# Autism multiplex family with 16p11.2p12.2 microduplication syndrome in monozygotic twins and distal 16p11.2 deletion in their brother 

Anne-Claude Tabet, Marion Pilorge, Richard Delorme, Frédérique Amsellem, Jean-Marc Pinard, Marion Leboyer, Alain Verloes, Brigitte Benzacken, Catalina Betancur

## Supplementary Material

## Supplementary Note



Inset of Figure 2.
The segmental duplications in the 16p11.2-p12.2 region have been assigned the alphanumeric IDs A1-A2, B1B3, C1-C2, D1-D6, E1-E3 and F1-F3. Segmental duplications A1 and A2 are 110 kb in size, are in the same orientation and share $>98 \%$ sequence identity. The distal (telomeric) breakpoint of the duplication in the twins (Patients 2 and 3 ) is located at A1, whereas the proximal (centromeric) breakpoint of the deletion in their nontwin brother (Patient 1) and the father is located at A2. Segmental duplications B1-B3 are $\sim 55 \mathrm{~kb}$ in size, are oriented in the same way and share $>99 \%$ sequence identity. As A1 and A2, segmental duplications B1 and B2 are located at the distal breakpoint of the duplication and the proximal breakpoint of the deletion, respectively, whereas B3 is located at the proximal breakpoint of the duplication. Segmental duplications C1 and C2 are $\sim 42$ kb in size, are oriented in the same way and share $>98 \%$ sequence identity. The proximal and distal breakpoints of the duplication are located at segmental duplications C1 and C2, respectively. Segmental duplications D1-D6 are 15-20 kb in size, are oriented in the same way and share $>98 \%$ sequence identity. D1D6 are present at all distal and proximal breakpoints of the deletion and the duplication. Segmental duplications E1-E3 are 15 kb in size, are in the same orientation and share $>98 \%$ sequence identity. Segmental duplications F1-F3 are 7.6 kb in size and share $>98 \%$ sequence identity.

Supplementary Table 1. Psychiatric, cognitive and developmental evaluations of the siblings

|  | Patient 1 | Patient 2 <br> (MZ twin) | Patient 3 (MZ twin) |
| :---: | :---: | :---: | :---: |
| Sex | Male | Male | Male |
| Copy number imbalance | 16p11.2 deletion (28.40-29.25 Mb) | 16p11.2p12.2 dupliication (21.28-30.23 Mb) | 16p11.2p12.2 duplication (21.28-30.23 Mb) |
| Inheritance | Paternal | de novo | de novo |
| Clinical and research diagnosis | Autism | Autism | Autism |
| ADI-R |  |  |  |
| Age at evaluation | 5 y 1 mo | 3 y 2 mo | 3 y 2 mo |
| Social (cutoff 10) | 17 | 23 | 22 |
| Communication (cutoff 7) | 14 (non verbal) | 14 (non verbal) | 13 (non verbal) |
| Repetitive behavior (cutoff 3) | 7 | 4 | 3 |
| Onset (cutoff 1) | 5 | 4 | 4 |
| ADI-R diagnosis | Autism | Autism | Autism |
| ADOS (module 1) |  |  |  |
| Age at evaluation | - | 18 y 5 mo | 18 y 5 mo |
| Communication (cutoff 4) | - | 6 | 6 |
| Social Interaction (cutoff 7) | - | 14 | 13 |
| Total (cutoff 12) | - | 20 | 19 |
| Play | - | 4 | 4 |
| Interests and Behavior | - | 8 | 8 |
| ADOS diagnosis | - | Autism | Autism |
| IQ measure |  |  |  |
| Scale | WISC-III | RCPM | RCPM |
| Age at evaluation | 16 y | 18 y 4 mo | 18 y 4 mo |
| Full scale IQ | 47 | <1st centile | <1st centile |
| Verbal IQ | 50 | - | - |
| Performance IQ | 50 | - | - |
| VABS $\\|^{1}$ |  |  |  |
| Age at evaluation | 5 y 2 mo | 18 y 5 mo | 18 y 5 mo |
| Communication | 13 | 11 | 9 |
| Daily living | 20 | 23 | 21 |
| Socialization | 15 | 1 | 1 |
| Maladaptive behaviors | 38 | 20 | 23 |
| CARS |  |  |  |
| Age at evaluation | - | 10 y 3 mo | 10 y 3 mo |
| Composite score | - | 37 | 38 |
| Severity | - | Mild-moderate autism | Severe autism |

