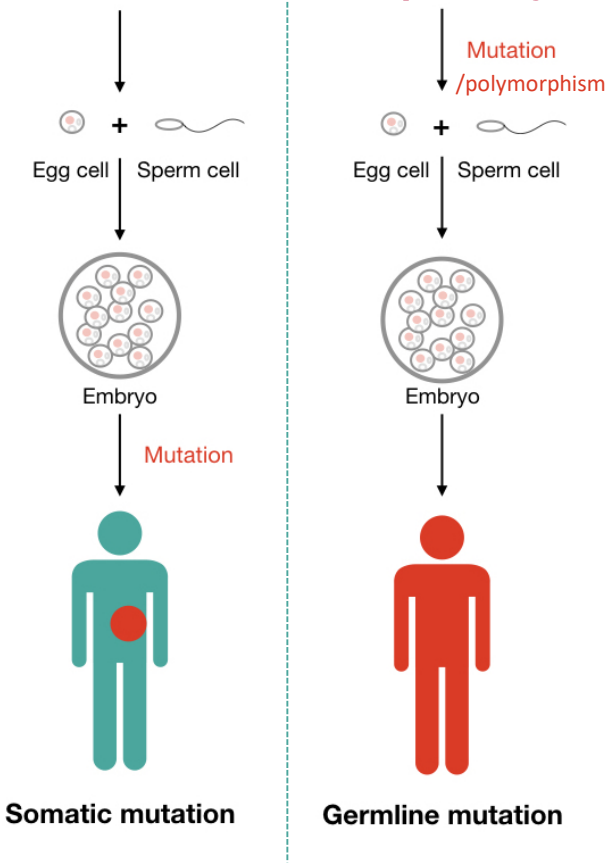
Prescription médicale — *Over-the-counter*

LaMal — *LCA* — *Pas de remboursement*

Mutations et variations (polymorphismes)

Acquises (somatiques)

- En général dans tumeurs
  - Biopsie tumorale
  - Diagnostic/ gradation/ indication thérapeutique



Héréditaires / constitutives (germline)

- Dans toutes les cellules du corps
- Biopsie salivaire ou sang
- Indications très diverses

Caffeine Consumption

Caffeine is the most widely consumed drug in the world. The amount of caffeine you consume – whether it's from coffee, tea, or soft drinks – may be influenced by your genes. The average 23andMe customer who drinks caffeinated beverages consumes about 265 mg of caffeine per day. This is equivalent to more than two cups of coffee.

Erin, 23andMe customers who are genetically similar to you tend to consume 61 mg more caffeine per day than average.

GeneLife

Skin type

MMP1 gene
Gene related to the decrease of tension and elasticity of skin due to the breakdown of collagen. Influences susceptibility to wrinkles.

GPX 1 gene
Gene related to spots due to decreased detoxification ability. Influences susceptibility to spots.

SOD2 gene
Gene related to antioxidant production ability inside the body. Influence's ability to produce antioxidants.

Upon analysis of these 3 genes, you will be classified into 4 skin types, each with their own different variations.

Type 1
People with Type 1 skin have a standard ability to maintain tension and elasticity, as well as standard enzyme activity inside the body.

People that have Type 1 skin are not affected by the 3 skin related genes. However, environmental factors (especially exposure to ultraviolet rays and active oxygen) still greatly influence skin health.

Type 2
People with Type 2 Skin are weak at maintaining tension and elasticity of the skin.

People that have Type 2 skin tend to have faster breakdown of collagen. This leads to the decline of tension and elasticity of the skin, which is the primary reason for the formation of wrinkles.

Type 3
People with Type 3 Skin have weak enzyme activity inside the body.

People that have Type 3 skin tend to have weak anti-oxidative ability. This means that the skin is more susceptible to oxidation due to its inability to expunge active oxygen. This is the primary reason for the formation of dark spots.

Type 4
People with Type 4 skin are weak in both their ability to maintain tension and elasticity, as well as enzyme activity inside the body—a combination of Type 2 and 3.

People that have Type 4 skin are more prone to wrinkles and dark spots.

Ancestry & santé