

NeuroDeGene® 2.0: EXPANDED GENETIC PANEL FOR IMPROVED PROGNOSIS AND EARLY-DETECTION OF NEURODEGENERATIVE DISEASES



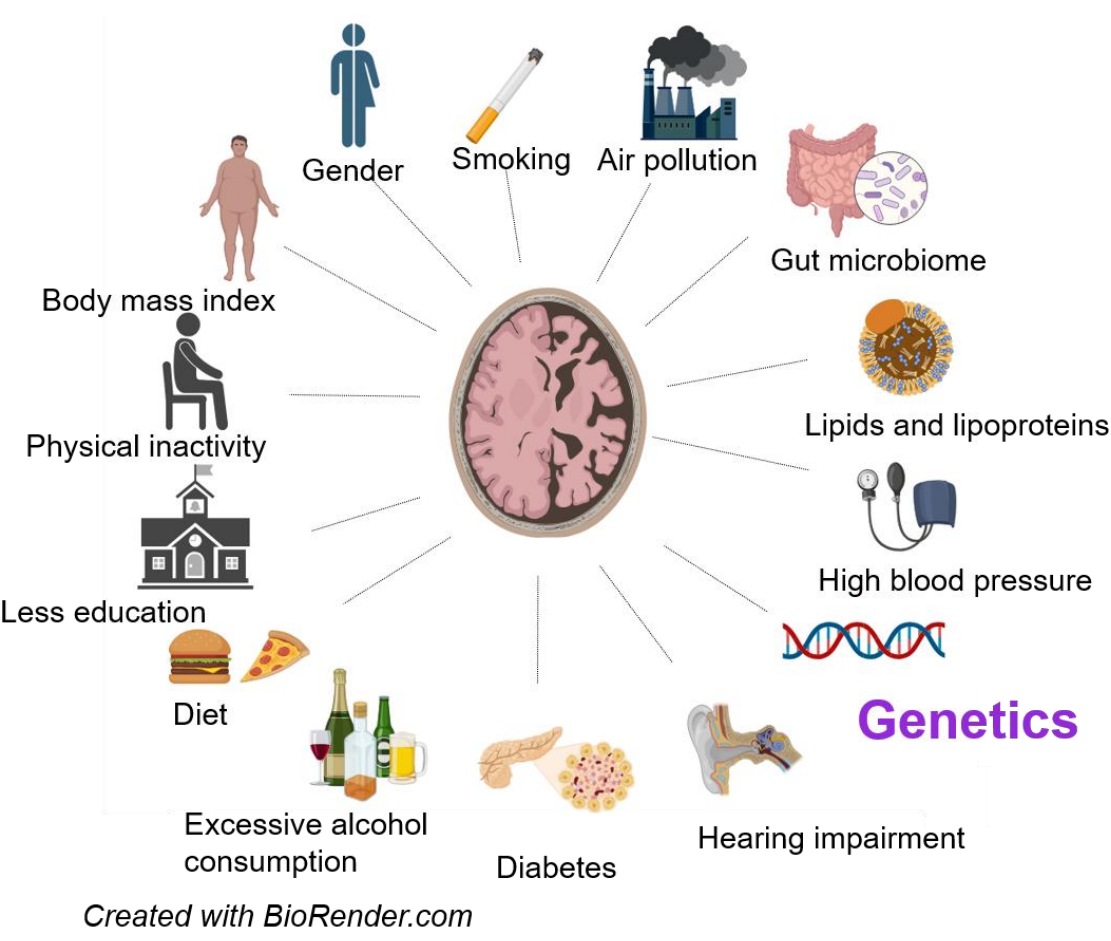
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1. Introduction

Neurodegenerative diseases (NDs) are multifactorial.



