TABLES

Supplemental Table I: Primers for real-time quantitative PCR analysis of the *HEY2* region

Primer Pair Name (Location hg38)	Forward Primer	Reverse Primer
LOC643623 (chr6:125,708,092-125,708,284)	TGAAAGAGGATGGGATCTGG	ATGCCATATGGTTTCCCTGA
3' LOC643623 (chr6:125,721,737-125,721,953)	GGCAAAACATGGGATCATTT	GGTGACTGGAATGGGTATGC
HEY2 A (chr6: 125,757,085-125,757,293)	TGGGGCTCCAATTCTGTTAG	AAGATTTCACATTTTGGTCCTCA
HEY2 B (chr6: 125,757,294- 125,757,525)	TCCATGAATACCTCTTCTTCAGG	TCCTAAAGCTAAAATTCCAACGA
HEY2 C (chr6:125,758,691- 125758913)	TCCAACTCATGTGACAGAGACA	GCCACTCACATGTGTGACAA
5' NCOA7 (chr6:125,780,731-125,780,899)	TCTGTCACGCGGATGTTAAG	CGTGCTATGAGGCTACGTGA
NCOA7 A (chr6: 125,795,569- 125,795,732)	ATTCCCACTGCCTCTGTTTG	TGTGCAGATTCCTTCCTGTG
NCOA7 B (chr6: 125,797,562- 125,797,768)	GGCCTCGCTACACAAACATT	GCTGTAAACACCTGCAACCA

Supplemental Table II: Published 6q duplications involving *HEY2*

Reference	Chromosomal Anomalies and Interval (hg38)	Clinical Summary
Molecularly Defined Cases of *HEY2* Duplication		
This report	12kb-84kb gain Minimum interval chr6:125,749,186-125,761,299 Maximum interval chr6:125,713,307-125,797,245 20-40kb intronic loss Minimum interval chr2:50,832,013-50,852,148 Maximum interval chr2:50,822,062-50,862,325	3-year-old Hispanic female; tetralogy of Fallot, infundibular and valvular pulmonary stenosis, hypotonia, lower extremity weakness, fine motor delay and speech delay, Chiari I malformation
[Thorsson et al. 2014]	~14.3 Mb gain chr6:113,244,335-127,583,668 ~0.53 Mb loss previously associated with autism and developmental delay[†] chr16:29,646,068-30,181,301	12-year-old male; referred to Signature Genomics for clinical CNV analysis due to "developmental delay, abnormal karyotype"
[Thorsson et al. 2014]	~74 Mb gain chr6:96,782,686-170,592,191 ~55 Mb deletion chrX:100608892-155998655	1-month-old female; unbalanced translocation, referred to Signature Genomics for clinical CNV analysis due to "dysmorphic features"
Cytogenetically Defined Cases of Isolated 6q Duplications		
[Chen et al. 1976], Patient 1	46,XY,der(5)ins(5;6)(q33;q15q27)mat	20-month-old male; small for gestational age, failure to thrive, gross motor delay, language delay
[Chen et al. 1976], Patient 2	46,XY,der(5)ins(5;6)(q33;q15q27)mat	19-year-old male; small for gestational age, joint contractures, scoliosis, gross motor delay, language delay, seizures, cognitive deficits
[Valerio et al. 2006]	46,XX,der(12)ins(12;6)(q22;q21q22)mat	17-month-old female; normal development, dysmorphic features
[Zneimer et al. 1998]	46,XX,dup(6)(q21q23)de novo	5-year-old female; small for gestational age, umbilical hernia, transient insulin dependent diabetes until 7 months of age, gross motor delay, cognitive delay, structurally normal heart with cardiomegaly of unknown etiology, dysmorphic features
[Pratt et al. 1998], Patient 1	46,XY,dup(6)(q21q23.3)de novo	8-month-old male; small for gestational age, bilateral club foot, right ventricular hypertrophy, thickened tricuspid valve, gross motor delay, dysmorphic features
[Pratt et al. 1998], Patient 2	46,XX,dup(6)(q21.15q23.3)de novo	11-year-old female; speech delay, cognitive deficits, ventricular septal defect, pulmonic valvular stenosis

[†] [Shinawi et al. 2010]

Chen H, Tyrkus M, Cohen F, Woolley PV, Jr., Mayeda K, Bhogaonker A, Espirtu CE, Simpson W. 1976. Familial partial trisomy 6q syndromes resulting from inherited ins (5;6) (q33;q15q27). Clinical genetics 9(6):631-637.

