MEDGENOME | Claria Reproductive Genetics

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KaryoSeq

Whole Genome Sequencing for Chromosomal Abnormalities

What is **KaryoSeq**?

KaryoSeq is a new genetic test that utilizes whole genome sequencing* for detection of **Aneuploidies** of all chromosomes and **Copy Number Variations** (deletions and duplications) **>1Megabase**.

Advantages

1. Cost effective
2. Comprehensive Genome Wide
3. Well Validated 100% concordance >1MB
4. Prenatal (AF, CVS, POC) and Postnatal Application.
5. High Resolution# Higher Diagnostic Yield

*Low pass Whole Genome Sequencing

#Compared to QF-PCR/Karyotyping

Comparison of available tests

Test	Karyotyping	QF-PCR	SNP Microarray	KaryoSeq (Low – Pass whole genome Sequencing)
Abnormalities detected	Aneuploidies, larger CNVs, **Structural Abnormalities.**	Aneuploidies in chromosomes 13, 18, 21, X and Y	Aneuploidies, CNVs, Triploidy, UPD, AOH	Aneuploidies and CNVs
Input	Live cells	DNA	DNA	DNA
TAT	14 Working days	**< 03 Working days**	10 Working days	8 Working days* (approximately)
CNV resolution	>5Mb Size Very Low Resolution	Not detected	**>200Kb Gain and >100Kb loss** **High Resolution**	Genome wide CNVs >1Mb size Moderate Resolution
Cost effectiveness	Cost effective but lower resolution	**Cost effective**	Expensive	**Cost effective**
MCC Test needed	**No**	Yes	Yes	Yes
Diagnostic Yield(Prenatal)	3-6%	11.1%	**17.56%**	**17.11%**

**TAT depends on test combination*

Validation

The validation process involved comparison of the CMA results with KaryoSeq.

Sample Size

- 10 normal
- 138 abnormal

DNA Sample Type

- Amniotic Fluid
- Chorionic villus biopsy
- Product of conception
- Direct fetal DNA
- peripheral blood DNA

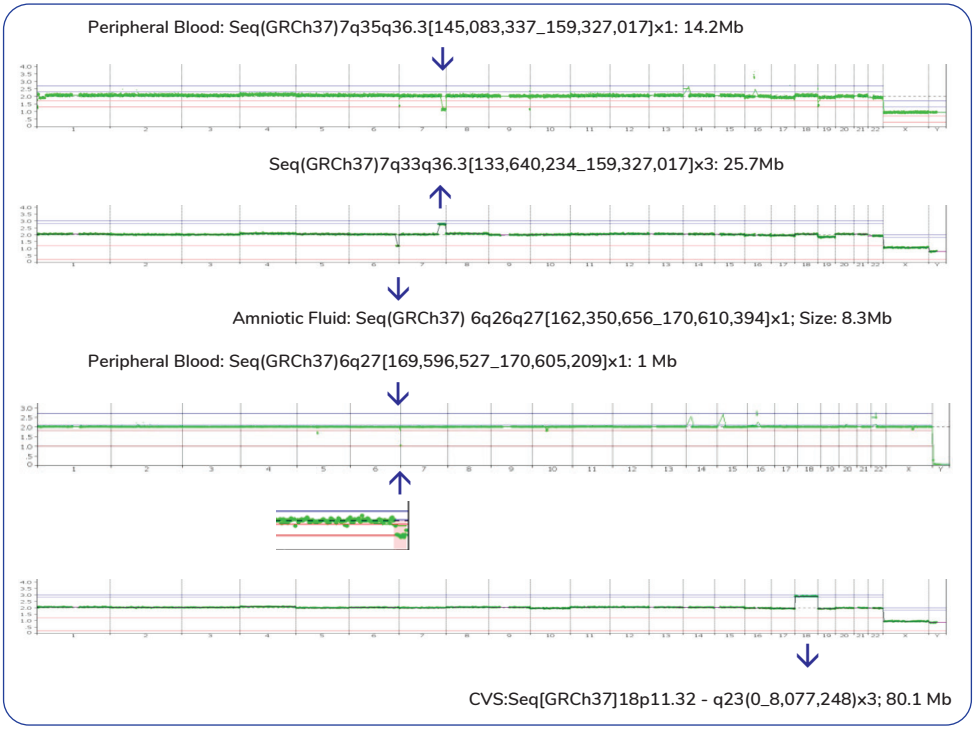
Aberrations Identified

- Whole chromosome aneuploidies
- CNVs

Concordance

- 100% concordance>1Mb CNVs

Examples of variants detected



Test Details

Test Code	Test Name	Sample Requirements	TAT	Methodology
MGM2754	Karyoseq (without MCC or other samples)	Peripheral Blood, Direct DNA	8 Working Days	NGS
MGM2777	KaryoSeq with MCC	Chorionic Villus Sampling (CVS)/Amniotic Fluid (AF)/ Cultured Amniotic Fluid/Cord Blood/Cardiac Blood/Products of Conception Tissue (POC)/Peripheral Blood, Direct DNA/DNA Isolated from Cell Lines or Cultured Cells	10 Working Days	NGS
MGM2761	Karyoseq with (prenatal cell culture if required)	Chorionic Villus Biopsy, Amniotic Fluid	8 + 12 Working Days	NGS