Major challenges

- Limited scalable, accessible tools for early-stage and preclinical diagnosis
- Current strategies include **invasive** (e.g. CSF sampling) and/or **expensive** (e.g. neuroimaging PET-scan) techniques

Our proposal

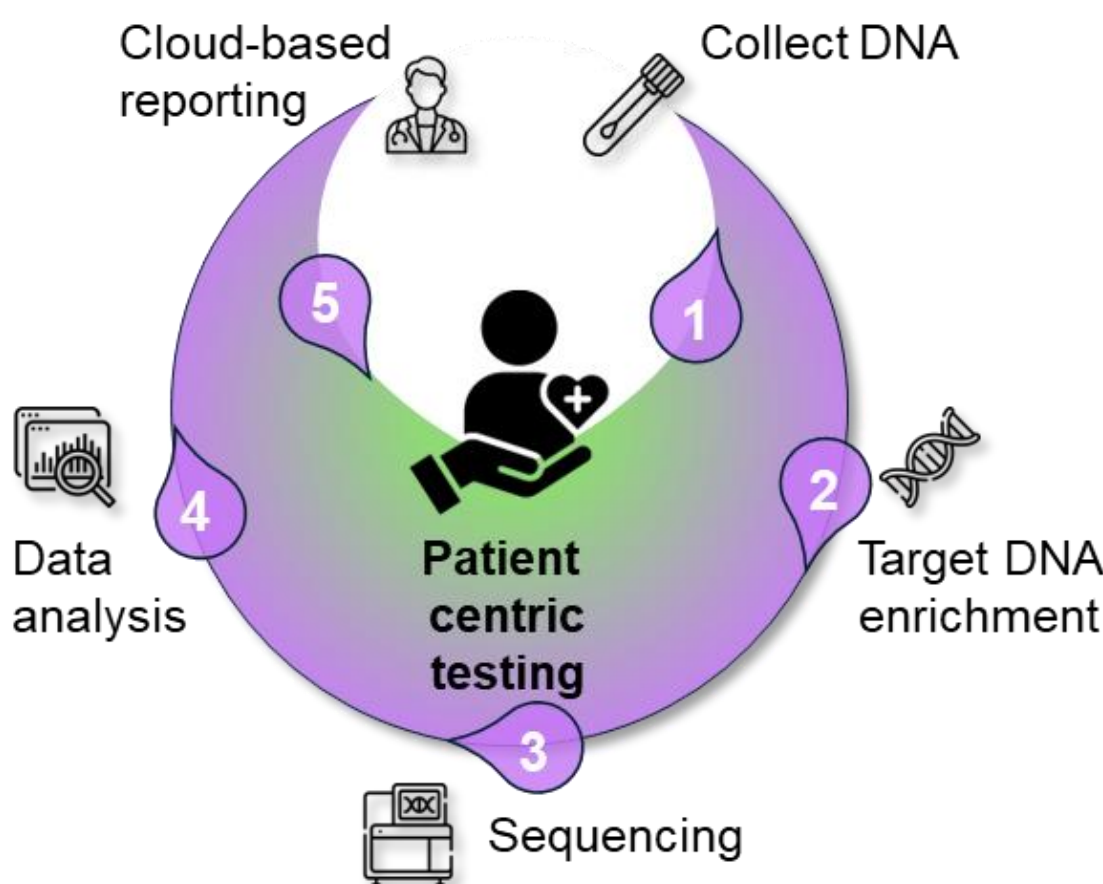
- Develop a genetic panel for **multiple NDs**
- Genetic panel for **genotyping/early-detection/differential diagnosis**
- Use **machine learning** approaches to improve prognostic value
- Predict **disease risk** and **response to drugs** from **multiple genetic variants**

