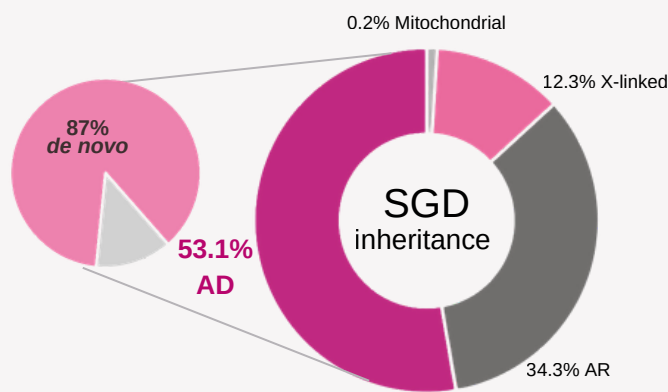


BambniTest™ NIPT-SGD

Background

Single gene disorders account for ~1% of birth defects [1], often driven by *de novo* mutations that parental carrier screening cannot detect. [2] With *de novo* risk increasing with parental age [3], prenatal screening provides a crucial, cost-effective preventive approach for severe early-onset conditions.



Information derived from reference [2]
AD: Autosomal Dominant; AR: Autosomal Recessive

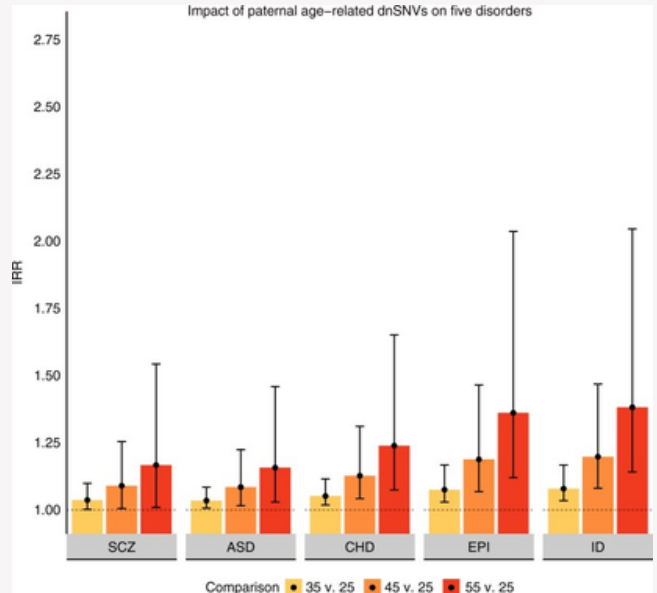


Figure adopted from reference [4]
dnSNVs: *de novo* single nucleotide variants; SCZ: schizophrenia; ASD: autism spectrum disorder; CHD: congenital heart disease; EPI: epilepsy; ID: intellectual disability;
IRR: Incidence rate ratio, which represents the increased risk of dnSNV-related diseases in the offspring of older fathers compared to those of younger fathers

BambniTest™ NIPT-SGD

BambniTest™ Non-Invasive Prenatal Testing of Single Gene Disorders (NIPT-SGD) targets specific mutations to detect *de novo* single gene abnormalities missed by carrier screening and standard NIPT. By identifying severe disorders independent of phenotypic heterogeneity or visible ultrasound anomalies, it minimizes missed diagnoses and facilitates early intervention without the risk of invasive procedures.

Testing Scope

66 autosomal dominant or X-linked disorders within 34 genes are selected based on the following criteria:

- Incidence rate
- High penetrance
- >50% caused by *de novo* mutations
- Early on-set (<10 years old) with severe phenotypes
- Variants detectable with NGS
- At risk of being missed by prenatal ultrasound

22 disorders: Intellectual / Developmental Disabilities
44 disorders: Structural Abnormalities / Others

Captures *De Novo* Mutations

Screens for spontaneous single-gene abnormalities that carrier screening misses — with zero risk of miscarriage

Facilitates Early Intervention

Identifies severe disorders before the onset of ultrasound abnormalities, and aids in the molecular diagnosis of nonspecific findings

