# Blueprint Genetics

## Rare3k

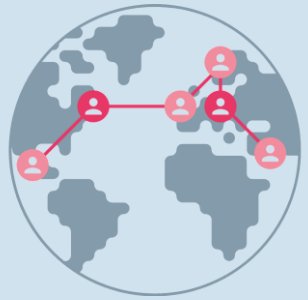
## December 4th, 2019

# Introduction to Blueprint Genetics

Dedicated Laboratory for Human Rare Diseases

- Founded in 2012 as a spin-off from Stanford University
- Specialty genetic testing business focused on broad hereditary genetic diseases
- End-to-end service from sample preparation to report delivery
- Single gene analysis, gene panels, Whole Exome Sequencing
- Unrivalled clinical interpretation practice supported by a highly qualified team
- Proprietary software platform and machine learning / AI capabilities

## Key Facts



**170** Employees

Founded in **2012**

**>4,000** Clinicians in **70** countries

## Core Operations In

Helsinki

Seattle

## Quality Management

**CLIA** Clinical laboratory certification by US regulatory authority

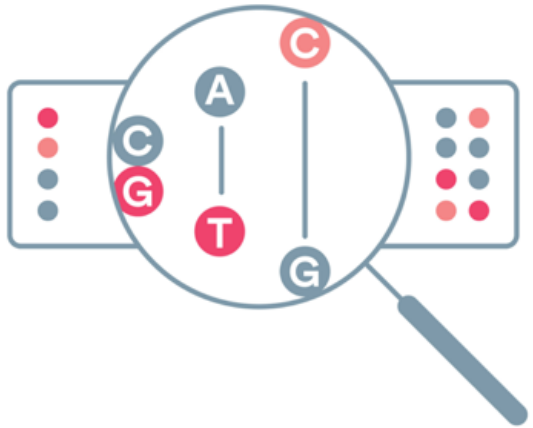
**CAP** All laboratory functions accredited by College of American Pathologists

**ISO 15189** Processes and documentation comply with the most widely used standards worldwide

**CE-IVD** All Blueprint Genetics' panel tests are CE marked, general IVD devices

**Patient sample**

**DNA sequencing**




**Analysis and interpretation**

**Clinical report**

# Superior analytic and clinical performance

| PERFORMANCE | WHOLE EXOME | CLINICAL EXOME |
|---|---|---|
| **Single nucleotide variants** | | |
| Sensitivity | 99.65% | 99.83% |
| Specificity | >99.99% | >99.99% |
| **Insertions, deletions and indels by sequence analysis** | | |
| 1-10 bps sensitivity | 96.94% | 99.33% |
| 1-10 bps specificity | >99.99% | >99.99% |
| 11-50 bps sensitivity | 99.07% | 99.16%* |
| 11-50 bps specificity | >99.99% | >99.99% |
| **Copy number variants (exon level dels/dups)** | | |
| 1 exon level deletion (heterozygous) sensitivity | NA | 100% (20/20) |
| 1 exon level deletion (homozygous) sensitivity | NA | 100% (5/5) |
| 1 exon level deletion (het or homo) sensitivity | 92.3% (24/26) | 100% (25/25) |
| 2-7 exon level deletion (het or homo) sensitivity | 96.0% (24/25) | 100% (44/44) |
| 1-9 exon level duplication (het or homo) sensitivity | NA | 75% (6/8) |
| **Microdeletion/-duplication sdrs (large CNVs)** | | |
| Size range (0.1-47 Mb) | 100% (37/37) | 100% (25/25) |
| **Simulated CNV detection** | | |
| 5 exons level deletion/duplication sensitivity | 98.63% | 98.7% |
| 5 exons level deletion/duplication specificity | 99.98% | 100.00% |

*11-30 bps

**Clinical sample indel sensitivity 100.0% (1-80bps)

# The rare disease challenge

Over **350** million people affected

It takes on average **5.6** years for the illness to be properly identified

Visiting **8** doctors during diagnostic odysseia

Only **10%** have an approved therapy

# Our solution

**Digitalizing rare disease diagnostics:**

AI programs can analyze huge quantities of information from medical records to identify high-risk individuals

Genome analysis and clinical interpretation can efficiently identify the underlying pathogenic mutations to establish a molecular diagnosis

# Rare3K - Introduction

- Helsinki Biobank, HUS and Blueprint Genetics are launching a research initiative to sequence a cohort of 3 000 donors representing different rare disease groups.
- The study establishes pilot programs for diagnosing patients with Wilson disease, aTTR polyneuropathy, achondroplasia, inherited retinal disorders (IRD) and age-related macular degeneration (AMD).
- This collaborative project aims to test, whether combination of HUS data lake, Helsinki Biobank specimen collections and AI tools and Blueprint Genetics' clinical genetic testing resources improves identification of rare disease patients.
- This pilot aims to assess the impact of the biobank approach for diagnostics of rare diseases.
- **The Rare3k approach creates an accredited clinical path from sample to diagnosis by combining resources in the biobank infrastructure, clinical data in data lake and clinical whole exome sequencing for efficient diagnostics of rare diseases.**