2. The NeuroDeGene® panel

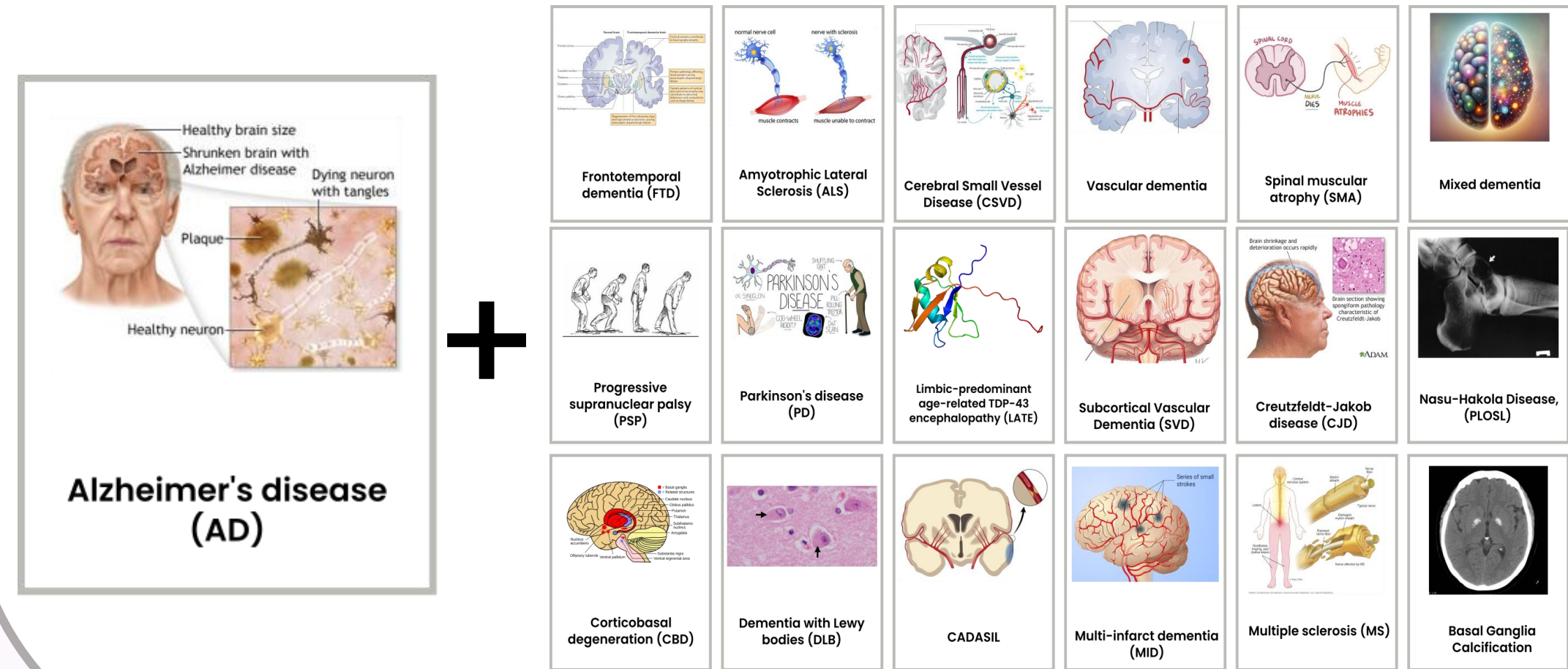
NeuroDeGene® is a **DNA-targeted sequencing** kit developed in collaboration with **Celemics**

Detection of **Single Nucleotide Polymorphisms (SNPs)** and **Insertions/Deletions (INDELs)** associated with **NDs**

Use of **state-of-the-art sequencing technology, bioinformatics pipelines and machine learning**, to develop **predictive models** for early diagnosis and stratification of NDs for **personalized medicine**



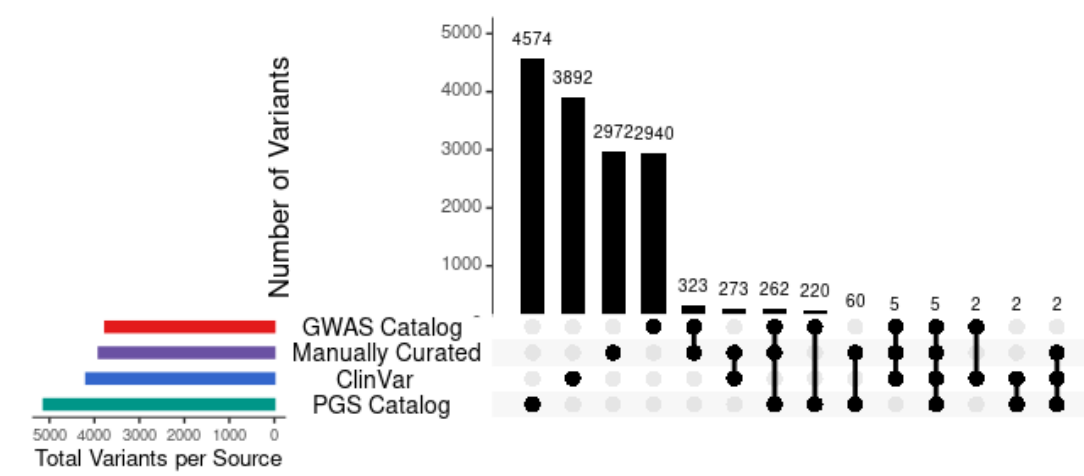
NeuroDeGene® includes **genetic variants associated with 19 neurodegenerative disorders**