Reduced Miss Rate

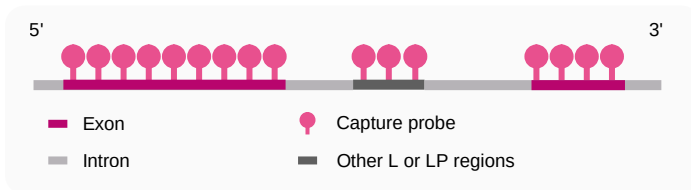
Bypasses the challenges of phenotypic heterogeneity—detecting cases with negative or difficult-to-observe ultrasound findings — to provide a more definitive risk assessment

Parameters	Description
Technology	Targeted sequencing, paired-end
Platform	Illumina SBS sequencing system
Sample type	Maternal blood with singleton pregnancy
Analysis offered	P/ LP SNVs and InDels ≤3bp within 34 genes (66 disorders) Note: P/ LP InDels >3bp within 34 genes (66 disorders) are reported as supplementary

Technology

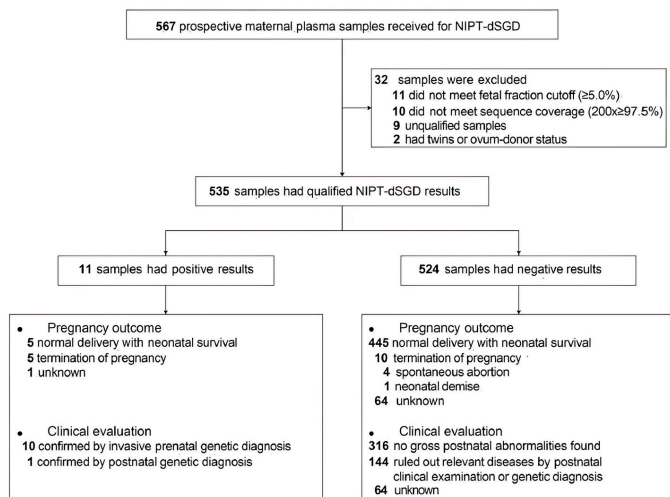
Targeted Capture NIPT

By focusing sequencing power ($\geq 97.5\%$ target region at 200x depth) on clinically significant regions (protein-coding regions and splice sites of 34 genes, as well as other regions classified as pathogenic or likely pathogenic according to the ClinVar and HGMD databases), we achieve higher depth and accuracy for small mutations in ccfDNA.

