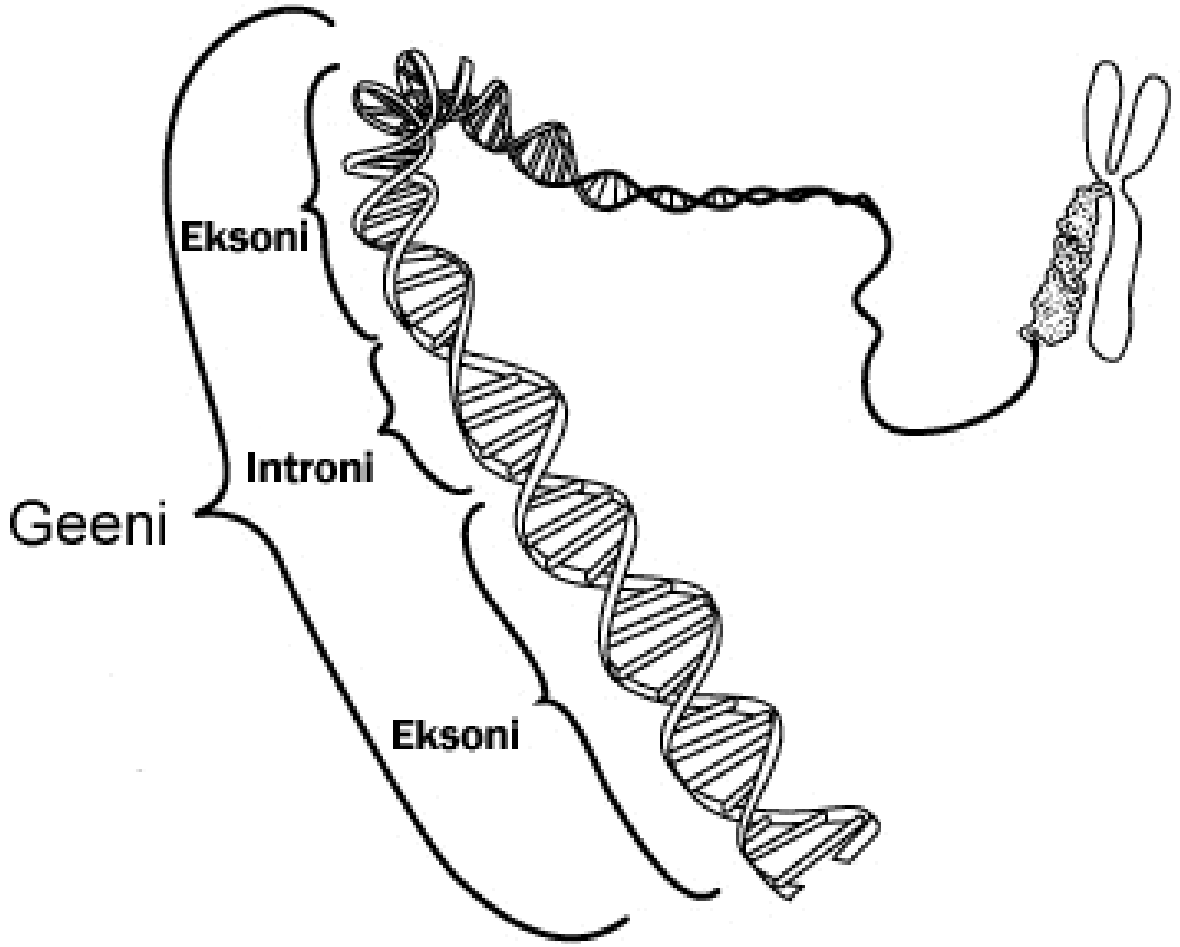
# Keuhkosairauksien genetiikkaa

Maria Haanpää, Dos.

Perinnöllisyyslääkäri

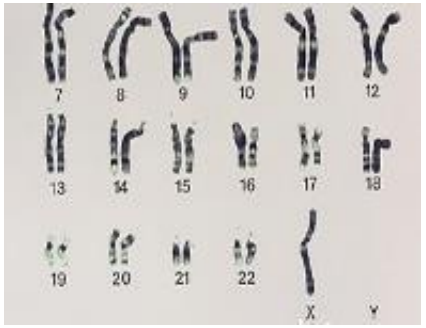
Osastonylilääkäri

# Termit; kromosomi, geeni, proteiini

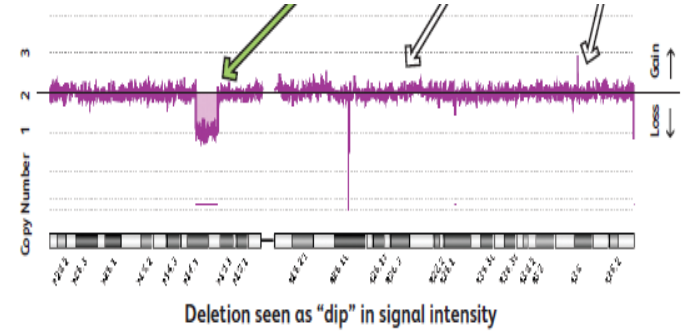


## Aneuploidia

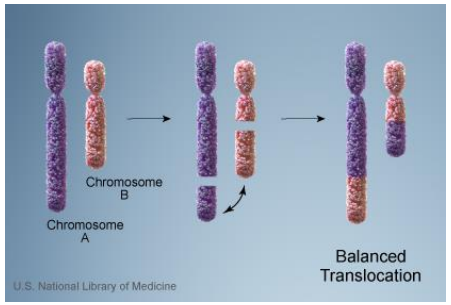
(13-, 18- ja 21-trisomiat, Turner)