${ }^{1}$ Age equivalent scores, expressed in months. Abbreviations: CARS, Childhood Autism Rating Scale; MZ, monozygotic; RCPM, Raven's Colored Progressive Matrices; VABS II, Vineland Adaptive Behavior Scales, second edition; WISC-III, Wechsler Intelligence Scale for Children, third edition

Supplementary Table 2. Other CNVs identified in the family

| Subject | Chr | Start ${ }^{1}$ | End ${ }^{1}$ | Size | Algorithms | CNV | Inheritance | DGV ${ }^{3}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Patient 1 | 2 | 4191253 | 4199818 | 8565 | CNV partition | deletion | paternal | yes |
|  | 3 | 74185282 | 74280502 | 95220 | CNV partition, PennCNV | deletion | maternal | partial |
|  | 4 | 69097539 | 69163188 | 65649 | CNV partition | deletion | maternal ${ }^{2}$ | yes |
|  | 6 | 79029649 | 79090197 | 60548 | CNV partition | deletion | paternal | yes |
|  | 6 | 170222030 | 170223555 | 1525 | CNV partition | deletion | paternal ${ }^{2}$ | yes |
|  | 8 | 39356825 | 39497557 | 140732 | CNV partition, PennCNV | deletion | paternal | yes |
|  | 9 | 370095 | 400312 | 30217 | CNV partition, PennCNV | duplication | maternal | yes |
|  | 11 | 55124465 | 55149014 | 24549 | CNV partition | deletion | paternal ${ }^{2}$ | yes |
|  | 11 | 80663196 | 80692622 | 29426 | CNV partition, PennCNV | deletion | maternal | yes |
|  | 12 | 7891603 | 8014573 | 122970 | CNV partition, PennCNV | deletion | paternal | yes |
|  | 13 | 56659471 | 56665094 | 5623 | CNV partition | deletion | paternal ${ }^{2}$ | yes |
| Patient 2 | 3 | 164004033 | 164085280 | 81247 | CNV partition | deletion | maternal ${ }^{2}$ | yes |
|  | 4 | 69097539 | 69163188 | 65649 | CNV partition | deletion | maternal ${ }^{2}$ | yes |
|  | 4 | 161271979 | 161291569 | 19590 | CNV partition | deletion | de novo? | yes |
|  | 6 | 67075448 | 67104015 | 28567 | CNV partition | deletion | paternal | yes |
|  | 6 | 79029649 | 79090197 | 60548 | CNV partition | deletion | paternal | yes |
|  | 6 | 170222030 | 170223555 | 1525 | CNV partition | deletion | paternal ${ }^{2}$ | yes |
|  | 8 | 39356825 | 39497557 | 140732 | CNV partition, PennCNV | deletion | paternal | yes |
|  | 11 | 55124465 | 55149014 | 24549 | CNV partition | deletion | paternal ${ }^{2}$ | yes |
|  | 11 | 80663196 | 80692622 | 29426 | CNV partition, PennCNV | deletion | maternal | yes |
|  | 12 | 7891603 | 8014573 | 122970 | CNV partition, PennCNV | deletion | paternal | yes |
|  | 14 | 18531500 | 19387587 | 856087 | CNV partition, PennCNV | duplication | paternal | yes |
|  | 19 | 20413668 | 20507068 | 93400 | CNV partition | deletion | maternal ${ }^{2}$ | yes |
| Father | 1 | 103941535 | 104107839 | 166304 | CNV partition, PennCNV | deletion |  | yes |
|  | 2 | 4191253 | 4199818 | 8565 | CNV partition | deletion |  | yes |
|  | 4 | 115398433 | 115401739 | 3306 | CNV partition | deletion |  | yes |
|  | 6 | 67075448 | 67104015 | 28567 | none (manual inspection) | deletion |  | yes |
|  | 6 | 79029649 | 79090197 | 60548 | CNV partition | deletion |  | yes |
|  | 6 | 170222362 | 170223555 | 1193 | CNV partition | deletion |  | yes |
|  | 8 | 39356825 | 39497557 | 140732 | CNV partition, PennCNV | deletion |  | yes |
|  | 10 | 66981540 | 66983475 | 1935 | CNV partition | deletion |  | yes |
|  | 11 | 55124465 | 55171592 | 47127 | CNV partition | deletion |  | yes |
|  | 12 | 7891603 | 8014573 | 122970 | CNV partition, PennCNV | deletion |  | yes |
|  | 13 | 56646795 | 56665094 | 18299 | CNV partition | deletion |  | yes |
|  | 14 | 18531500 | 19387587 | 856087 | none (manual inspection) | duplication |  | yes |
|  | 16 | 81590327 | 81706426 | 116099 | CNV partition, PennCNV | deletion |  | no |
|  | 18 | 36515599 | 36519446 | 3847 | CNV partition | deletion |  | yes |
| Mother | 2 | 82794772 | 82891026 | 96254 | CNV partition | deletion |  | yes |
|  | 2 | 159667833 | 159679609 | 11776 | CNV partition | deletion |  | partial |
|  | 3 | 74185282 | 74280502 | 95220 | CNV partition, PennCNV | deletion |  | partial |
|  | 3 | 133194645 | 133195707 | 1062 | CNV partition | deletion |  | yes |
|  | 3 | 164004033 | 164101579 | 97546 | CNV partition | deletion |  | yes |
|  | 4 | 69064675 | 69163188 | 98513 | CNV partition | deletion |  | yes |
|  | 4 | 70164518 | 70246877 | 82359 | CNV partition | deletion |  | yes |
|  | 5 | 148738220 | 149321472 | 583252 | CNV partition, PennCNV | deletion |  | partial |
|  | 5 | 150167998 | 150194892 | 26894 | CNV partition | deletion |  | yes |
|  | 9 | 370095 | 400312 | 30217 | CNV partition, PennCNV | duplication |  | yes |
|  | 9 | 43515795 | 43720352 | 204557 | CNV partition | deletion |  | yes |
|  | 11 | 80663196 | 80692622 | 29426 | none (manual inspection) | deletion |  | yes |
|  | 15 | 19777876 | 19967366 | 189490 | CNV partition | deletion |  | yes |
|  | 18 | 36514913 | 36519446 | 4533 | CNV partition | deletion |  | yes |
|  | 19 | 20404485 | 20507068 | 102583 | CNV partition, PennCNV | deletion |  | yes |
|  | 19 | 53898415 | 53900677 | 2262 | CNV partition | deletion |  | yes |

