Genomic Prediction
Clinical Laboratory

Samples received: 08/21/2020
Report signed: 08/29/2020
Analysis version v22.7: 06/15/2020
Clinical report v2.2.0: 05/03/2021

Case ID: 00001
Sample Type: Trophectoderm
Test Type: EPGT-A, EPGT-P 24 Chromosome Microarray

Referring Clinician

Dr. John Doe

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Processing Laboratory

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PGT-P: Caucasian Panel

Patient (or egg donor) self-reported ancestry: Caucasian
Partner (or sperm donor) self-reported ancestry: Caucasian

Report for:

Jane Doe

&

John Doe

Euploid embryos

#	PGT-A	Sex	Embryo Health Score
25	46,XY	Male	+0.85
13	46,XX	Female	+0.66
5	46,XX	Female	+0.55
14	46,XY	Male	-0.22
3	46,XX	Female	-0.73

Patient

Jane Doe

Sex: female
DOB:
Address:
Phone:
Email:

Partner

John Doe

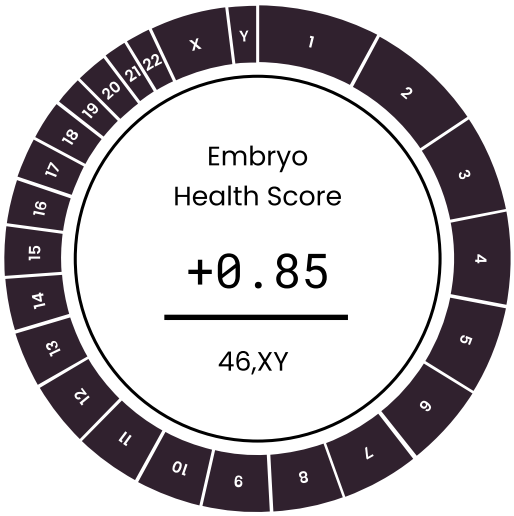
Sex: male
DOB:
Address:
Phone:
Email:

Aneuploid embryos

#	PGT-A	Sex	Embryo Health Score
1	47,XY+13	Male	-
4	47,XX+15	Female	-
6	47,XY+15	Male	-

Embryo #25

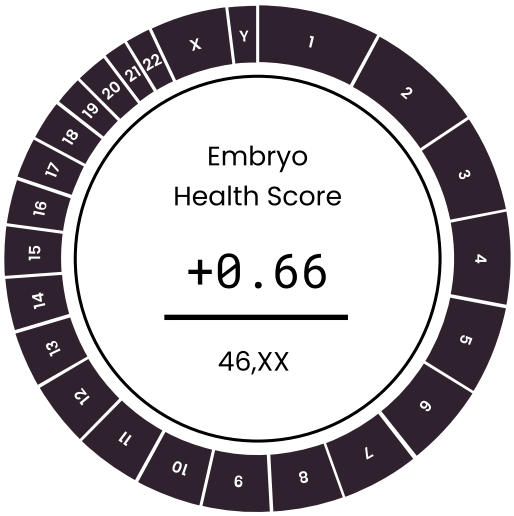
Euploid Male



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	10%	26%	0.4x	20
Hypertension	67%	74%	0.9x	41
Heart Attack	23%	19%	1.2x	60
Coronary Artery Disease	45%	41%	1.1x	55
Type 1 Diabetes	0.37%	0.53%	0.7x	35
Type 2 Diabetes	41%	41%	1x	52
Basal Cell Carcinoma	22%	31%	0.7x	35
Malignant Melanoma	3.8%	2.5%	1.5x	75
Testicular Cancer	0.40%	0.31%	1.3x	65
Prostate Cancer	23%	13%	1.5x	75
Schizophrenia	1.4%	1.7%	0.8x	40