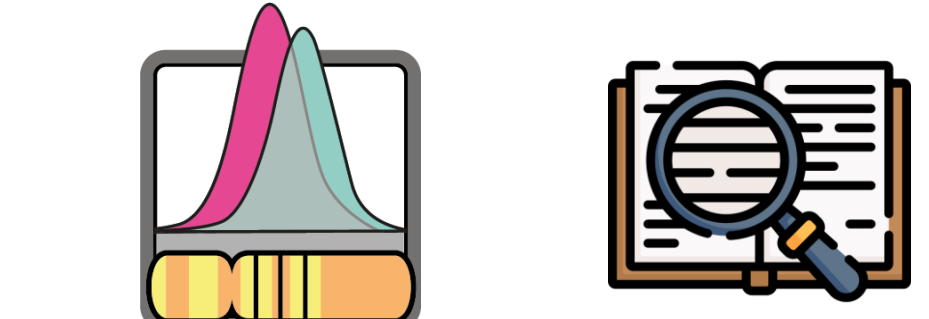
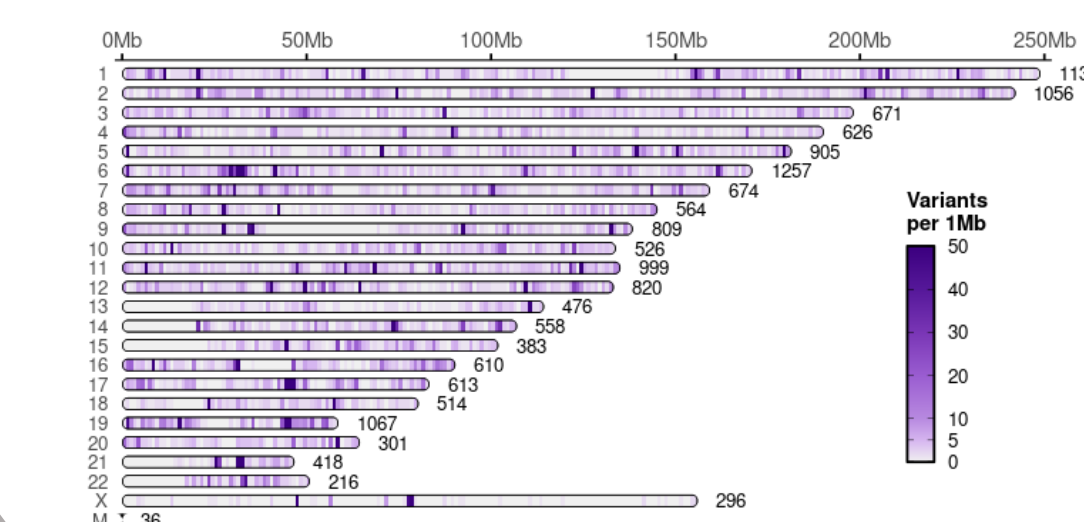
3. NeuroDeGene®: Variant selection and key features

ClinVar

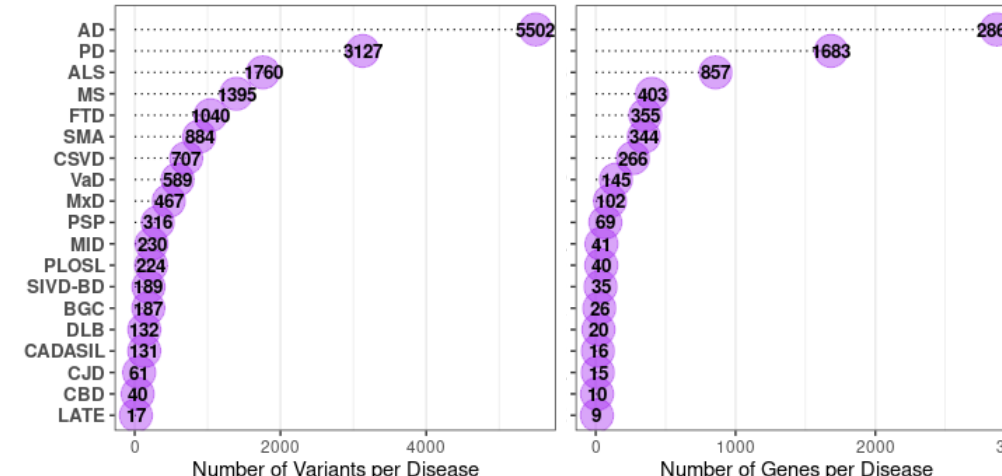
Genetic variants collected from **ClinVar, GWAS, PGS** catalogs and **manually curated**



