



## Test Information Sheet

### *FISHonChipDx and FISH tests for microdeletion/microduplication syndromes and subtelomeric/pericentromeric copy number analysis*

**Purpose:** GeneDx offers FISHonChipDx as an economical microarray-based replacement test for subtelomere FISH panel testing and also to evaluate for 65 microdeletion and microduplication syndromes. Positive findings on the FISHonChipDx array are confirmed by FISH to determine the nature of a genomic imbalance. This array also provides size information for any identified deletions or duplications since it has a resolution of 50 kb in targeted regions. GeneDx also offers individual FISH assays for the genomic disorders listed below, and also for chromosomal rearrangements that extend to the telomere (terminal rearrangements), for subtelomeric imbalances, and for pericentromeric imbalances (supernumerary marker chromosomes).

#### **Genomic regions assayed by FISHonChipDx array and by individual FISH tests:**

All subtelomeric and pericentromeric regions		Cornelia DeLange syndrome	5p13.1
1p36 deletion syndrome	1p36	Cowden syndrome	10q23.31
1q21 microdeletion (TAR)	1q21.1	Cri-du-chat syndrome	5p15.2
1q21 distal microdeletion	1q21.1	DiGeorge/Velocardiofacial syndrome	22q11.2
1q41-1q42 microdeletion	1q41-1q42	Gonadal dysgenesis	Yp11.3
2p15 microdeletion	2p15	Greig cephalopolysyndactyly	7p14.1
2q32.2-2q33 microdeletion	2q32.2-2q33	Hemophilia A	Xq28
2q37 microdeletion	2q37	Hemophilia B	Xq27.1
3q29 microdeletion	3q29	Hereditary neuropathy with pressure palsies	17p11.2
6p25 microdeletion	6p25	Kallmann syndrome	Xp22.31
7q11 Williams region duplication	7q11.32	Langer-Giedion syndrome	8q24.11
8p23 microdeletion	8p23.1	Leri-Weill dyschondrosteosis	Xp22.33
9q34 subtelomeric deletion	9q34	MECP2 duplication MR syndrome	Xq28
10q22-10q23 deletion	10q22-10q23	Miller-Dieker syndrome	17p13.3
12q24 microdeletion	12q24.2	Nabbus mask-like facial syndrome	8q21.3-8q22.1
14q11.2 microdeletion	14q11.2	Neurofibromatosis type 1	17q11.2
15q13.3 microdeletion	15q13.1-15q13.3	Neurofibromatosis type 2	22q12.2
15q24.2 microdeletion	15q24.2-15q24.3	Pelizaeus-Merzbacher syndrome	Xq22.2
16p11.2 microdeletion/duplication	16p11.2	Polycystic kidney disease	16p13.3
16p11.2-16p12.2 microdeletion	16p11.2-p12.2	Potocki-Lupski syndrome	17p11.2
16p13.1 microdeletion/duplication	16p13.1	Potocki-Shaffer syndrome	11p11.2
17q12 microdeletion	17q12	Prader-Willi syndrome	15q11.2-15q13.1
17q21 microdeletion/duplication	17q21	Retinoblastoma	13q14.2
22q11.2 microdeletion/duplication	22q11.2	Rett syndrome	Xq28
22q11.2 distal microdeletion	22q11.2	Rubenstein-Taybi syndrome	16p13.3
22q13.3 microdeletion	22q13.3	Saethre-Chotzen syndrome	7p21.1
Alagille syndrome	20p12.2	Smith-Magenis syndrome	17p11.2
Alpha thalassemia / mental retardation	16p13.3	Sotos syndrome	5q35.3
Angelman syndrome	15q11.2-15q13.1	Steroid sulfatase deficiency	Xp22.31
Basal cell nevus syndrome	9q22.32	Tuberous sclerosis type 2	16p13.3
Beckwith-Wiedeman syndrome	11p15.5	WAGR syndrome	11p13
Cat-eye syndrome	22q11.21	Williams-Beuren syndrome	7q11.23
Charcot-Marie tooth disease	17p11.2	Wilms tumor	11p13
CHARGE syndrome	8q12.2	Wolf-Hirschhorn syndrome	4p16.3

#### **Reasons for referral:**

1. Suspected common microdeletion/duplication syndrome (FISHonChipDx or FISH)
2. Replacement test for subtelomere FISH panel (FISHonChipDx)
3. First-pass genome scan in patients with mental retardation and a normal karyotype (FISHonChipDx)
4. Confirmation of certain karyotypes with terminal rearrangements (FISHonChipDx or FISH)
5. Mosaicism for a genomic imbalance (FISH)