Embryo #13

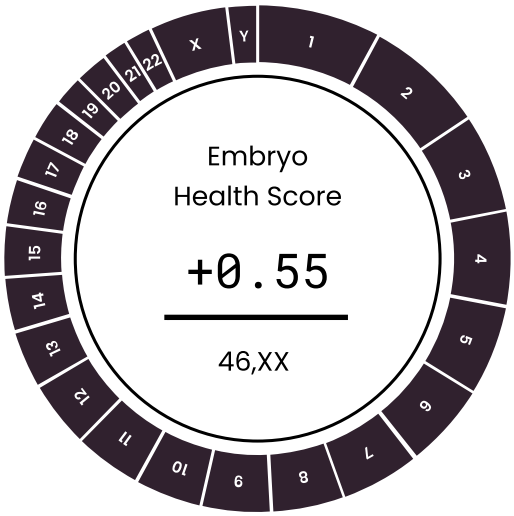
Euploid Female



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	8%	28%	0.3x	15
Hypertension	57%	82%	0.7x	35
Heart Attack	32%	18%	1.8x	88
Coronary Artery Disease	39%	28%	1.4x	69
Type 1 Diabetes	0.9%	0.53%	1.7x	73
Type 2 Diabetes	28%	46%	0.6x	30
Breast Cancer	9%	11%	0.8x	42
Basal Cell Carcinoma	34%	26%	1.3x	65
Malignant Melanoma	1.9%	1.9%	1x	50
Schizophrenia	0.96%	1.6%	0.6x	30

Embryo #5

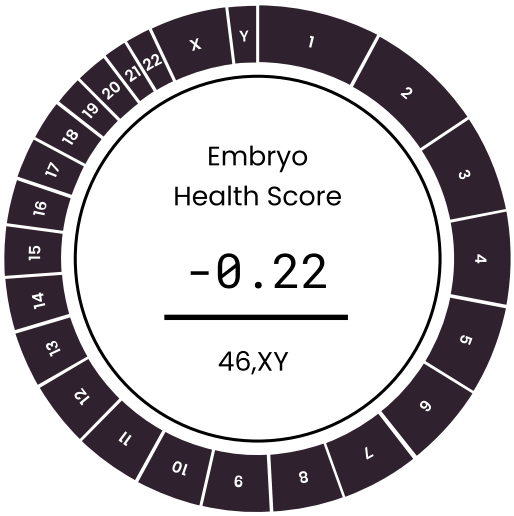
Euploid Female



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	34%	28%	1.2x	62
Hypertension	57%	82%	0.7x	35
Heart Attack	32%	18%	1.8x	88
Coronary Artery Disease	39%	28%	1.4x	69
Type 1 Diabetes	0.37%	0.53%	0.7x	35
Type 2 Diabetes	37%	46%	0.8x	40
Breast Cancer	9%	11%	0.8x	42
Basal Cell Carcinoma	10%	26%	0.4x	20
Malignant Melanoma	1.9%	1.9%	1x	50
Schizophrenia	0.96%	1.6%	0.6x	30

Embryo #14

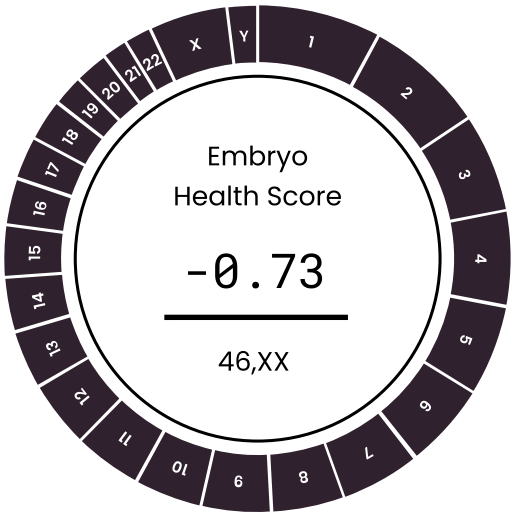
Euploid Male



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	29%	26%	1.1x	55
Hypertension	81%	74%	1.1x	59
Heart Attack	19%	19%	1.0x	50
Coronary Artery Disease	45%	41%	1.1x	55
Type 1 Diabetes	0.80%	0.53%	1.5x	70
Type 2 Diabetes	45%	41%	1.1x	55
Prostate Cancer	20%	13%	1.5x	75
Basal Cell Carcinoma	28%	31%	0.9x	45
Malignant Melanoma	4.0%	2.5%	1.6x	75
Testicular Cancer	0.59%	0.31%	1.9x	86
Schizophrenia	3%	1.7%	1.8x	88