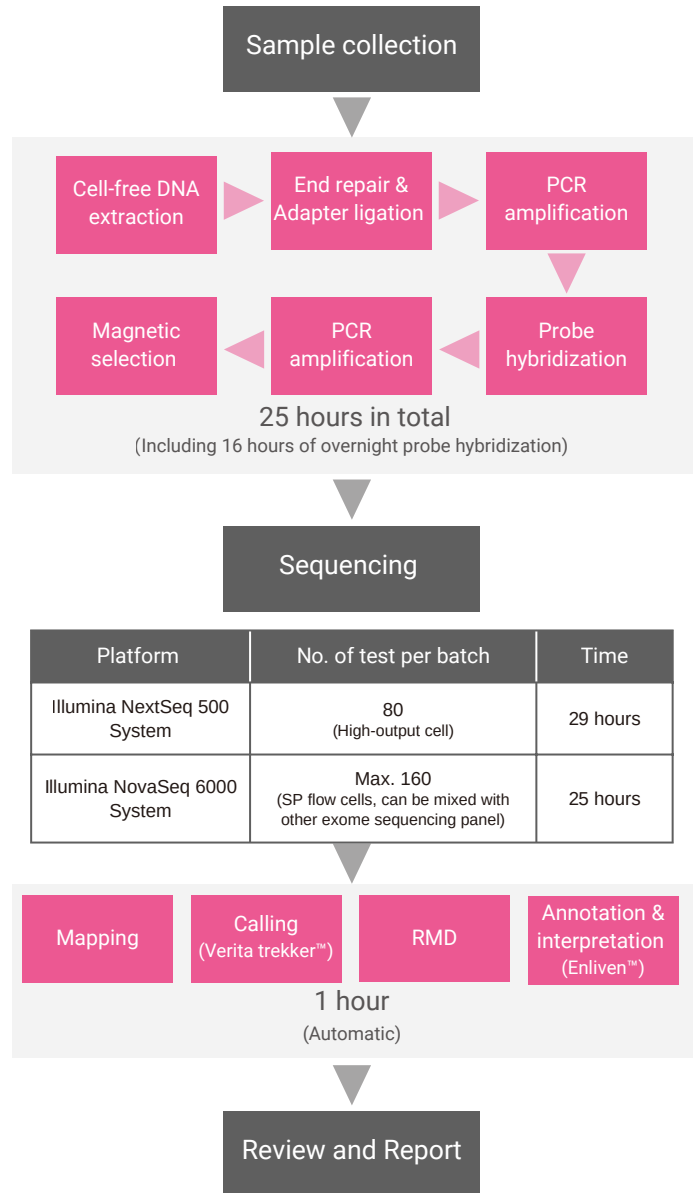


Accuracy and Utility

BambniTest™ NIPT-SGD demonstrates sensitivity and specificity of up to 100%. In a prospective study of 537 pregnancies, the test identified pathogenic variants in 2.2% of cases (72.2% *de novo*). Crucially, 45.5% of these positive cases presented with normal ultrasound parameters, highlighting the test's ability to identify risks that ultrasound misses. Furthermore, postnatal evaluation confirmed the absence of disease in all followed-up negative cases. [5]



NIPT-dSGD: BambniTest™ NIPT-SGD; Figure adopted from reference [5]



References:

- [1] Chitty LS. Advances in the prenatal diagnosis of monogenic disorders. *Prenat Diagn.* 2018;38(1):3-5.
- [2] Yang Y, Muzny DM, Xia F, et al. Molecular findings among patients referred for clinical whole-exome sequencing. *JAMA.* 2014;312(18):1870-1879.
- [3] Jónsson H, Sulem P, Kehr B, et al. Parental influence on human germline *de novo* mutations in 1,548 trios from Iceland. *Nature.* 2017;549(7673):519-522.
- [4] Taylor JL, Debost J, Morton SU, et al. Paternal-age-related *de novo* mutations and risk for five disorders. *Nat Commun.* 2019;10(1):3043.
- [5] Zhang H, He J, Teng Y, et al. Non-invasive prenatal testing for dominant single-gene disorders using targeted next-generation sequencing. *QJM.* Published online February 21, 2025.

Non-Invasive Prenatal Testing of Single Gene Disorders (NIPT-SGD)

Screens for pathogenic/ likely pathogenic variants (SNVs, InDels < 3bp) for 66 autosomal dominant or X-linked disorders within 34 genes

Intellectual / Developmental Disabilities (22)

Disorders	Genes	Incident/Prevalence
CHARGE syndrome	CHD7	1-9/ 100 000
Intellectual developmental disorder, autosomal dominant 5	SYNGAP1	--
Bainbridge-Ropers syndrome	ASXL3	<1/ 1 000 000
Coffin-Siris syndrome 1	ARID1B	<1/ 1 000 000
Rett syndrome	MECP2	1-9/ 100 000
Developmental delay with variable intellectual impairment and behavioral abnormalities	TCF20	--
Kleefstra syndrome 2	KMT2C	<1/ 1 000 000
Intellectual developmental disorder, autosomal dominant 52	ASH1L	--
Intellectual developmental disorder, autosomal dominant 7	DYRK1A	<1/ 1 000 000
Developmental and epileptic encephalopathy 4	STXBP1	1-9/ 100 000
White-Sutton syndrome	POGZ	<1/ 1 000 000
Developmental and epileptic encephalopathy 27	GRIN2B	1-9/ 100 000
Intellectual developmental disorder, autosomal dominant 6, with or without seizures	GRIN2B	--
Developmental and epileptic encephalopathy 2	CDKL5	1-9/ 100 000
Developmental and epileptic encephalopathy 94	CHD2	--
Menke-Hennekam syndrome 1	CREBBP	--
Rubinstein-Taybi syndrome 1	CREBBP	1-9/ 100 000
Helsmoortel-van der Aa syndrome	ADNP	1-9/ 100 000
Rett syndrome, congenital variant	FOXG1	--
Cornelia de Lange syndrome 1	NIPBL	1-9/ 100 000
Intellectual developmental disorder, autosomal dominant 43	HIVEP2	--
Mowat-Wilson syndrome	ZEB2	1-9/ 100 000