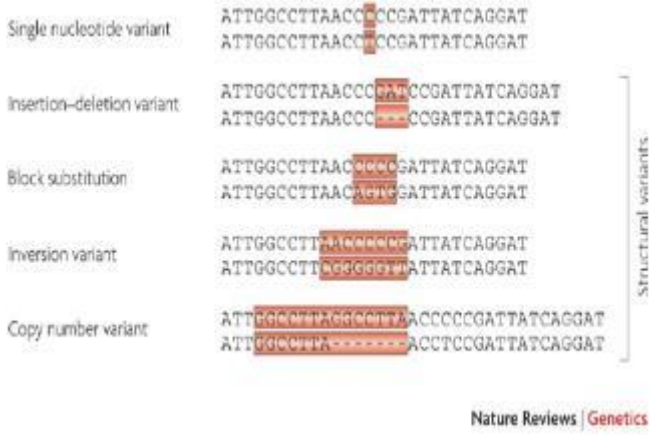
## CNVs (mikrodeleetiot/duplikaatiot)



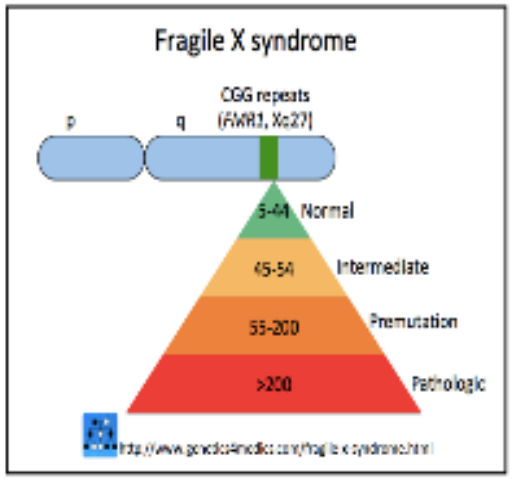

## Muu kromosomitason vaihtelu
(translokaatiot, inversiot)



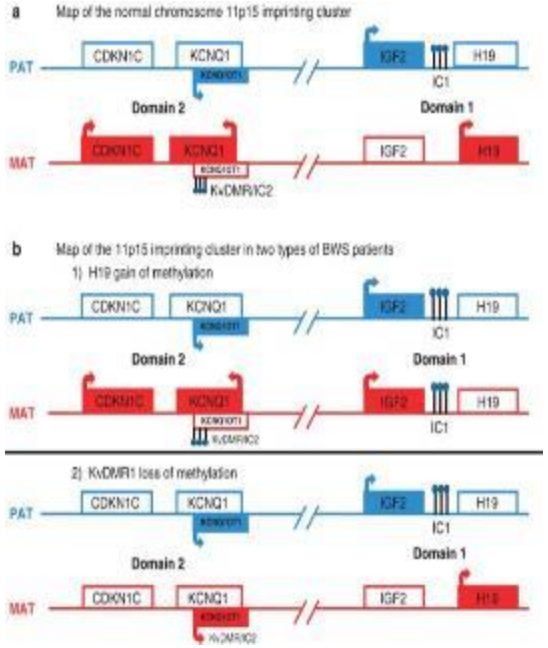

## Emästason vaihtelu NGS




## Toistojaksomutaatiot




## Metylaatiomuutokset




**Perimän vaihtelun eri muodot**

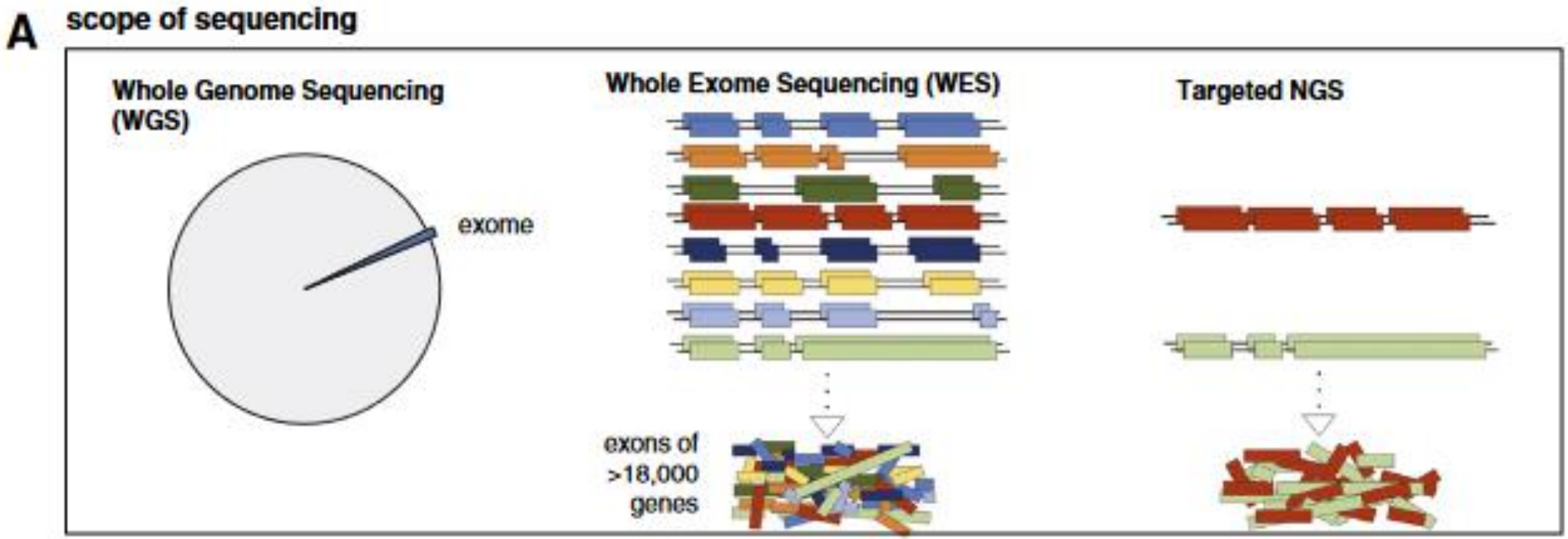
***Tarvitaan erilaisia menetelmiä geneettisessä diagnostiikassa***