Embryo #3

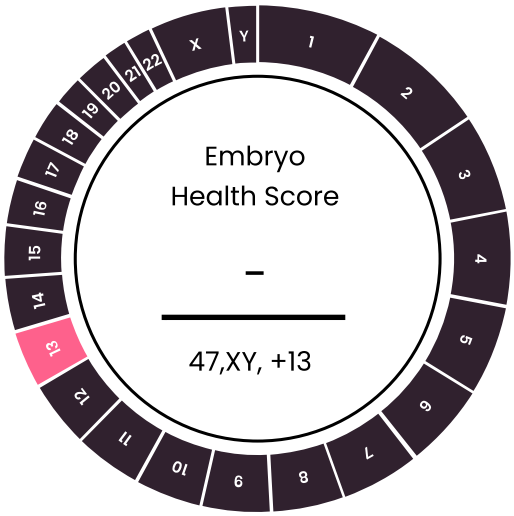
Euploid Female



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	53%	28%	1.9x	95
Hypertension	66%	82%	0.8x	40
Heart Attack	31%	18%	1.8x	77
Coronary Artery Disease	39%	28%	1.4x	69
Type 1 Diabetes	0.37%	0.53%	0.7x	35
Type 2 Diabetes	74%	46%	1.6x	70
Breast Cancer	39%	11%	2.8x	99
Basal Cell Carcinoma	55%	26%	2.1x	95
Malignant Melanoma	1.9%	1.9%	1.0x	50
Schizophrenia	4.5%	1.6%	2.8x	98

Embryo #1

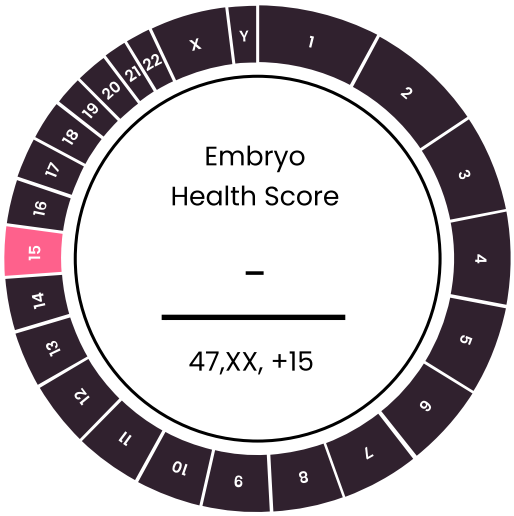
Aneuploid Male



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	-	-	-	-
Hypertension	-	-	-	-
Heart Attack	-	-	-	-
Coronary Artery Disease	-	-	-	-
Type 1 Diabetes	-	-	-	-
Type 2 Diabetes	-	-	-	-
Prostate Cancer	-	-	-	-
Basal Cell Carcinoma	-	-	-	-
Malignant Melanoma	-	-	-	-
Testicular Cancer	-	-	-	-
Schizophrenia	-	-	-	-

Embryo #4

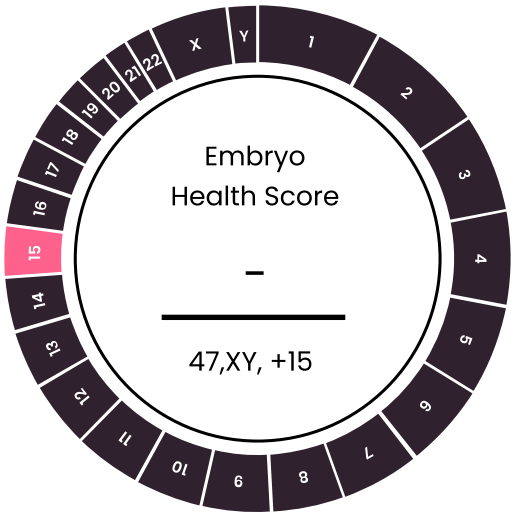
Aneuploid Female



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	-	-	-	-
Hypertension	-	-	-	-
Heart Attack	-	-	-	-
Coronary Artery Disease	-	-	-	-
Type 1 Diabetes	-	-	-	-
Type 2 Diabetes	-	-	-	-
Breast Cancer	-	-	-	-
Basal Cell Carcinoma	-	-	-	-
Malignant Melanoma	-	-	-	-
Schizophrenia	-	-	-	-