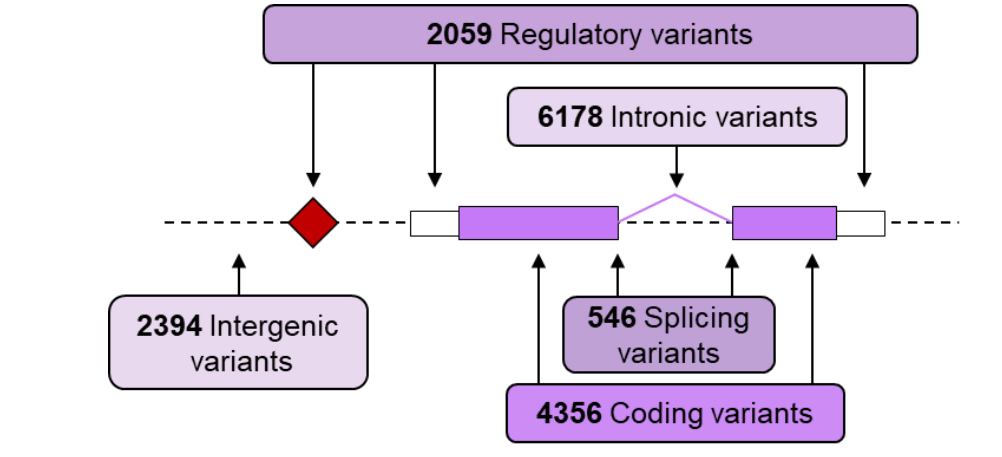
Genome-wide coverage of variants



15 533 variants distributed across 19 NDs and mapped to 5219 genes



More than **70% non-coding** variants

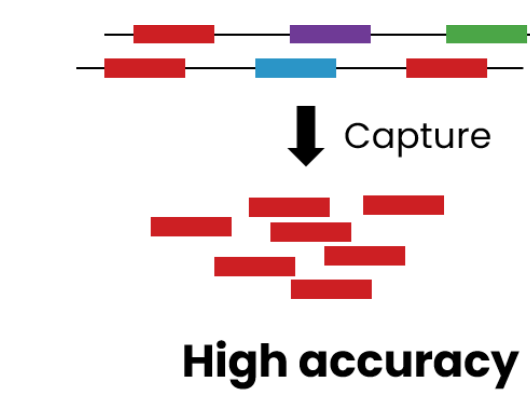
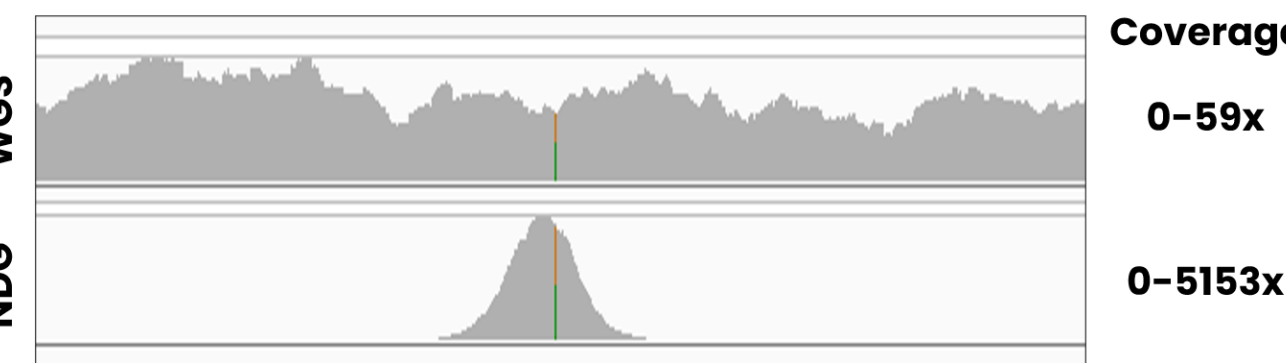