E.Salminen

# The Pulmonary Genetics:

- atopic disease
- severe asthma
- bronchiectasis
- bronchiolitis obliterans
- congenital diaphragmantic hernia
- congenital hypoventilation
- cystic fibrosis (CF)
- cystic lung diseases
- childhood interstitial lung disease (IDL)
- hereditary hemorrahagic telangiectasia (HHT)
- lymphangiectasia
- Pneumothorax
- pulmonary hypertension and other pulmonary vascular diseases
- primary ciliary dyskinesia
- recurrent lung infections
- sleep-related breathing disorders/ sleep apnea
- tracheoesophageal fistula

# Mikä tutkimus? Yksittäinen geeni, vai paneelin vai eksomi?



# Esimerkkejä paneeleista

## Pulmonology panels

- Bronchiectasis Panel
- Central Hypoventilation and Apnea Panel
- Comprehensive Pulmonology Panel
- Cystic Lung Disease Panel
- Hermansky-Pudlak Syndrome Panel
- Interstitial Lung Disease Panel
- Neonatal Respiratory Distress – Surfactant Dysfunction Panel
- Primary Ciliary Dyskinesia Panel
- Pulmonary Artery Hypertension (PAH) Panel

# NGS geenipaneeli

- Paneelin koko ei korreloi sen ”hyvyyteen”
- Tärkeintä että kaikki oleelliset geenit ovat mukana paneelissa
- Hyvin kuratoitu paneeli on tärkein!

# Vuonna 2012

## Genetic testing for respiratory disease: Are we there yet?

Peter D Paré MD, Editor-in-Chief

# Vuonna 2022

**Genetic testing in interstitial lung disease: An international survey**

Michelle Terwiel[1] | Raphael Borie[2,3] | Bruno Crestani[2,3] | Liam Galvin[4] | Francesco Bonella[5] | Aurelie Fabre[6] | Antoine Froidure[7] | Matthias Griese[8] | Jan C. Grutters[1] | Kerri Johannson[9] | Caroline Kannengiesser[3,10] | Leticia Kawano-Dourado[3,11,12] | Maria Molina-Molina[13] | Antje Prasse[14] | Elisabetta A. Renzoni[15,16] | Jasper van der Smagt[17] | Venerino Poletti[18] | Katerina Antoniou[19] | Coline H. M. van Moorsel[1]

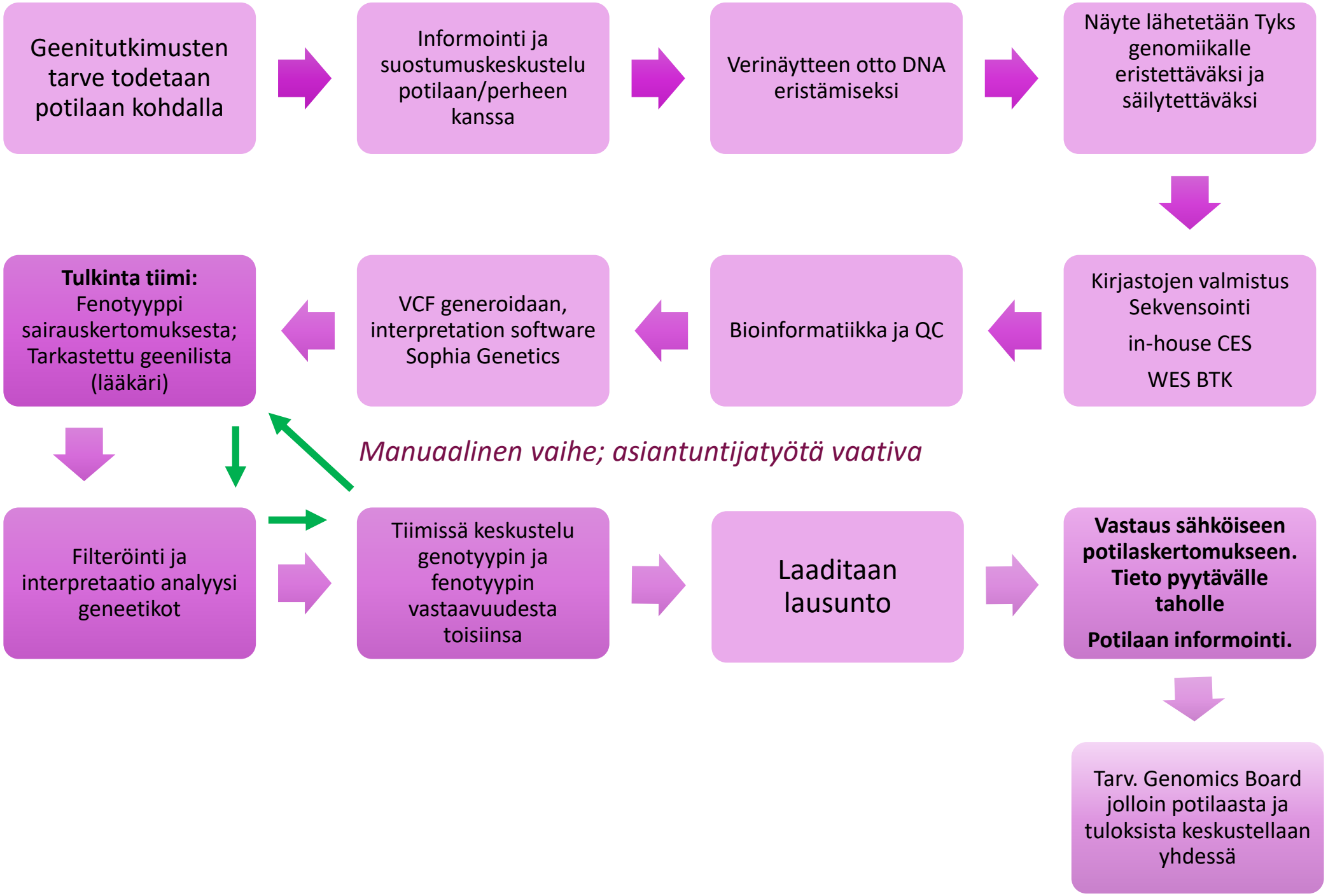
- Genetic analysis is emerging for interstitial lung diseases(ILDs); however, ILD practices are not yet standardized. We surveyed patients', and pulmonologists' experiences and needs on genetic testing in ILD to evaluate the current situation and identify future needs.