HumanCNV370-Duo BeadChip (Illumina) data were analyzed using CNV partition and PennCNV. In addition, the results were inspected manually to determine inheritance of genomic variants in the children. Because none of the CNVs detected in Patients 1 and 2 appeared to be rare, no attempt was made to validate these findings with an independent method. ${ }^{1}$ Genomic coordinates correspond to the hg18 genome assembly (Build 36). ${ }^{2}$ Apparently inherited CNV with one breakpoint differing from the parent. ${ }^{3}$ DGV, Database of Genomic Variants (http://projects.tcag.ca/variation/).

Supplementary Table 3. Clinical features of individuals with duplications of the 16p11.2p12 region

|  | Engelen et al. (2002) <br> Patient 1 (mother) | Engelen et al. (2002), Finelli et al. (2004) Patient 2 (daughter) | Finelli et al. (2004) <br> Patient 1 | $\begin{aligned} & \text { Ballif et al. (2007) } \\ & \text { Patient 5 } \end{aligned}$ | Present study <br> Patient 2 (MZ twin) | Present study <br> Patient 3 (MZ twin) |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Duplicated region | 16p11.2p12.2 (21.24-29.41 Mb) | 16p11.2p12.2 (21.24-29.41 Mb) | 16p11.2p12.2 (21.24-29.41 Mb) | $\operatorname{trp}(16)(\mathrm{p} 11.2 \mathrm{p} 12.1) \mathrm{dup}(16)(\mathrm{p} 12$. $1 \mathrm{p} 12.2)(21.4-28.2 \mathrm{Mb})(5.7 \mathrm{Mb}$ trp; 1.1 Mb dup) | 16p11.2p12.2 (21.28-30.23 Mb) | 16p11.2p12.2 (21.28-30.23 Mb) |
| Molecular studies | FISH (WCP16 and specific BAC probes) | FISH (WCP16 and specific BAC probes) | FISH (WCP16 and specific BAC probes) | array-CGH, SNP array 250K | SNP array 370K | SNP array 370K |
| Inheritance | unknown | inherited from mother (Patient 1) | mother's karyotype normal; father's karyotype not available | de novo | de novo | de novo |
| Gender | F | F | M | F | M | M |
| Age | 40 y | 5 y | 25 y | 10 y 11 mo | 17 y 6 mo | 18 y 4 mo |
| Weight | NA | 16.3 kg ( $50^{\text {th }}$ centile) | 42 kg ( $<3^{\text {rd }}$ centile) | -2 SD | 49 kg (-2 SD) | 55 kg (-1 SD) |
| Stature | 158 cm ( $<3^{\text {rd }}$ centile) | 103 cm ( $3^{\text {rd }}$ centile -2 cm ) | 151 cm ( $<3^{\text {rd }}$ centile) | -3 to -4 SD, growth hormone deficiency | 173 cm (normal range) | 172 cm (normal range) |
| HC | 52.5 cm (<3 ${ }^{\text {rd }}$ centile) | 49 cm ( $3^{\text {rd }}$ centile) | $54 \mathrm{~cm}\left(25^{\text {th }}\right.$ centile) | -1 SD | 55 cm (-1 SD) | $55 \mathrm{~cm}(-1$ SD) |
| Development | learning difficulties | normal in the first year of life | severe neurodevelopmental delay | significant neurodevelopmental delay | normal development followed by regression at 26 mo | normal development followed by regression at 24 mo |
| IQ | IQ 83 (PIQ 64, VIQ 100, WAIS) | IQ 80 | $25<1 Q<39$ at $3 y$ | IQ 42 (WISC-IV at age 9) | severe ID | severe ID |
| ASD | autism | ASD | autism | - | autism | autism |
| Language | automatic speech, echolalia | poor expressive language, echolalia | first words at 10 y , no functional language | $12^{\text {th }}$ percentile for reading, $<1^{\text {st }}$ percentile for spelling and math | language regression at 26 mo ; non verbal | language regression at 24 mo ; non verbal |