MCC – Maternal Cell Contamination Testing is a prerequisite for prenatal samples.

The gender of prenatal samples will not be reported in accordance with the Pre-Conception and Pre-Natal Diagnostic Techniques Act, 1994 – MedGenome Labs Ltd. Registered no. 1451.

Examples of CNVs detected

Sl. No.	Sample Type	Microarray detected CNV's	Size (Mb)	KaryoSeq Detected CNV's	Size (Mb)	Concordance (Microarray vs KaryoSeq)
1	CVS	arr[GRCh38] (18)x3 **[Edwards syndrome]**	80.1	Seq[GRCh37]18p11.32 - q23(0_8,077,248)x3	78	✓
2	CVS	arr[GRCh38] (21)x3 **[Down syndrome]**	33.1	Seq[GRCh37]21p13-q22.3(0-48,129,895)x3	33.1	✓
3	POC	arr[GRCh38] (12)x3	133.5	Seq[GRCh37]12p13.33 - q24.33(0-133,851,895)x3	133.8	✓
4	Peripheral Blood	arr[GRCh38]11p15.5q23.3(230,616_116,744,147)x3, arr[GRCh38]22q11.1q11.21(16,408,174_20,291,006)x1 **[DiGeorge syndrome]**	116.5 3.88	Seq[GRCh37]11p15.5-q23.3(230,616_116,744,147)x3 Seq[GRCh37]22q11.1-q11.21(16,408,174_20,291,006)x1	103 4	✓
5	AF	arr[GRCh38] 15q13.2q13.3(30,820,717_32,622,039)x1	1.8	Seq[GRCh37]15q13.2-q13.3(30,885,000_32,485,000)x1	1.02	✓
6	Peripheral Blood	arr[GRCh38] 5q35.2q35.3(175,989,093_178,055,505)x1	2.0	Seq[GRCh37]5q35.2 - q35.3(75,568,094_177,768,094)x1	2.2	✓
7	Peripheral Blood	arr[GRCh38] 22q13.32q13.33(48,199,706_50,759,338)x1 **[Phelan-McDermid syndrome]**	2.5	Seq[GRCh37]22q13.32 - q13.33(48,470,380_51,304,566)x1	2.8	✓
8	Peripheral Blood	arr[GRCh38] 22q11.21(18,950,000_21,108,369)x1 **[DiGeorge syndrome]**	2.1	Seq[GRCh37]22q11.21(18,762,659_21,870,380)x1	3	✓
9	POC	arr[GRCh38]Yq11.23(25,519,063_26,318,566)x2 Yq11.223q11.23(23,717,662_24,887,532)x2	1.1 0.8	Seq[GRCh37]Yq11.223 - q11.23(124,655,552_28,476,607)x2	3.8	✓
10	AF	arr[GRCh38] 9q22.1q22.31(87,988,200_92,870,072)x1	4.8	Seq[GRCh37]9q22.1-q22.31(90,521,336_95,971,336)x1	5.4	✓
11	POC	arr[GRCh38] 10q22.3(79,625,681_80,213,053)x1, arr[GRCh38]15q11.2q13.1(23,102,621_28,458,904)x1 **[Angelman syndrome/ Prader-Willi syndrome]**	0.6 5.3	Seq[GRCh37]10q11.22(18,762,659_21,870,380)x1 Seq[GRCh37]15q11.2 - q13.1(18,762,659_21,870,380)x1	3.3 5.1	✓
12	Peripheral Blood	arr[GRCh38] 18q21.2q21.33(54,720,552_62,003,701)x1	7.2	Seq[GRCh37]18q21.2 - q21.33(52,309,136_59,709,136)x1	7.4	✓
13	Peripheral Blood	arr[GRCh38] 13q32.3q34(101,067,948_114,342,258)x1, arr[GRCh38]16p13.3p13.2(35,881_8,831,829)x3	13.2 8.7	Seq[GRCh37]13q33.1-q34(101,770,197_115,169,878)x1 Seq[GRCh37]16p13.3-p13.2(5,260,000_8,910,000)x3	13.3 3.6	✓
14	AF	arr[GRCh37] 10p15.3p14(100,048_7,701,527)x1	7.6	Seq[GRCh37]10p15.3-p14(0_7,660,000)x1	10	✓