# Maailmalla

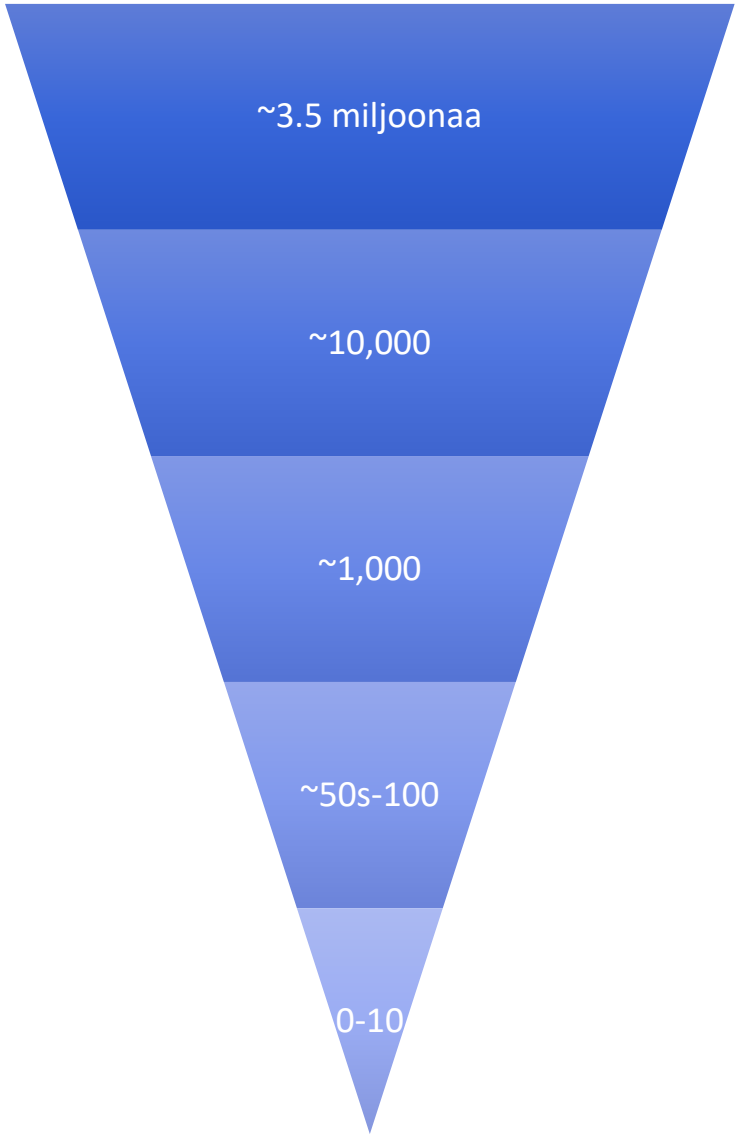
- The PulmoGene Panel, a next-generation sequencing test, **provides focused results for more than 60 genes that have been implicated in inherited (monogenic) lung disease**. We customize our testing strategy by focusing on the handful of genes most relevant for a patient's specific symptoms.

- **Many lung and respiratory diseases have an underlying genetic cause**.