Embryo #6

Aneuploid Male



	Risk	Avg Risk	Ratio	Risk Percentile
Hypercholesterolemia	-	-	-	-
Hypertension	-	-	-	-
Heart Attack	-	-	-	-
Coronary Artery Disease	-	-	-	-
Type 1 Diabetes	-	-	-	-
Type 2 Diabetes	-	-	-	-
Prostate Cancer	-	-	-	-
Basal Cell Carcinoma	-	-	-	-
Malignant Melanoma	-	-	-	-
Testicular Cancer	-	-	-	-
Schizophrenia	-	-	-	-

PGT-P:

Result Interpretation:

PGT-A: “Euploid” indicates that the proper combination of chromosomes was detected (46,XX or 46,XY) and no whole chromosome or segmental aneuploidy >10Mb wasdetected. “Aneuploid” indicates that at least one whole chromosome or segmental (>10Mb) aneuploidy was detected. Aneuploidy is associated with an increased risk ofimplantation failure, miscarriage and medical problems including congenital anomalies and intellectual disability. In general, biopsy samples designated as “Aneuploid” are notconsidered suitable for transfer. “Inconclusive” indicates that a too high level of noise was detected in the sample to determine copy number, and a repeat biopsy isrecommended to complete the analysis. “No Amp” indicates that no DNA was detected in the sample, and a repeat biopsy is recommended to complete the analysis.

PGT-P: Each PGT-P predictor is trained on a large repository of hundreds of thousands of genomes with associated clinical phenotypes, as part of validating a polygenic riskscore (PRS) model. An “Embryo Health Score” is given for each euploid sample. This is calculated by combining polygenic scores of different disease predictors and may be used to compare overall disease risk between embryos to help decide which embryo(s) to select for transfer. An Embryo Health Score of “0” is defined as average. Embryo Health Scores greater than zero are calculated as having a lower than average disease risk and scores less than zero have a higher than average disease risk. In general, the higher the Embryo Health Score, the lower the overall disease risk. The Embryo Health Score is included when more than one disease trait is selected.

Additional data is reported as follows:
• Risk: The lifetime chance of developing a particular condition based on the polygenic risk score calculations from this embryo’s genotype.
• Average Risk: The chance of developing the condition in the general population.
• Ratio: The calculated embryo disease risk compared to the average disease risk in thegeneral population.
• Risk Percentile: The fraction of other genomes in the population which is lower than the polygenic risk scores of this embryo. In this way, a 98th percentile score is in the top2% of highest risk. Generally, a lower risk (and a lower percentile) is preferable.

Additional results are defined as the following: "Inconclusive" indicates that a too high level of noise was detected in the sample to determine polygenic risk scores/copynumber, and a repeat biopsy is recommended to complete the analysis. "No Amp" indicates that no DNA was detected in the sample, and a repeat biopsy is recommended to complete the analysis.

Accuracy:

Validation on positive controls demonstrated a diagnostic accuracy of 98.6% for PGT-A.
Validation on positive controls demonstrated a variant concordance with the controls which exceeded 99% for PGT-P genotyping. The genotyping concordance refers to theability of the test to correctly characterize genetic variants using the PGT-P genotyping platform. Demonstration of the utility of PGT-P based sibling selection to reduce therelative risk of disease has been validated. Specific risk reduction depends on disease trait. For further information, please refer to the publications below.

Data above pertains to samples created using intracytoplasmic sperm injection (ICSI). In samples created with conventional insemination, diagnostic accuracy is reduced.

Treff et al, "Preimplantation Genetic Testing for Polygenic Disease Relative Risk Reduction: Evaluation of Genomic Index Performance in 11,883 Adult Sibling Pairs," Genes 2020, 11, 648
Treff et al, "Validation of concurrent preimplantation genetic testing for polygenic and monogenic disorders, structural rearrangements, and whole and segmental chromosome aneuploidy with a single universal platform", European Journal of Medical Genetics, 2019 April 23.

