Supplementary Materials

The role of alpha-synuclein and other Parkinson’s genes in neurodevelopmental and neurodegenerative disorders

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References

Figure S1: Comparative genomic hybridization and optical mapping detect size and orientation of *SNCA* copy number variants

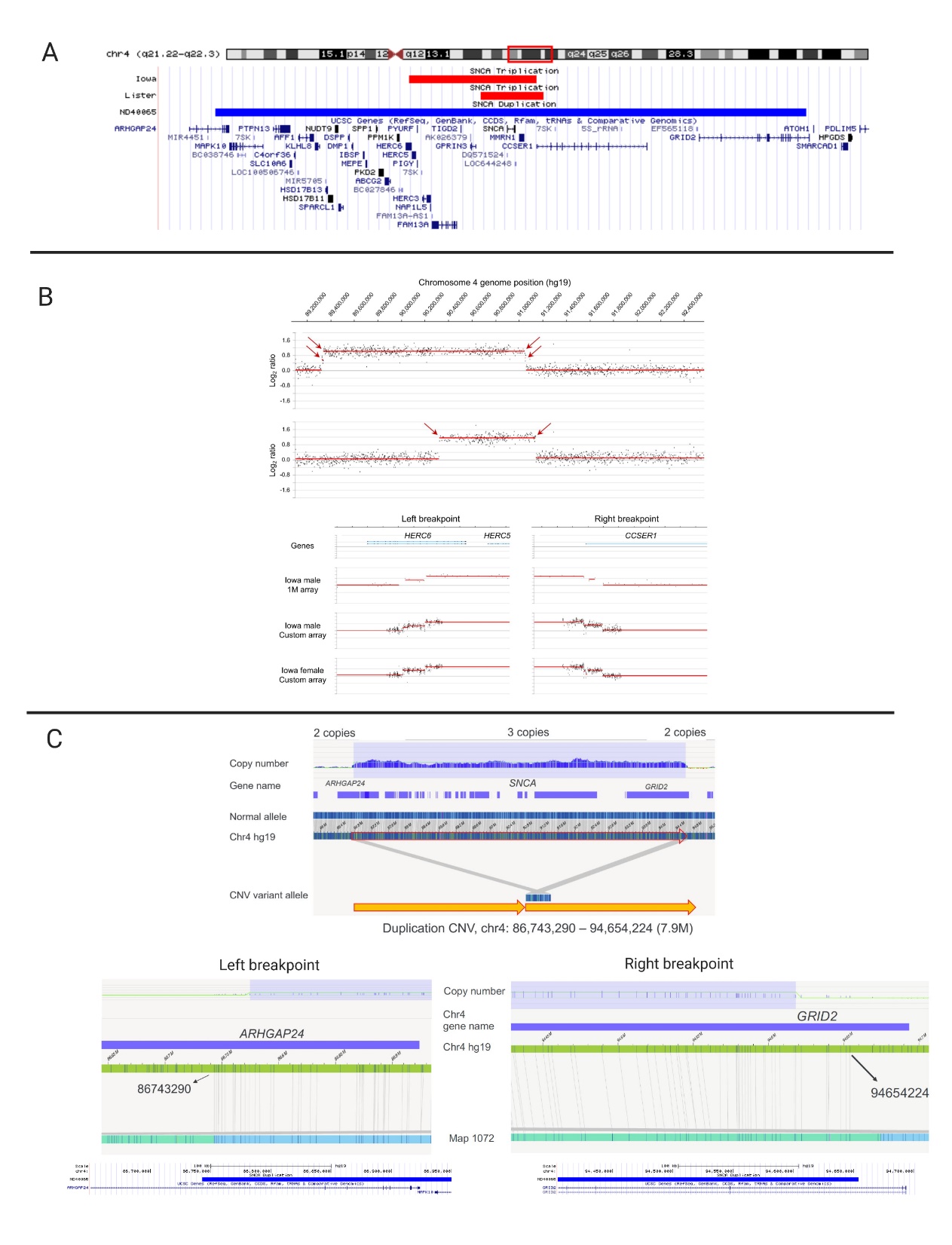
Figure S1: A. UCSC genome browser custom tracks (genome build GRCh37/hg19, February 2009) for two SNCA triplication cases (red) and one SNCA duplication (blue). B. Illustration of comparative genomic hybridization (CGH) for two SNCA triplication cases. The lower panel of B shows the left and right breakpoint with a ‘step’ that indicated two different recombination events [1]. C. Optical mapping using Saphyr Genome Imaging (Bionano) allows for CNV sizing (resolution 500bp) and orientation of CNVs. Case is from NINDS Cell repository (Cell line ID: ND40065) and presents with a 7.9Mb duplication disrupting the Rho GTPase-activating protein 24 (ARHGAP24) and Glutamate receptor delta-2 (GRID2) gene. (GRID2) is also implicated in autism (https://gene.sfari.org/database/human-gene/GRID2 ; [2].