| Other behavior | ADHD, borderline psychotic symptoms, flat affect, anxiety disorder, obsessive-compulsive symptoms | stubbornness | never achieved continence, needs help in eating, dressing and self care; hyperactive, poor attention | friendly and talkative, ADHD, anxiety and nervousness with nail biting and skin picking | not fully toilet trained, hyperactivity, short and agitated sleep | not fully toilet trained, hyperactivity, aggressive behavior, self-injurious behavior, severe sleep disturbance |
| Dysmorphism |  |  |  |  |  |  |
|  | - | - | asymmetric, squared, bitemporal constriction, sparse hair | round face with full cheeks | triangular face, broad forehead, prominent orbital ridge | triangular face, broad forehead, prominent orbital ridge |
| eyes | - | upslanting palpebral fissures | hypertelorism | narrow and slightly short palpebral fissures, relative hypertelorism, ptosis, strabismus, hyperopia | deep set eyes, upslanting palpebral fissures, thick upslant eyebrows, myopia, strabismus | deep set eyes, upslanting palpebral fissures, thick upslant eyebrows, myopia, strabismus |
| nose | - | - | broad nasal bridge, broad nasal tip, prominent columella | short nose, wide nasal bridge and round tip, anteverted nares | large, prominent nasal bridge, wide, bulbous tip, anteverted nares | large, prominent nasal bridge, wide, bulbous tip, anteverted nares |
| mouth and jaw | - | - | large mouth, thick lips, large irregular teeth, short philtrum | wide mouth, high-arched palate, thin upper lip, long philtrum, retrognathia | everted lower lip, tented philtrum wide cupid's bow, overbite, retrognathia with marked chin | everted lower lip, tented philtrum wide cupid's bow, overbite, retrognathia with marked chin |
| ears | - | - | long | low and posteriorly rotated, hyperacusis | backward tilted | backward tilted |
| Other malformations | - | - | bilateral club foot | bridged palmar creases, short fifth fingers, prominent finger tip pads, bilateral hallux valgus, minimal 2,3 toe syndactyly | ventricular septal defect, slender habitus, sternum deformity, mild scoliosis, cubitus valgus, long fingers and toes, bilateral single palmar creases and sandal gap | no heart defect, slender habitus, sternum deformity, mild scoliosis, cubitus valgus, long fingers and toes, bilateral single palmar creases and sandal gap |
| Infections | - | - | recurrent bronchitis, otitis, and gastroenteritis in childhood | - | recurrent otitis, nose and throat infections in childhood | recurrent otitis, nose and throat infections in childhood |
| Neurological | distal coreoathetotic movements, cervical dystonia | - | walked unassisted at 8 y , ataxic gait | hypotonia | hyporeflexia, no motor deficit | absent reflexes, no motor deficit |
| Epilepsy | - | - | yes | - | - | - |
| Brain imaging | brain CT normal | NA | MRI: slight ventricular dilatation, moderate diffuse cortical atrophy | NA | MRI: white matter hyperintensities, moderate cortical atrophy and thin corpus callosum | MRI: white matter hyperintensities, moderate cortical atrophy and thin corpus callosum |