4. Efficient capture sequencing and genotyping

Targeted panel sequencing

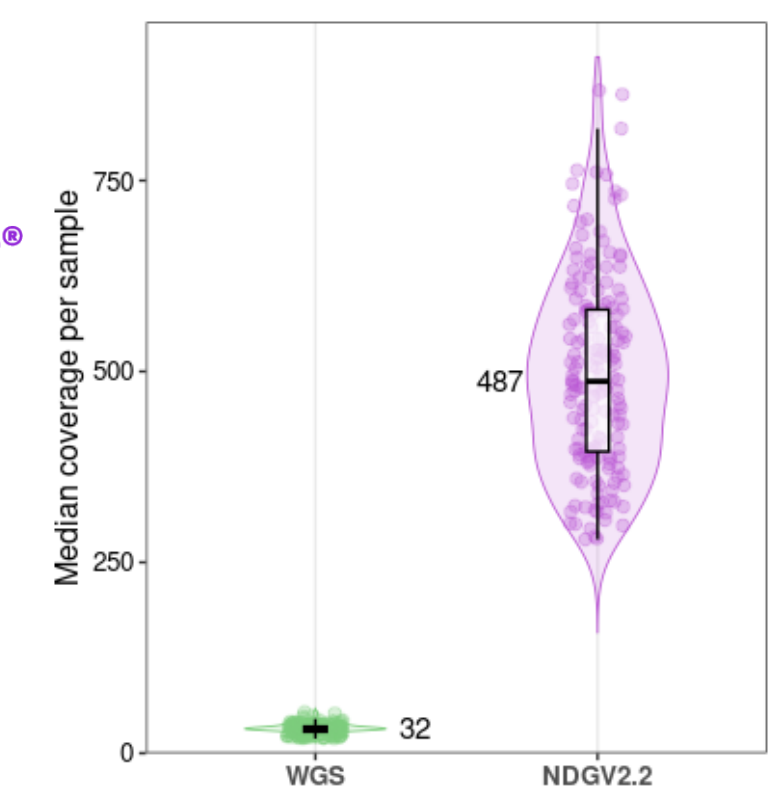
- Up to thousands of genes/variants
- High coverage and depth
- Low cost

NeuroDeGene® provides **higher coverage** around **sharp capture peaks** compared to WGS

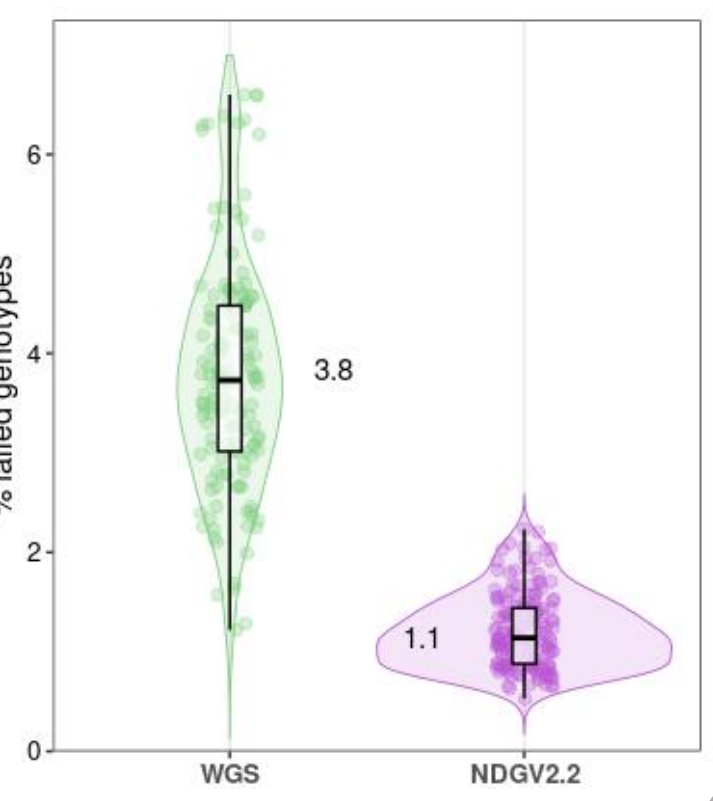


Exome ~ 1,32%
Human genome (3,1 Gb)
NeuroDeGene® ~ 0,3%

NeuroDeGene® provides **higher median coverage** for selected variants compared to WGS