Pratt VM, Roberson JR, Weiss L, Van Dyke DL. 1998. Duplication 6q21q23 in two unrelated patients. American journal of medical genetics 80(2):112-114.

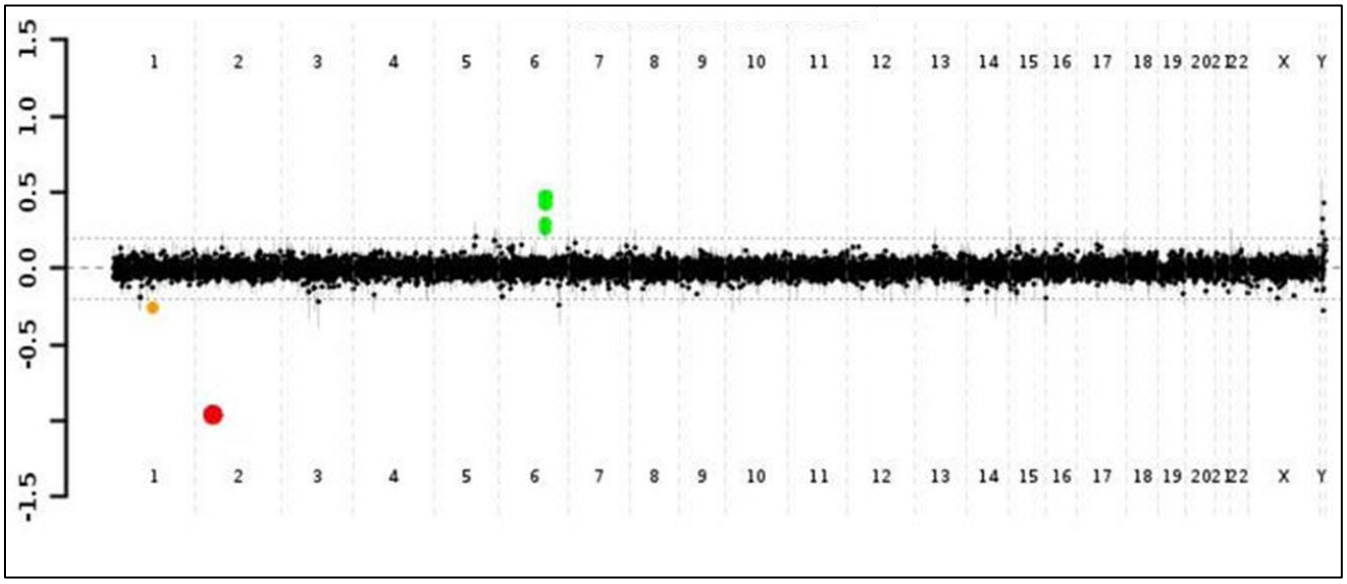
Shinawi M, Liu P, Kang SH, Shen J, Belmont JW, Scott DA, Probst FJ, Craigen WJ, Graham BH, Pursley A, Clark G, Lee J, Proud M, Stocco A, Rodriguez DL, Kozel BA, Sparagana S, Roeder ER, McGrew SG, Kurczynski TW, Allison LJ, Amato S, Savage S, Patel A, Stankiewicz P, Beaudet AL, Cheung SW, Lupski JR. 2010. Recurrent reciprocal 16p11.2 rearrangements associated with global developmental delay, behavioural problems, dysmorphism, epilepsy, and abnormal head size. Journal of medical genetics 47(5):332-341.

Thorsson T, Russell WW, El-Kashlan N, Soemedi R, Levine J, Geisler SB, Ackley T, Tomita-Mitchell A, Rosenfeld JA, Topf A, Tayeh M, Goodship J, Innis JW, Keavney B, Russell MW. 2014. Chromosomal Imbalances in Patients with Congenital Cardiac Defects: A Meta-analysis Reveals Novel Potential Critical Regions Involved in Heart Development. Congenital heart disease.