### **Limitations of FISHonChipDx:**

1. Cannot provide fine-resolution breakpoint mapping for unbalanced chromosomal rearrangements
2. Cannot detect small (<1 Mb) rearrangements in genomic regions that are not specifically targeted
3. Cannot determine the nature of some chromosomal imbalances (e.g., translocations, insertions)
4. Cannot detect balanced rearrangements
5. Cannot detect polyploidy

**Test method:** FISHonChipDx is a custom-designed microarray containing 15,000 oligonucleotides (60-mers) specifically placed about 50 kb apart across 3 Mb of each subtelomeric region and at loci associated with 65 common or novel microdeletion/microduplication syndromes. The rest of the genome is covered with probes spaced roughly 400-500 kb apart. FISH analysis is based on the hybridization of a fluorescently labeled probe to metaphase spreads and interphase nuclei prepared from cell cultures derived from peripheral blood, amniotic fluid, or a chorionic villus sample. FISH probes have a specific sequence that is complementary to a particular region of the genome. The presence, absence, amplification, or transposition of the targeted region is analyzed with a fluorescent microscope. Additionally, FISH methodology can be used to test for suspected low-level mosaicism by increasing the number of cells scored.

**Confirmations:** Positive results from the FISHonChipDx assay are confirmed with individual FISH probes. Confirmations in the proband are performed free of charge; parental samples can be tested upon request at a nominal cost.

**Test sensitivity:** FISHonChipDx is designed for evaluating disorders with a high frequency of large deletions or duplications rather than single-gene mutations and is expected to be highly sensitive for detecting these large rearrangements. FISHonChipDx and FISH typically have a technical sensitivity close to 100% for genomic disorders (~90% FISH sensitivity for microduplications). FISH probes may hybridize to non-targeted sequences in <2% of cells. With an analytical sensitivity of 99%, FISH detection of a non-mosaic normal or abnormal cell line can be ruled out with 95% confidence by scoring 50 nuclei (American College of Medical Genetics, Standards and Guidelines, E10.5.8). This laboratory ensures the specificity of each lot of FISH probe.

### **Exclusions:**

FISH and FISHonChipDx testing does not include investigation of interstitial regions, except those related to the listed microdeletion/duplication syndromes. For small interstitial imbalances, the whole-genome GenomeDx array is appropriate or, if a specific region is under suspicion, the CopyDx (qPCR) technology should be requested. FISH may not detect abnormalities that involve a small part of a targeted locus.

### **Specimen Requirements and Shipping/Handling:**

- **Blood:** A single tube with 2-5ml whole blood in EDTA and a second tube of 2-5ml whole blood in heparin. If ordering FISH only, a sample of blood in heparin is sufficient (no EDTA blood needed). Ship overnight at ambient temperature, using a cool pack in hot weather. Do not refrigerate blood samples.
- **Tissue cultures:** Two T25 flasks of cultured cells at 75% confluency. Ship overnight at ambient temperature, using a cool pack in hot weather. Retain backup cultures.
- **Extracted DNA:** High-grade DNA preparation is requested. We require a **minimum total amount of DNA of 5 micrograms**, with a **concentration of at least 50 ng/ul** (50 nanograms per microliter).

### **Required Forms:**

- Sample submission form (Molecular Cytogenetics form) – complete all pages, including
- Payment options form or institutional billing instructions

**Prices and turn-around-time (fees are subject to change without notice):**

Test #337: FISHonChipDx targeted array for microdeletion/microduplication syndromes and subtelomeric/pericentromeric analysis	\$650	Approx. 2 weeks
Test #336: FISH, one probe for hybridization	\$555	Approx. 2 weeks

**CPT codes for FISHonChipDx array CGH analysis in a new patient - All codes and units apply:**

Test #337: FISHonChipDx targeted array for microdeletion/microduplication syndromes and  
subtelomeric/pericentromeric analysis

88230 x 2 unit = \$ 160  
88271 x 2 units = \$ 60  
88283 x 2 units = \$ 95  
88273 x 4 units = \$ 180  
88291 x 2 units = \$ 60

**TOTAL                    \$650**

**CPT codes for FISH analysis of a single genomic locus in a new patient - All codes and units apply:**

Test #336: FISH for a single locus

88230 x 1 unit = \$ 160  
88271 x 2 units = \$ 60  
88283 x 1 units = \$ 95  
88273 x 4 units = \$ 180  
88291 x 2 units = \$ 60

**TOTAL                    \$555**

**Possible ICD9 Codes:**    Clinical information can vary.