# Workflow Turun Genomii-kalla



# Interpretaation / tulkinnan  workflow




Genomi sekvenssi

⇩

Allele frekvenssi: harvinaisia ja uusia variantteja

⇩

Eksonitason variantteja

⇩

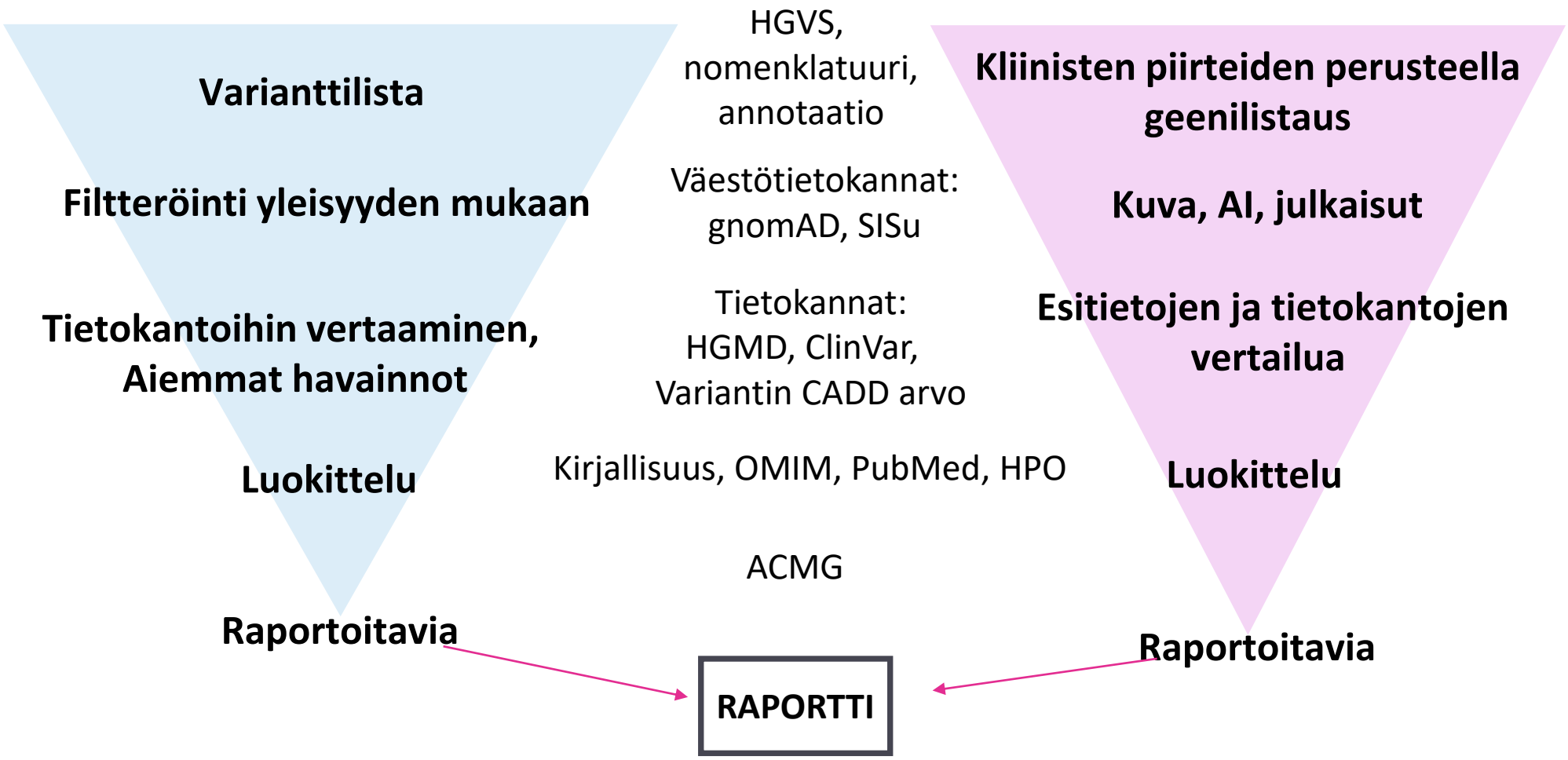
Geneettinen analyysi (yhdistettynä periytymismalli hypoteesiin) ja fenotyyppi filtteröinti