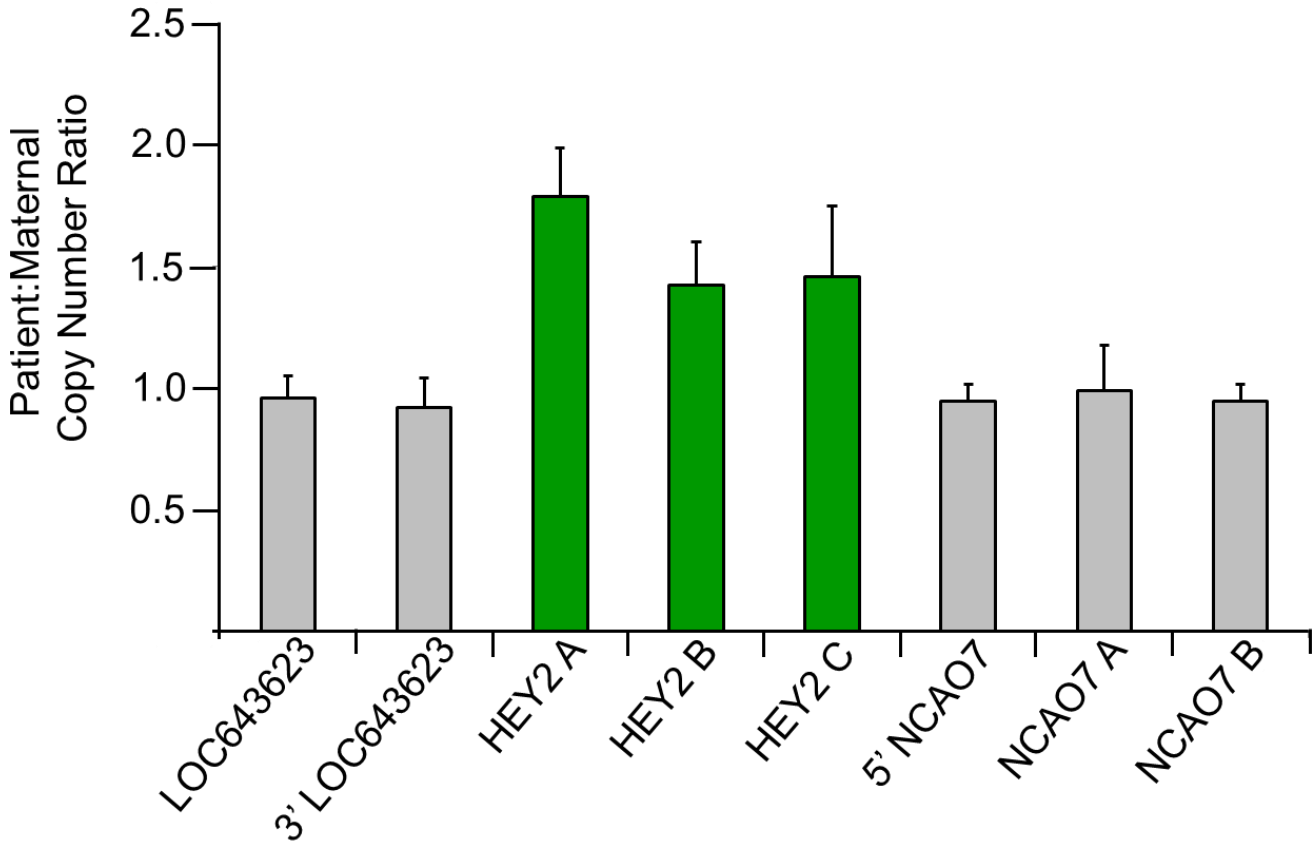
Valerio D, Di Domenico A, Felicetti M, La Boccetta A, Ferrara C, Antonio N, Borrelli AL. 2006. Prenatal diagnosis of a partial 6q trisomy: a case report. Prenatal diagnosis 26(10):917-919.

Zneimer SM, Ziel B, Bachman R. 1998. Partial trisomy of chromosome 6q: an interstitial duplication of the long arm. American journal of medical genetics 80(2):133-135.

FIGURES



Supplemental Figure I. Array-based copy number variation (CNV) data plotted on a $\log_2$ scale shows the duplication of *HEY2* on chromosome 6 (green dots) and the deletion of *NRXN1* intronic sequence on chromosome 2 (red dot).



Supplemental Figure II. Real-time quantitative PCR analysis revealed a normal copy number ratio between the patient and her mother (patient:maternal) for probes within and 3' of *LOC643623* and within and 5' of *NCAO7*. In contrast all probes within *HEY2* showed an increased patient:maternal copy number ratio. This suggests that the patient carries a single gene duplication of *HEY2* that does not include *LOC643623* or *NCAO7*.