Methods and Limitations

DNA is amplified from this sample of cells and evaluated by DNA microarray analysis. Copy number of each chromosome (PGT-A) is predicted by comparing the copy number from each chromosome in the embryo biopsy to the copy number observed in known normal sample. This test screens for whole chromosome aneuploidy, some forms of polyploidy such as triploidy or haploidy and some forms of tetraploidy, segmental (partial) chromosome aneuploidy of 10Mb size or larger, and uniparental isodisomy (but not heterodisomy, unless additional PGT studies requiring parental bloodsamples are being performed concurrently). This test will not detect balanced structural rearrangements including translocations and inversions or segmental aneuploidy less than 10Mb in size. There is a risk of false negative and false positive results. The most likely cause of a false negative or false positive result is mosaicism, which is present in approximately 5% of embryos. The higher the level of mosaicism, the higher chance theembryo will be called abnormal. Not all mosaic embryos will be diagnosed as abnormal. Other reasons for a false negative or false positive result include, but are not limited to: sample contamination, specimen marking issues, rare genetic variants interfering with analysis, and other technical issues. Overall, the chance for a false

negative or a false positive result unrelated to mosaicism is 2%. Diagnostic studies to confirm the karyotype in an ongoing pregnancy are recommended. Genetic counseling is recommended. Results are reported in reference to the normal human genome (hg19). Positive and negative controls performed as expected.

These results were generated using the Affymetrix UK BioBank SNP array.

PGT-P results are based upon polygenic risk scores (PRS) for each given disease trait. Polygenic studies are designed to provide a risk estimate only. This is NOT a diagnostictest. PRS are not a guarantee of the presence or absence of disease. PGT-P is designed to provide a PRS only for the specific condition(s) requested by the ordering provider. Additional PRS for other polygenic diseases are NOT included in analysis. In demographics different from the caucasian training set, sensitivity will be reduced. This is further reduced in embryos with mixed ethnic backgrounds.

Disease risk is adjusted to the sex of the embryo and the familial disease history, whereavailable. PGT-P is not a replacement for PGT-M, and is not capable of detectingmonogenic causes of diseases tested. For most polygenic conditions, disease risk will be additionally influenced by environmental, and other non-genetic factors. PGT-P doesnot address these factors as part of the analysis. Less frequently, conditions that are generally considered polygenic may be highly affected by rare, monogenic variants, which are inherited in certain families. If these variants are rare, the polygenic risk scoremay not take these into account, and the polygenic risk score accuracy may perform with severely reduced prediction of true disease risk. For cases with known monogenic variants causing a Mendelian inheritance pattern of disease, these variants should beaddressed using PGT-M. Therefore, based on these limitations, testing for the polygenicdisorder(s) in individuals conceived following PGT-P testing is recommended accordingto standard clinical criteria. In cases of aneuploidy, chromosomal abnormality interferes with polygenic disease risk calculation. PRS are therefore not reported in aneuploidembryos.

Furthermore, a history of a stem cell or bone marrow transplant in a biological parent may impact the accuracy of the results, and must be reported to Genomic PredictionClinical Laboratory. Although every effort is made to complete testing, in rare cases it may be determined that we are not able to proceed with PGT-P testing. GenomicPrediction Clinical Laboratory will notify the associated clinician as soon as possible in these cases.

Following conception, there is a 3-5% chance in every pregnancy of genetic and/or non-genetic medical problems, including birth defects and intellectual disability. PGT does not reduce this risk, nor does this screening eliminate the need for prenatal screening/testing as recommended during pregnancy.

Although rare, it is possible for samples to be damaged by human error or lost/destroyed due to weather, transit issues or other problems beyond the control of Genomic Prediction Clinical Laboratory. Sample contamination from biological (such as DNA) or non-biological sources may potentially lead to an inaccurate result.

This test was developed, and its performance characteristics determined by Genomic Prediction Clinical Laboratory. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA).

Nathan R. Treff, PhD, HCLD (ABB)
Clinical Laboratory Director
Genomic Prediction Clinical Laboratory

04/08/2021

CAP: 8488628, CLIA: 31D2152380, New Jersey DOH: 00056206