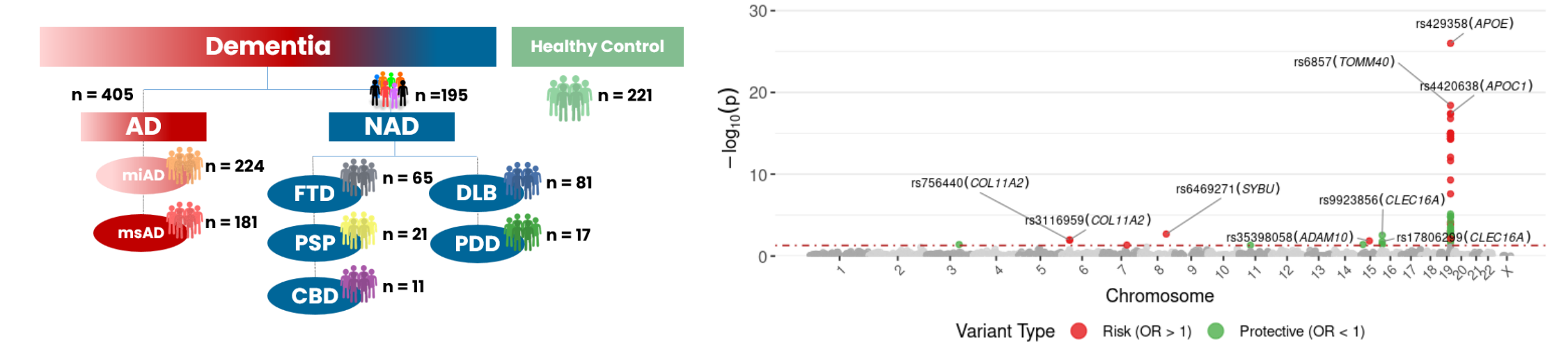
NeuroDeGene® delivers a **lower error rate (~1%)** compared to WGS



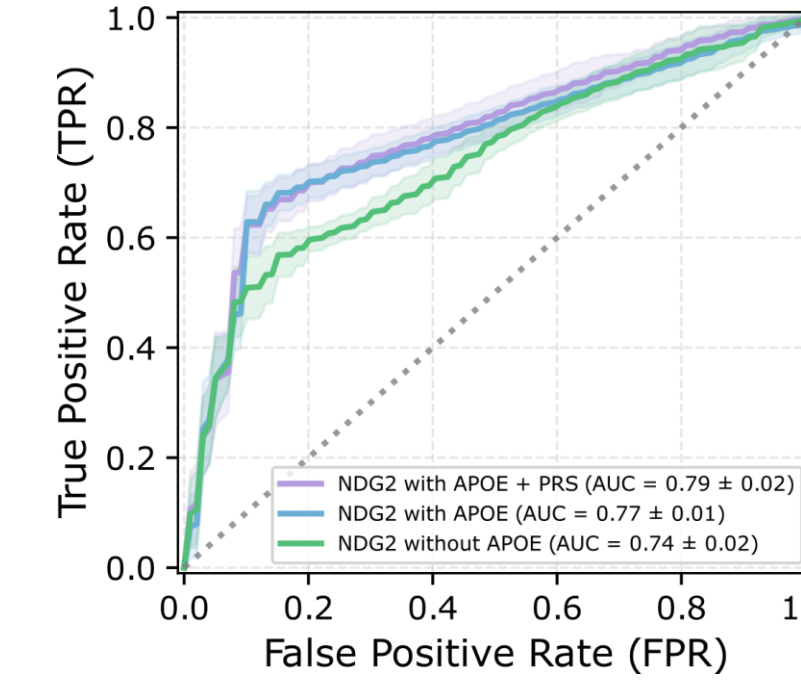
5. NeuroDeGene® genetic risk prediction

NeuroDeGene® was tested in the **ADDIA** cohort (NCT03030586)

Univariate analysis confirms the **APOE locus** as the strongest genetic risk factor for AD