[^0]
## Supplementary Table 4. Genes within the 220-kb minimal region of overlap of distal 16p11.2 deletions (28.73-28.95 Mb)

| Symbol | Name | Coordinates (hg 18) | Function | Associated disease |
| :---: | :---: | :---: | :---: | :---: |
| ATXN2L | Ataxin 2 related protein | $\begin{aligned} & 28741915- \\ & 28756059 \end{aligned}$ | ATXN2L is a member of the spinocerebellar ataxia family, suggested to be a component of the cytokine signaling system | No associated disease |
| TUFM | Tu translation elongation factor, mitochondrial | $\begin{aligned} & 28761233- \\ & 28765230 \end{aligned}$ | TUFM participates in protein translation in mitochondria | An homozygous missense mutation in TUFM was described in a baby with mitochondrial encephalopathy (combined oxidative phosphorylation deficiency 4, OMIM 610678) |
| SH2B1 | SH2B adaptor protein 1 | $\begin{aligned} & 28782725- \\ & 28793027 \end{aligned}$ | SH2B1 is an adaptor protein involved in leptin, insulin, cytokine and growth factor receptor signaling. In addition to its role in central nervous system-mediated obesity, SH2B1 facilitates neurite outgrowth | Severe early-onset obesity (OMIM 613444) |
| ATP2A1 | ATPase, Ca++ transporting, cardiac muscle, fast twitch 1 | $\begin{aligned} & 28797310- \\ & 28823331 \end{aligned}$ | ATP2A1 is a magnesium-dependent enzyme involved in muscular excitation and contraction | Autosomal recessive Brody myopathy (OMIM 601003), characterized by impaired muscular relaxation during exercise |
| RABEP2 | RAB GTPase binding effector protein 2 | $\begin{aligned} & 28823243- \\ & 28844033 \end{aligned}$ | RABEP2 plays a role in membrane trafficking, regulating endosomal vesicle docking and fusion | No associated disease |
| CD19 | CD19 antigen | $\begin{aligned} & 28850761- \\ & 28858164 \end{aligned}$ | CD19 is a cell surface molecule that regulates the antigen receptor-dependent stimulation of $B$ lymphocytes | Antibody-deficiency syndrome (OMIM 613493), autosomal recessive |
| NFATC2IP | Nuclear factor of activated T-cells | $\begin{aligned} & 28869819- \\ & 28885268 \end{aligned}$ | NFATC2IP plays a role in the inducible expression of cytokine genes in $T$ cells | No associated disease |
| SPNS1 | Spinster homolog 1 | $\begin{aligned} & 28893650- \\ & 28904339 \end{aligned}$ | SPNS1 appears to be involved in programmed cell death. The homologue of SPNS1, SPNS2, encodes a transporter of the sphingolipid metabolite sphingosine 1-phosphate (S1P), which plays a central role in neural, cardiovascular, and immunological development and function | No associated disease |
| LAT | Linker for activation of T cells | $\begin{aligned} & 28903648- \\ & 28909605 \end{aligned}$ | LAT is a transmembrane protein that when phosphorylated leads to the recruitment of multiple signaling molecules implicated in T cell activation | No associated disease |

