Test (TAT) ***Signed Consent***	**Indication**	**Diagnostic Yield**	**Result Types**	**Variant Detected (Type and Size)**
Non Invasive Prenatal Screen	▪ Prenatal **Screen**	Non Diagnostic (assesses risk)	▪ Sex chromosomes ▪ Low risk ▪ High risk	▪ Aneuploidy (e.g., T13, T18, T21, XO, XXY) ▪ Limited microduplication / microdeletion syndromes
Karyotype (3-4 days) ***Not required***	▪ MCA ▪ Advanced Maternal Age ▪ Multiple miscarriage	Varies by indication	▪ Normal ▪ Abnormal ▪ Uncertain	▪ Aneuploidy (e.g., T13, T18, T21, XO, XXY) Deletions , duplications and structural rearrangements (≥ 5 Mb)
Microarray (3-4 weeks) ***Encouraged***	▪ ID/DD/ASD ▪ MCA ▪ Microdup/del syn	15 – 20% *Miller et al., 2010*	▪ Normal ▪ Abnormal ▪ Uncertain ▪ Consanguinity* ▪ Nonpaternity* (*SNP Array)	▪ Deletions and duplications (≥ 50–100kb) aka CNVs ▪ Aneuploidy
Fragile X by PCR w Methylation (3-4 weeks) ***Not required***	▪ ID/DD/ASD ▪ Family History of FX ▪ POI, FXTAS	2.5% (Males w/ ID/DD) 2% (Males w/ ASD)	▪ Normal ▪ Pre-mutation Carrier ▪ Intermediate ▪ Full mutation	▪ Trinucleotide repeat size
Nucleotide Repeat Expansion (2-3 weeks) ***Often required, especially for HD***	▪ Huntington Disease (HD) ▪ Myotonic Dystrophy ▪ Freidriech Ataxia	Varies	▪ Normal ▪ Pre-mutation Carrier ▪ Intermediate ▪ Full mutation	▪ Nucleotide repeat size
Methylation Studies ***Not required***	▪ Prader-Willi, Angelman, Beckwith-Wiedemann, Russell-Silver	Varies		
Single or Multi Gene (3-4 weeks) ***Required by some labs***	▪ Varies	Varies	▪ Negative ▪ Uncertain ▪ Positive	▪ SNV ▪ Small insertions/deletions (indels) ▪ Within exons and their flanking intronic regions of the tested gene(s)
Exome Sequencing (Rapid: 7 days, Standard: 8-12 weeks) ***Required***	▪ Atypical / early-onset /nonspecific presentation, broad differential	36% - Overall 31% - Isolated NDD 16% - Primarily ASD 39% - Primarily ID 37% - ASD/ID 53% - NDD plus *Srivastava et al., 2019*	▪ Negative ▪ Uncertain ▪ Positive ▪ Secondary Findings ▪ Incidental Findings	▪ SNVs within nearly all exons and 10 bp of their flanking intronic regions for nearly all genes ▪ Indels ▪ CNVs ≥ 4 exons. <u>Not analyzed:</u> ▪ Regulatory domains ▪ Deep intronic regions ▪ Chromosomal rearrangements ▪ Nucleotide repeat expansions ▪ Mitochondrial genome
Genome Sequencing (12 weeks) ***Required***	*Not yet widely available for clinical use*		▪ Negative ▪ Uncertain ▪ Positive ▪ Secondary Findings ▪ Incidental Findings	▪ SNVs within nearly all exons and introns for nearly all genes, including mitochondrial genome ▪ Indels ▪ CNVs ≥ 4 exons ▪ Regulatory domains <u>Not analyzed</u>: ▪ Chromosomal rearrangements ▪ Nucleotide repeat expansions

ASD: Autism Spectrum Disorder; **CNV:** Copy Number Variant ; **DD:** Developmental Delay; **FX**: Fragile X; **FXTAS:** Fragile X Tremor/Ataxia Syn; **ID:** Intellectual Disability; **MCA**: Multiple Congenital Anomalies; **NDD:** Neurodevelopmental Disorder; **POI:** Premature Ovarian Insufficiency; **SNV:** Single Nucleotide Variant