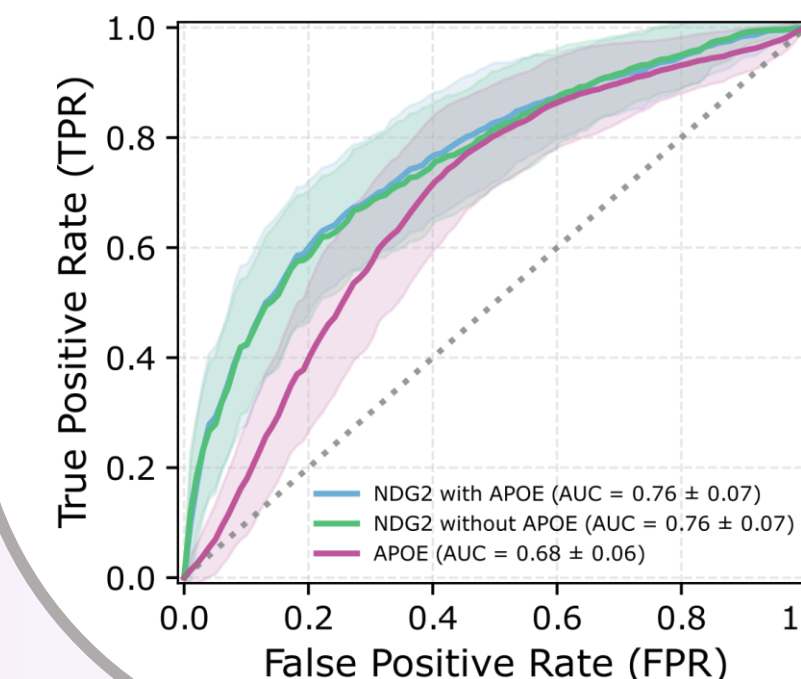
ML-based AD vs HC classification using **NeuroDeGene®** captures a **substantial proportion of the genetic signal (~75%)**, consistent with published estimates of AD heritability (~60-80%)



Model	Accuracy	Sensitivity	Specificity
NDG2 with APOE + PRS	0.748 [0.64-0.79]	0.656	0.859
NDG2 with APOE	0.753 [0.64-0.78]	0.668	0.856
NDG2 without APOE	0.686 [0.60-0.71]	0.596	0.793

Beyond APOE: **NeuroDeGene®** captures the **wider genetic architecture of AD**

ML models improve differential diagnosis of AD vs DLB, achieving **promising accuracy**, supporting **NeuroDeGene®** potential in **differential diagnosis and clinical decision-making**



Model	Balanced Accuracy	Sensitivity	Specificity
NDG2 with APOE	0.70 [0.57-0.87]	0.67	0.72
NDG2 without APOE	0.69 [0.53-0.82]	0.65	0.73
APOE	0.65 [0.46-0.76]	0.68	0.62

Beyond clinical overlap: **NeuroDeGene®** distinguishes AD from other dementias

6. Conclusions

- NeuroDeGene® supports **early genetic risk stratification** and shows strong potential for **differential diagnosis across NDs**
- Validation in AD demonstrates **robust performance for diagnosis, prognosis, and patient stratification**, supporting its translational potential
- Preliminary results indicate high potential for **differential diagnosis between AD and other dementias**, but broader validation is required

We are actively seeking access to well-characterized NAD cohorts to expand and validate NeuroDeGene® for multi-disease differential diagnosis

If you want to test **NeuroDeGene®** for your **clinical** and **academic** studies, please visit us at **booth #849** or get in touch with us at



Learn more about us!

1. Bing M. Zhang et al. An Overview of Characteristics of Clinical Next-Generation Sequencing-Based Testing for Hematologic Malignancies. Arch Pathol Lab Med. 2021 Sep 1;145(9):1110-1116. 2. Lee Han-Byoel et al. Development and Validation of a Next-Generation Sequencing-Based Multigene Assay to Predict the Prognosis of Estrogen Receptor-Positive, HER2-Negative Breast Cancer. Clin Cancer Res. 2020 Dec 15;26(24):6513-6522. 3. Bellenguez, Céline et al. New insights into the genetic etiology of Alzheimer's disease and related dementias. Nat Genet. 2022 Apr;54(4):412-436. 4. Solis, Elliot et al. The NHGRI-EBI GWAS Catalog: knowledgebase and deposition resource. Nucleic Acids Res. 2023 Jan 6;51(D1):D977-D985. 5. Landrum Melissa J. et al. ClinVar: improving access to variant interpretations and supporting evidence. Nucleic Acids Res. 2018 Jan 4;46(D1):D1062-D1067. 6. Lambert, Samuel A. et al. The Polygenic Score Catalog as an open database for reproducibility and systematic evaluation. Nat Genet. 2021 Apr;53(4):420-425.



This project has received funding from the European Union's Horizon 2020 research and innovation program under the grant agreement No. 674474