*Manuaalinen kuratointi*

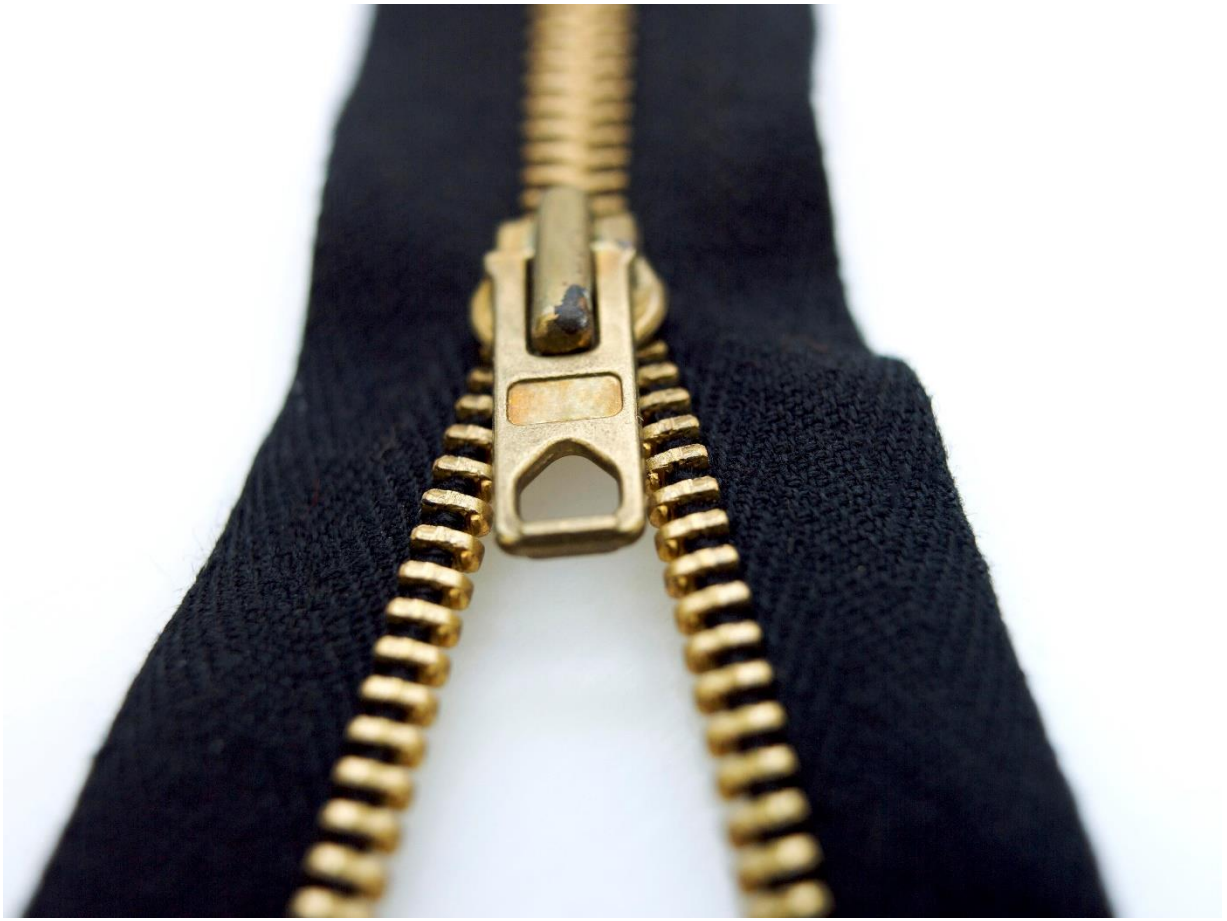
⇩

Kliinisesti relevantit variantit ⇨ Raportin laatiminen

# NGS-tulosten tulkinnan lähestymistavat