# Research objectives

- **The project is defined as biobank research, in which:**
  - patients with biobank consent and permission to recontacting (94%) are analyzed,
  - biobank donors want to receive “terveydelle merkityksellistä tietoa” (99%),
  - with help of the participating clinical experts, we aim to be able to recontact the patients to improve their diagnostics.
- **The Rare3k project aims to identify 3 000 donors in the Helsinki Biobank that have a clinical suspicion of a rare inherited disease by:**
  - developing algorithms to identify potential rare disease patients based on clinical information in the HUS data lake and
  - applying computational methods and machine learning to identify disease subclasses and establish disease classifiers.
- **The project’ objective is to perform whole exome sequencing and clinical interpretation for the 3000 donors with suspected rare disease to identify the underlying pathogenic mutations**

# Pilot programs in Rare3k

**Wilson disease**

- Underdiagnosed disease that leads to copper build-up affecting liver and brain

**TTR amyloidosis**

- Neurodegenerative disorder with several phenocopies

**Achondroplasia**

- 80% of mutations are *de novo* and lead to short statue

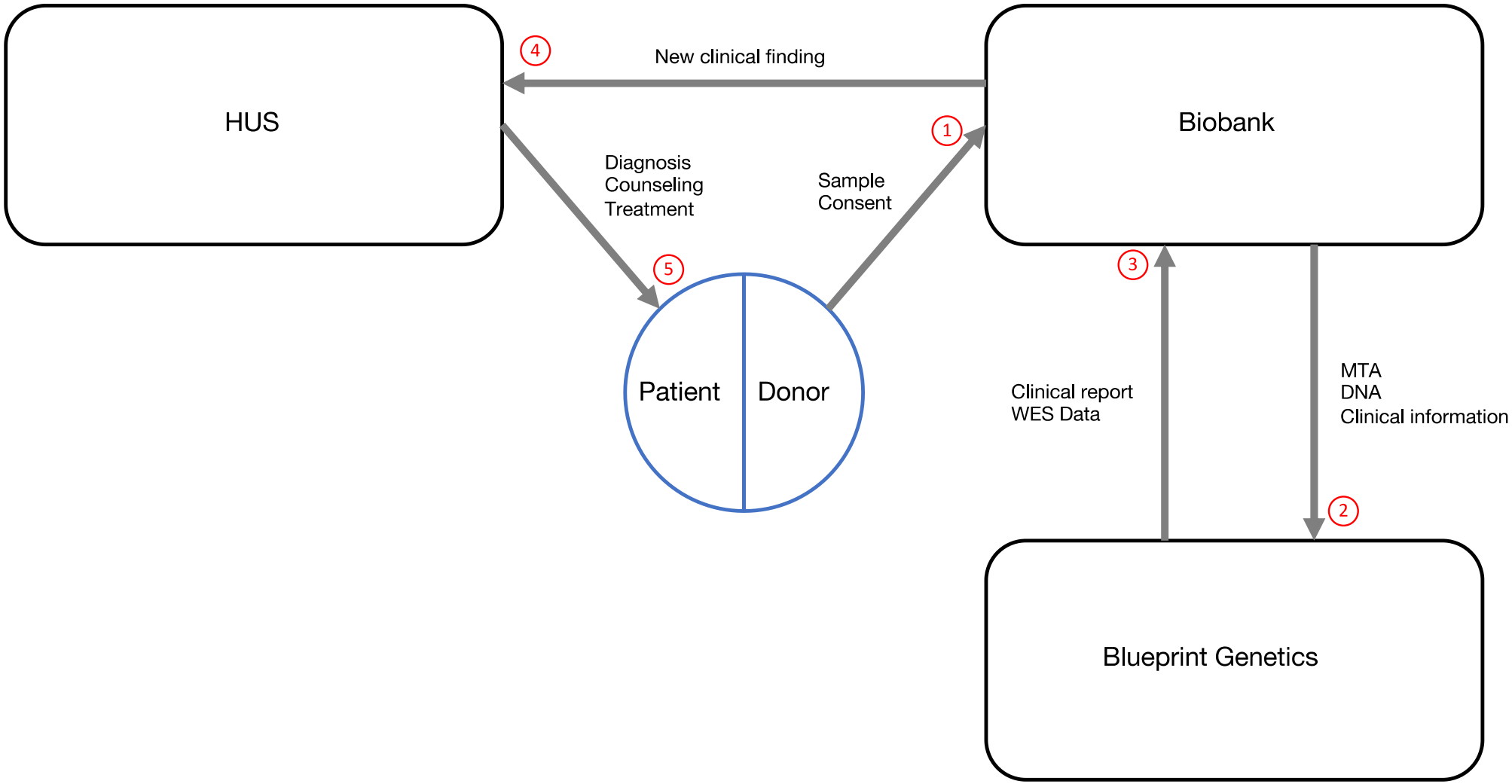
**Inherited retinal disorders**

- Heterogeneous disorders affecting retina where accurate molecular diagnosis is key in selecting treatments