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Supplementary Table 5. B allele frequency and genotypes of the short arm of chromosome 16

| SNP | Position | Father |  | Mother |  | Patient 1 |  | Patient 2 (twin) |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  | B all freq | Genotype | B all freq | Genotype | B all freq | Genotype | B all freq | Genotype |
| rs11865131 | 103667 | 0.5 | AB | 0.9 | BB | 0.5 | AB | 0.5 | AB |
| rs11248914 | 233563 | 0.5 | AB | 1.0 | BB | 0.5 | $A B$ | 0.5 | AB |
| rs9921222 | 315783 | 0.5 | AB | 1.0 | BB | 0.4 | $A B$ | 0.5 | AB |
| rs11645697 | 435663 | 0.6 | AB | 0.0 | AA | 0.0 | AA | 0.0 | AA |
| rs12446663 | 5906038 | 0.5 | AB | 1.0 | BB | 1.0 | BB | 1.0 | BB |
| rs6500827 | 6764824 | 0.5 | AB | 1.0 | BB | 0.5 | $A B$ | 0.5 | AB |
| rs4261521 | 7872048 | 0.6 | $A B$ | 0.0 | AA | 0.4 | AB | 0.5 | $A B$ |
| rs1058967 | 8854537 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 0.6 | AB |
| rs8064140 | 9576189 | 0.6 | AB | 1.0 | BB | 0.5 | $A B$ | 0.5 | AB |
| rs6498229 | 11607016 | 0.5 | AB | 0.0 | AA | 0.5 | $A B$ | 0.5 | AB |
| rs1794302 | 12498592 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 0.5 | AB |
| rs1438701 | 13173810 | 0.6 | AB | 1.0 | BB | 0.5 | $A B$ | 0.5 | AB |
| rs7405176 | 14365847 | 0.6 | AB | 0.0 | AA | 0.6 | $A B$ | 0.6 | AB |
| rs4780577 | 15675498 | 0.5 | AB | 0.0 | AA | 0.5 | $A B$ | 0.5 | AB |
| rs2100401 | 16867138 | 0.4 | $A B$ | 0.0 | AA | 0.0 | AA | 0.0 | AA |
| rs4781952 | 17616369 | 0.6 | AB | 0.5 | AB | 0.5 | AB | 0.0 | AA |
| rs9937539 | 18941493 | 0.5 | AB | 1.0 | BB | 1.0 | BB | 1.0 | BB |
| rs739565 | 19624006 | 0.5 | $A B$ | 1.0 | BB | 1.0 | BB | 1.0 | BB |
| rs2214195 | 20406898 | 0.5 | $A B$ | 0.0 | AA | 0.0 | AA | 0.0 | AA |
| rs858205 | 20979000 | 0.6 | $A B$ | 1.0 | BB | 0.6 | AB | 0.6 | AB |
| rs9933675 | 21161736 | 0.6 | $A B$ | 0.0 | AA | 0.0 | AA | 0.0 | AA |
| rs2238478 | 21190256 | 0.5 | $A B$ | 0.0 | AA | 0.5 | $A B$ | 0.5 | AB |
| rs226035 | 21202238 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 0.5 | AB |
| rs194548 | 21515973 | 0.5 | $A B$ | 0.5 | AB | 1.0 | BB | 0.7 | $A B$ |
| rs226005 | 21528048 | 0.5 | $A B$ | 1.0 | BB | 0.5 | AB | 0.3 | $A B$ |
| rs238547 | 23267700 | 0.6 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 0.3 | $A B$ |
| rs8048821 | 23886863 | 0.5 | $A B$ | 0.0 | AA | 0.5 | $A B$ | 0.6 | $A B$ |
| rs4787697 | 25111249 | 0.6 | AB | 0.0 | AA | 0.5 | $A B$ | 0.7 | $A B$ |
| rs4592663 | 25810187 | 0.5 | $A B$ | 0.5 | AB | 0.0 | AA | 0.3 | $A B$ |
| rs321441 | 26611178 | 0.5 | $A B$ | 0.0 | AA | 0.4 | $A B$ | 0.6 | $A B$ |
| rs10400960 | 26738119 | 0.5 | AB | 1.0 | BB | 0.5 | $A B$ | 0.4 | $A B$ |
| rs17200687 | 26743810 | 0.5 | $A B$ | 0.0 | AA | 0.0 | AA | 0.0 | AA |