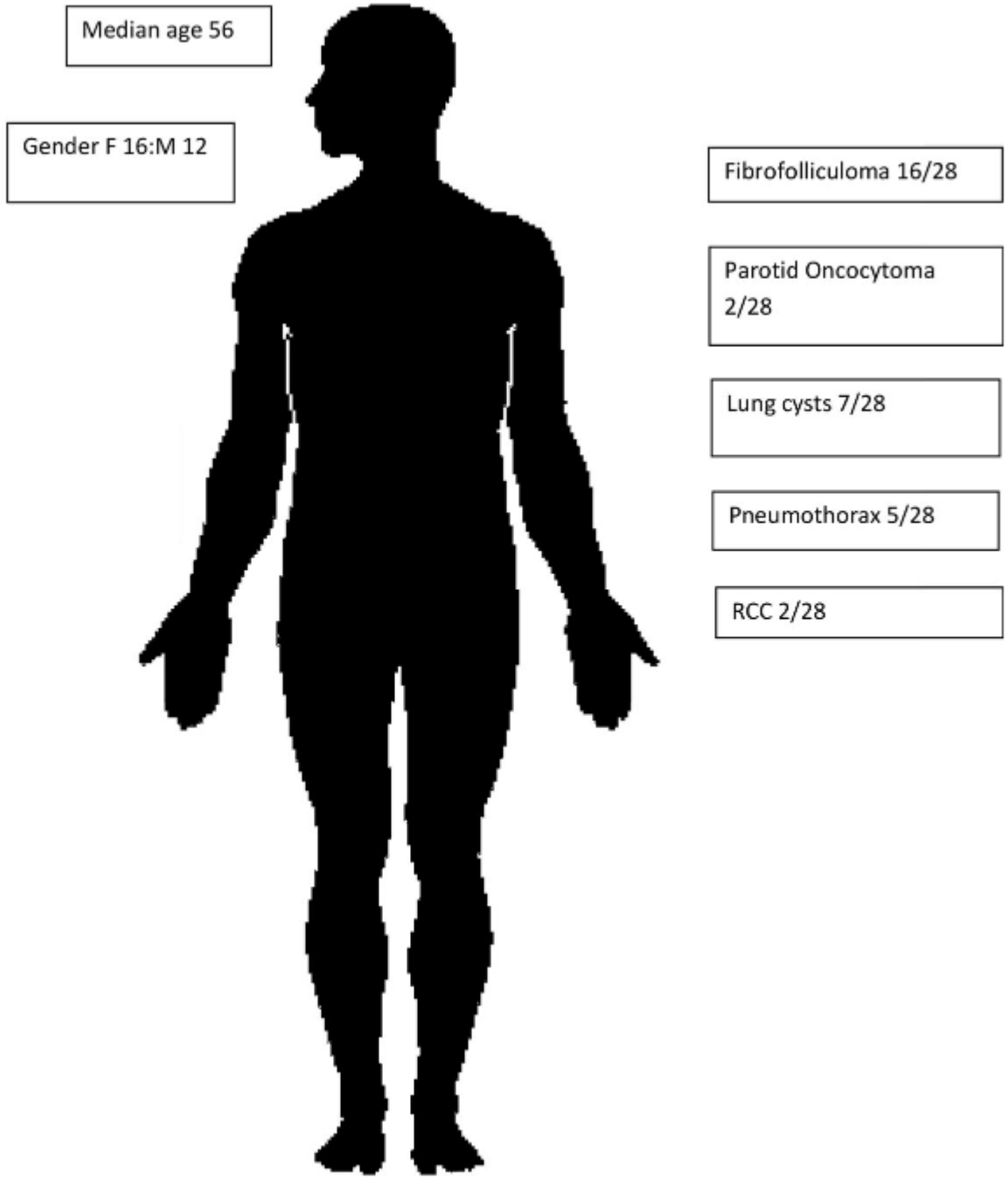


# Akateemista yhteistyötä, salapoliisin työtä!



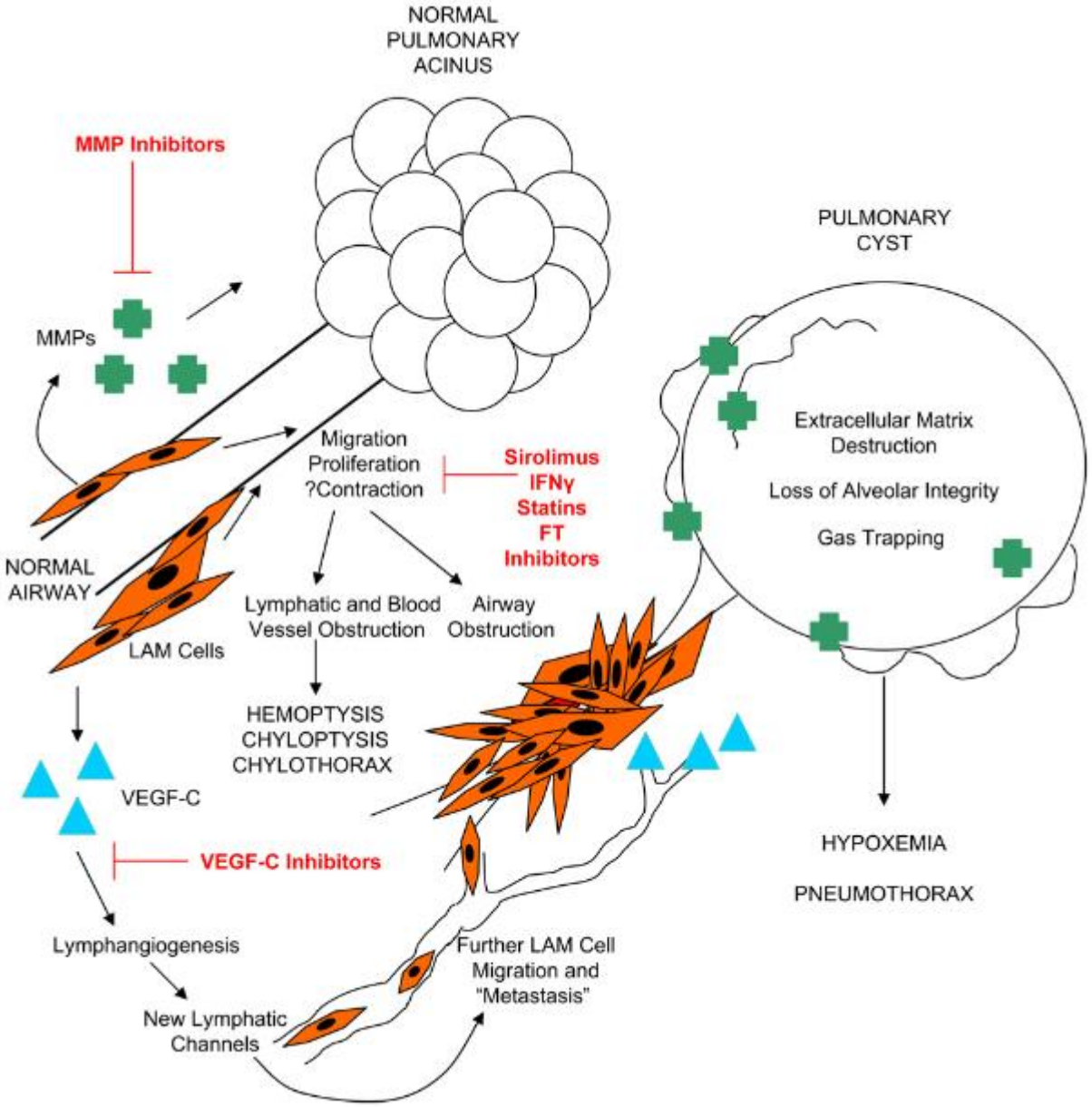
# Potilastapauksia ja teoriaa tietyistä keuhkosairauksista