Structural Abnormalities / Others (44)

Disorders	Genes	Incident/Prevalence
Developmental and epileptic encephalopathy 6B, non-Dravet	SCN1A	--
Dravet syndrome	SCN1A	1-9/ 100 000
Generalized epilepsy with febrile seizures plus, type 2/ Febrile seizures, familial, 3A	SCN1A	--
Migraine, familial hemiplegic, 3	SCN1A	1-5/ 10 000

Disorders	Genes	Incident/Prevalence	
Caffey disease	COL1A1	3/ 1 000	
Combined osteogenesis imperfecta and Ehlers-Danlos syndrome 1	COL1A1	<1/ 1 000 000	
Combined osteogenesis imperfecta and Ehlers-Danlos syndrome 2	COL1A2		
Osteogenesis imperfecta, type I	COL1A1	1-5/ 10 000	
Osteogenesis imperfecta, type II	COL1A1		
	COL1A2		
Osteogenesis imperfecta, type III	COL1A1		
	COL1A2		
Osteogenesis imperfecta, type IV	COL1A1	--	
	COL1A2		
Ehlers-Danlos syndrome, arthrochalasia type, 1	COL1A1	--	
Ehlers-Danlos syndrome, arthrochalasia type, 2	COL1A2		
Tuberous sclerosis 1	TSC1	1-9/ 100 000	
Tuberous sclerosis 2	TSC2		
Achondroplasia	FGFR3	1-9/ 100 000	
Crouzon syndrome with acanthosis nigricans	FGFR3	1-9/ 1 000 000	
Hypochondroplasia	FGFR3	1-9/ 100 000	
Muenke syndrome	FGFR3	1-9/ 100 000	
Achondroplasia, severe, with developmental delay and acanthosis nigricans	FGFR3	<1/ 1 000 000	
Thanatophoric dysplasia, type I	FGFR3	1-9/ 100 000	
Thanatophoric dysplasia, type II	FGFR3		
Lacrimoauriculodentodigital syndrome 1	FGFR2	<1/ 1 000 000	
Lacrimoauriculodentodigital syndrome 2	FGFR3		
Antley-Bixler syndrome without genital anomalies or disordered steroidogenesis	FGFR2	--	
Apert syndrome	FGFR2	1-9/ 100 000	
Beare-Stevenson cutis gyrata syndrome	FGFR2	<1/ 1 000 000	
Bent bone dysplasia syndrome 1	FGFR2	<1/ 1 000 000	
Pfeiffer syndrome/ Craniofacial-skeletal-dermatologic dysplasia	FGFR2	1-9/ 100 000	
Crouzon syndrome	FGFR2	1-9/ 1 000 000	
Jackson-Weiss syndrome	FGFR2	--	
Saethre-Chatzen syndrome	FGFR2	1-9/ 100 000	
Kabuki syndrome 1	KMT2D	1-9/ 100 000	
LEOPARD syndrome 1	PTPN11	--	
LEOPARD syndrome 2	RAF1		
LEOPARD syndrome 3	BRAF		
Noonan syndrome 1	PTPN11	1-5/ 10 000	
Noonan syndrome 3	KRAS		
Noonan syndrome 4	SOS1		
Noonan syndrome 5	RAF1		
Noonan syndrome 7	BRAF		
Noonan syndrome 8	RIT1		
Cardiofaciocutaneous syndrome 1	BRAF		1-9/ 1 000 000
Cardiofaciocutaneous syndrome 2	KRAS		

All incident/ prevalence are obtained from Orphanet, MedlinePlus, and others.