| rs4787393 | 26857335 | 0.6 | AB | 1.0 | BB | 0.6 | AB | 1.0 | BB |
| rs4238945 | 26882508 | 0.6 | $A B$ | 0.0 | AA | 0.5 | AB | 0.0 | AA |
| rs7206078 | 26955737 | 0.6 | $A B$ | 1.0 | BB | 1.0 | BB | 0.3 | AB |
| rs205432 | 27992496 | 0.6 | $A B$ | 0.0 | AA | 0.5 | AB | 0.0 | AA |
| rs205355 | 28012030 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 1.0 | BB |
| rs4075049 | 28150790 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 1.0 | BB |
| rs2650492 | 28240912 | 0.6 | AB | 1.0 | BB | 0.5 | AB | 1.0 | BB |
| rs1064886 | 28396413 | 1.0 | BB | 1.0 | BB | 1.0 | BB | 1.0 | BB |
| rs26528 | 28425210 | 1.0 | BB | 0.0 | AA | 0.0 | AA | 0.7 | AB |
| rs153107 | 28432806 | 1.0 | BB | 0.0 | AA | 0.0 | AA | 0.7 | AB |
| rs151228 | 28470527 | 1.0 | BB | 0.0 | AA | 0.0 | AA | 0.6 | $A B$ |
| rs151230 | 28490716 | 0.0 | AA | 1.0 | BB | 1.0 | BB | 0.3 | $A B$ |
| rs7201929 | 28779467 | 0.0 | AA | 1.0 | BB | 1.0 | BB | 0.3 | $A B$ |
| rs4072401 | 28844776 | 1.0 | BB | 0.0 | AA | 0.0 | AA | 0.7 | AB |
| rs7184953 | 29223380 | 1.0 | BB | 1.0 | BB | 1.0 | BB | 1.0 | BB |
| rs4787478 | 29256578 | 0.4 | AB | 0.6 | AB | 1.0 | BB | 0.0 | AA |
| rs8054172 | 29563365 | 0.5 | $A B$ | 0.0 | AA | 0.6 | AB | 0.0 | AA |
| rs11150564 | 29574237 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 1.0 | BB |
| rs7202714 | 30085308 | 0.5 | AB | 1.0 | BB | 0.5 | AB | 1.0 | BB |
| rs9938125 | 30195224 | 1.0 | BB | 1.0 | BB | 1.0 | BB | 1.0 | BB |
| rs4238961 | 30287987 | 0.6 | AB | 0.0 | AA | 0.6 | AB | 0.0 | AA |
| rs1064524 | 30400324 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 1.0 | BB |
| rs8058961 | 30716564 | 0.5 | $A B$ | 0.0 | AA | 0.6 | AB | 0.0 | AA |
| rs8048583 | 31187037 | 0.5 | $A B$ | 1.0 | BB | 1.0 | BB | 0.5 | AB |
| rs12927233 | 32045466 | 0.6 | $A B$ | 0.0 | AA | 0.5 | AB | 0.0 | AA |
| rs8047974 | 34079200 | 0.5 | $A B$ | 1.0 | BB | 0.5 | $A B$ | 1.0 | BB |
| Centromere |  |  |  |  |  |  |  |  |  |

Informative SNPs were selected to illustrate the rearrangements and the parental origin. The 16 p 11.2 p 12.2 region duplicated in Patient 2 (and in his twin brother, Patient 3) is highlighted in blue, the 16 p 11.2 region deleted in Patient 1 and his father is highlighted in red. Informative SNPs for which Patient 1 and Patient 2 share the same paternal allele are shown in blue font, those for which they inherited a different allele are shown in red font. A crossing-over in the father's germline inherited by Patient 1 occurred between 26743810 bp and 26857335 bp. Non-informative SNPs at the start and end of the duplication and the deletion are shown in black. Genomic coordinates correspond to NCBI Build 36 (hg18).


[^0]:     SD, standard deviation; VIQ, verbal IQ; WCP16, whole chromosome painting 16