# BHD



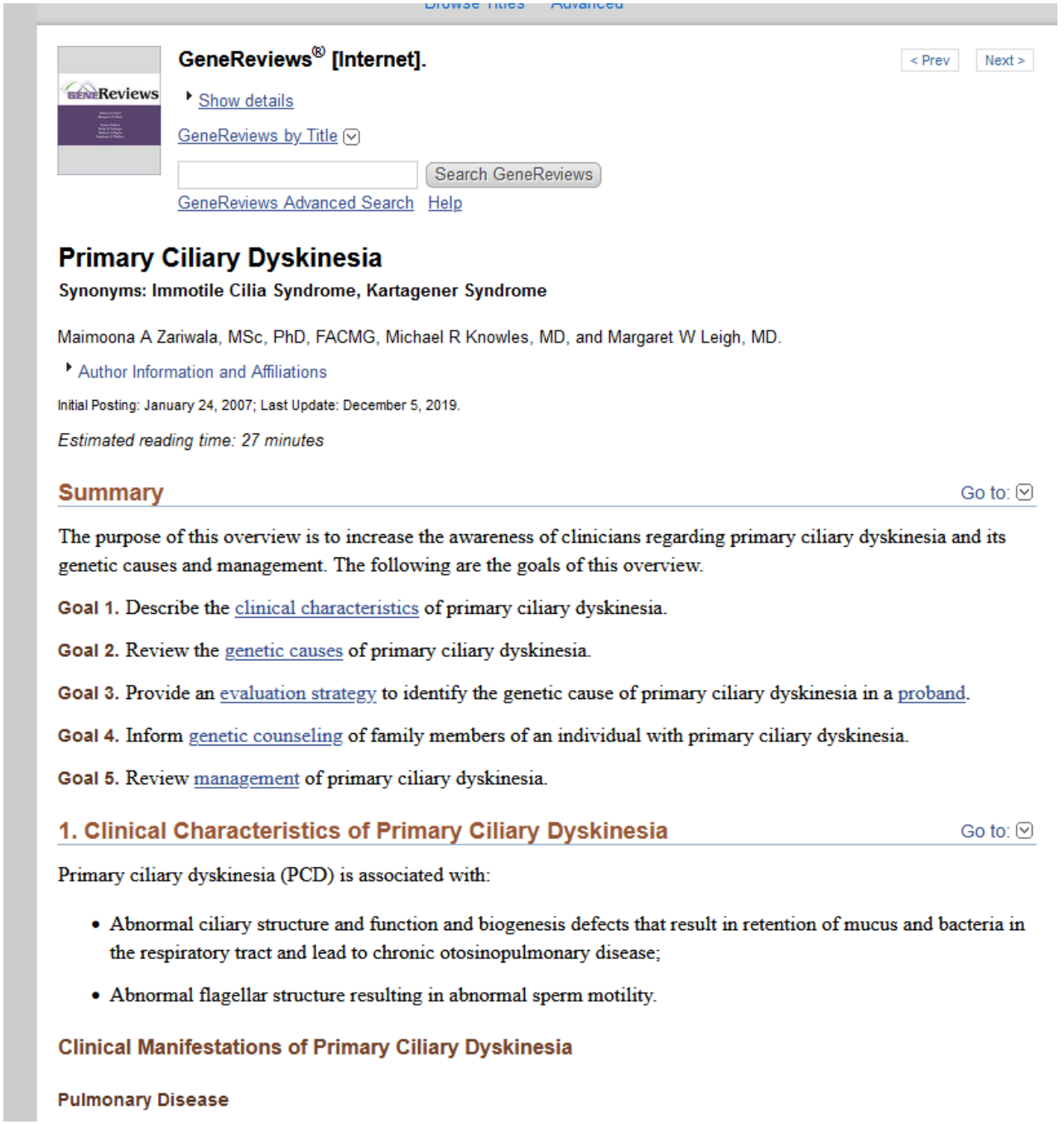

- Al-Shinnag et al, 2021

# LAM




- Juvet et al, American Journal of Respiratory Cell and Molecular Biology. May 2007

# Primaari ciliaari dyskinesia



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## Primary Ciliary Dyskinesia

**Synonyms: Immotile Cilia Syndrome, Kartagener Syndrome**

Maimoona A Zariwala, MSc, PhD, FACMG, Michael R Knowles, MD, and Margaret W Leigh, MD.

Author Information and Affiliations

Initial Posting: January 24, 2007; Last Update: December 5, 2019.

*Estimated reading time: 27 minutes*

### Summary

Go to:

The purpose of this overview is to increase the awareness of clinicians regarding primary ciliary dyskinesia and its genetic causes and management. The following are the goals of this overview.

**Goal 1.** Describe the clinical characteristics of primary ciliary dyskinesia.

**Goal 2.** Review the genetic causes of primary ciliary dyskinesia.

**Goal 3.** Provide an evaluation strategy to identify the genetic cause of primary ciliary dyskinesia in a proband.

**Goal 4.** Inform genetic counseling of family members of an individual with primary ciliary dyskinesia.

**Goal 5.** Review management of primary ciliary dyskinesia.

### 1. Clinical Characteristics of Primary Ciliary Dyskinesia

Go to:

Primary ciliary dyskinesia (PCD) is associated with:

- Abnormal ciliary structure and function and biogenesis defects that result in retention of mucus and bacteria in the respiratory tract and lead to chronic otosinopulmonary disease;
- Abnormal flagellar structure resulting in abnormal sperm motility.

#### Clinical Manifestations of Primary Ciliary Dyskinesia

**Pulmonary Disease**

# Keuhkolääkärin take home message

- Uskalla pyytää tarvittaessa geenitutkimuksia
- B-NGS-D paneeli jossa pyynnössä on mahdollisimman hyvin kuvattu kliininen kuva jolloin geenipaneeli osataan tehdä oikein (=riittävän laajana, muttei liian laajana)
- Geenitutkimuksella voidaan päästä täsmädiagnoosiin.
- Voi mahdollisesti vaikuttaa hoitoon ja/tai seurantaan
- Periytymistapa -> sukulaisten riskin arvio onnistuu.

# KIITOS