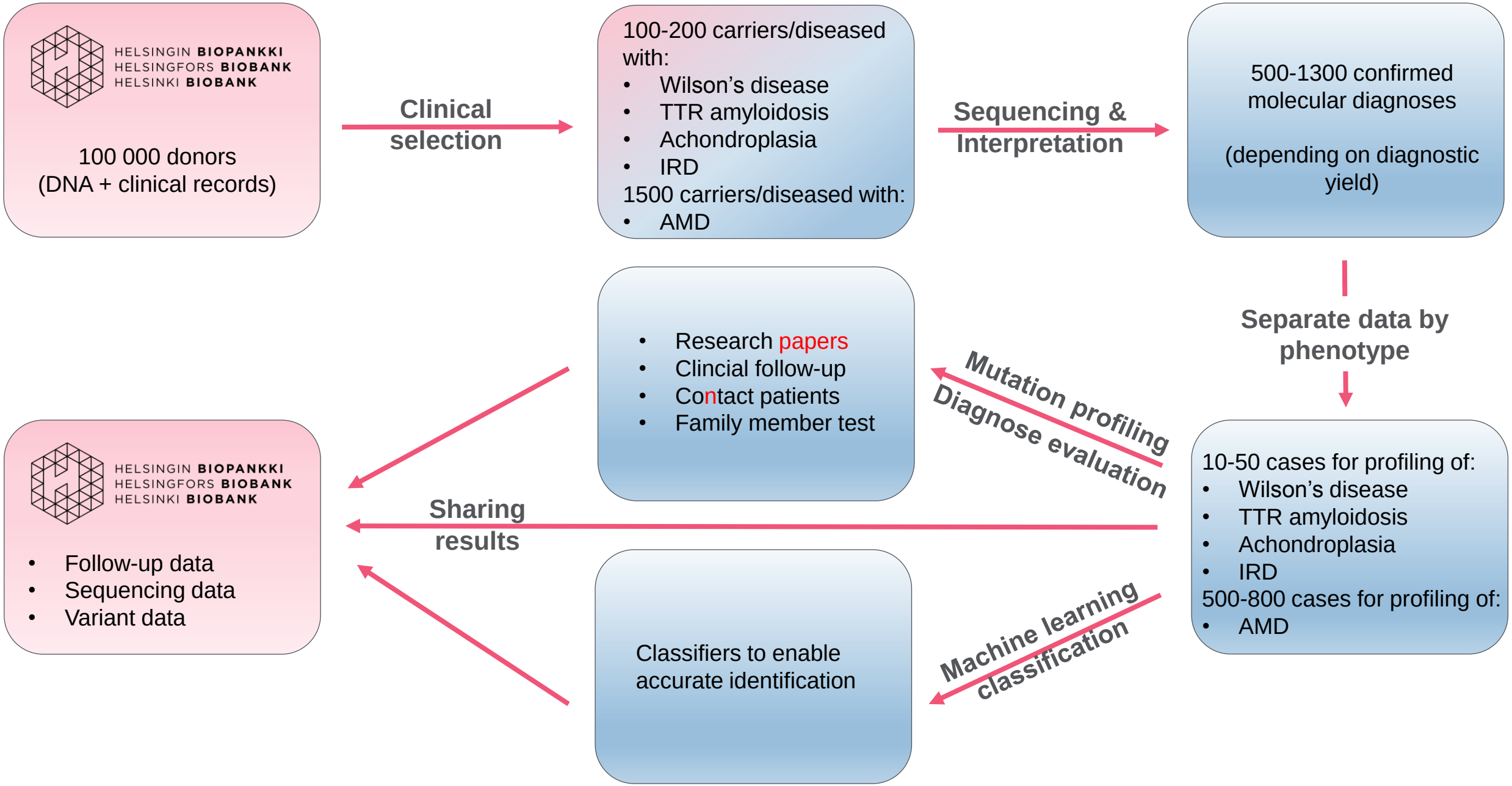
**Age-related macular degeneration**

- Progressive disease affecting macula where genetic factors explain up to 71% of disease variation

# Collaboration model



# Project work-flow



# Team

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