15	Peripheral Blood	arr[GRCh38] 2q12.3q13(108,652,368_110,116,258)x1	1.2	Seq[GRCh37]2q12.3 - q13(109,200,000_111,051,337)x1	1.4	✓
16	Peripheral Blood	arr[GRCh38] 21q11.2q21.3(13,644,166_25,925,065)x1	12.2	Seq[GRCh37]21q11.2 - q21.3(15,500,000_26,800,422)x1	11.3	✓
17	Peripheral Blood	arr[GRCh38] 8q24.21q24.3(130,350,392_145,070,385)x3	14.7	Seq[GRCh37]8q24.21-q24.3(131,400,277_144,250,277)x3	12.9	✓
18	Peripheral Blood	arr[GRCh38]5p15.33p15.2(113,462_13,788,173) x1 **[Cri du chat syndrome]** arr[GRCh38]20p13p12.1(80,929_15,514,914)x3	13.7 15.5	Seq[GRCh37]5p15.33 - p15.2(0_13,810,000)x1 Seq[GRCh37]20p13 - p12.1(0_13,810,000)x3	13.8 15.6	✓
19	Peripheral Blood	arr[GRCh38] 16p11.2(29,568,701_30,166,595)x1	0.5	Seq[GRCh37]16p11.2 - q11.2(31,910,000_46,800,515)x1	14.8	✓
20	Peripheral Blood	arr[GRCh38] 7p21.3p15.2(10571965-26444007)x1	15.8	Seq[GRCh37]7p21.3 - p15.2(10,560,000_26,460,000)x1	15.9	✓
21	Peripheral Blood	arr[GRCh38] 13q22.2q31.3(75,664,252_91,427,209)x1	15.7	Seq[GRCh37]13q22.2 - q31.3(76,120,197_92,110,324)x1	16	✓
22	Peripheral Blood	arr[GRCh38] 9q34.3(137,434,967_138,124,196)x1	0.7	Seq[GRCh37]9p13.1 - q12(38,814,048_55,146,786)x1	16.33	✓
23	Peripheral Blood	arr[GRCh38] 4q34.1q35.2(172,079,686_190,036,305)x1	17.9	Seq[GRCh37]4q34.1 - q35.2(172,981,307_191,154,276)x1	18.2	✓
24	POC	arr[GRCh38] (13)x3 **[Patau syndrome]**	95.6	Seq[GRCh37]13p13.1 - q12(0_115,169,878)x3	23	✓
25	AF	arr[GRCh38]6q26q27(162,350,656_170,610,394)x1, arr[GRCh38]7q33q36.3(133,640,234_159,327,017)x3	8.3 25.7	Seq[GRCh37]6q26-q27(162,025,576_171,115,067)x1 Seq[GRCh37]7q33-q36.3(133,113,445_159,138,663)x3	9 26	✓
26	POC	arr[GRCh37] (19)x1	58.6	Seq[GRCh37]19q13.2(8,404,119_49,024,030)x1	40.6	✓
27	CVS	arr[GRCh38] (20)x3 arr[GRCh38](21)x3 **[Down syndrome]**	64.2 33.1	Seq[GRCh37]20p13 - q13.33(0-63,025,520)x3 Seq[GRCh37]21p13 - q21.2(0_25,800,422)x3; Seq[GRCh37]21q21.2 - q22.3(25,800,422_48,129,895)x3	63 25.8 22.3	✓
28	POC	arr[GRCh38] Xp22.33q28(251,880-156,004,066)x1 **[Turner syndrome]**	155.7	Seq[GRCh37]Xp22.33 - q28(0_149,158,438)x1 Seq[GRCh37]Xq28(:149,158,438_153,908,438)x1 Seq[GRCh37]Xq28(153,908,438_155,270,560)x1	149 4.7 1.3	✓
29	POC	arr[GRCh38] Xp22.33q28(2,785,592_155,691,858)x2 **[Klinefelter syndrome]**	155.7	Seq[GRCh37]Xp22.33 - q28(0_155,270,560)x3	155.2	✓
30	CVS	arr[GRCh38]Xp22.33q28(2,785,592_155,691,858)x2 **[Klinefelter syndrome]**	155.7	Seq[GRCh37]Xp22.33 - q28(0_155,270,560)x3	155.2	✓

CVS: Chorionic Villus Sampling; POC: Products of conception; AF: Amniotic Fluid;

Talk to the Experts:

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