Table S1: Partial exonic PARK2 CNV deletion/duplication coordinates for UCSC genome browser custom tracks (genome build GRCh37/hg19, February 2009)

In this Table S1, we listed genome coordinates for Figure 1. Case data were analyzed from Autism Genome Project (AGP) [3].

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Count | Type | Exon | Size (bp) | Chrom. | Start | Stop | ID |
| 1 | Deletion | 8/9 | 197,372 | chr6 | 161892760 | 162090131 | 6016\_3 |
| 2 | Deletion | 5/6 | 265,769 | chr6 | 162275484 | 162541252 | 14103\_1780 |
| 3 | Duplication | 3/4 | 274,643 | chr6 | 162495289 | 162769931 | 20163\_1672002 |
| 4 | Duplication | 2/3/4 | 408,545 | chr6 | 162495289 | 162903833 | 13100\_1173 |
| 5 | Duplication | 2/3/4 | 389,593 | chr6 | 162511301 | 162900893 | 4156\_1 |
| 6 | Duplication | 2/3/4 | 351,673 | chr6 | 162552161 | 162903833 | 6362\_3 |
| 7 | Deletion | 3/4 | 226,621 | chr6 | 162580056 | 162806676 | 5326\_3 |
| 8 | Deletion | 4 | 41,060 | chr6 | 162588879 | 162629938 | 8612\_201 |
| 9 | Deletion | 3/4 | 160,236 | chr6 | 162601734 | 162761969 | 2267\_1 |
| 10 | Duplication | 3/4 | 212,453 | chr6 | 162622524 | 162834976 | 14220\_3530 |
| 11 | Duplication | 3/4 | 212,453 | chr6 | 162622524 | 162834976 | 6347\_3 |
| 12 | Duplication | 3 | 192,238 | chr6 | 162637688 | 162829925 | 13119\_1364 |
| 13 | Duplication | 3 | 185,689 | chr6 | 162644237 | 162829925 | 5335\_3 |
| 14 | Duplication | 2/3 | 190,740 | chr6 | 162644237 | 162834976 | 5431\_4 |
| 15 | Deletion | 3 | 143,617 | chr6 | 162666349 | 162809965 | 3382\_5 |

|  |
| --- |
| Genome Browser Custom Tracks (GRCh37/hg19) |
| browser position chr6:161756581-163162564 |
| track name="PARK2 - 6q26" description="PARK2 - 6q26" visibility=2 itemRgb="On" |
| chr6 161892760 162090131 6016\_3 0 . 161892760 162090131 34,139,34 |
| chr6 162275484 162541252 14103\_1780 0 . 162275484 162541252 34,139,34 |
| chr6 162495289 162769931 20163\_1672002 0 . 162495289 162769931 65,105,225 |
| chr6 162495289 162903833 13100\_1173 0 . 162495289 162903833 65,105,225 |
| chr6 162511301 162900893 4156\_1 0 . 162511301 162900893 65,105,225 |
| chr6 162552161 162903833 6362\_3 0 . 162552161 162903833 65,105,225 |
| chr6 162580056 162806676 5326\_3 0 . 162580056 162806676 34,139,34 |
| chr6 162588879 162629938 8612\_201 0 . 162588879 162629938 34,139,34 |
| chr6 162601734 162761969 2267\_1 0 . 162601734 162761969 34,139,34 |
| chr6 162622524 162834976 14220\_3530 0 . 162622524 162834976 65,105,225 |
| chr6 162622524 162834976 6347\_3 0 . 162622524 162834976 65,105,225 |
| chr6 162637688 162829925 13119\_1364 0 . 162637688 162829925 65,105,225 |
| chr6 162644237 162829925 5335\_3 0 . 162644237 162829925 65,105,225 |
| chr6 162644237 162834976 5431\_4 0 . 162644237 162834976 65,105,225 |
| chr6 162666349 162809965 3382\_5 0 . 162666349 162809965 34,139,34 |

Table S2: 22q11.21 deletions coordinates for UCSC genome browser custom tracks (genome build NCBI36/hg18, March 2006)

In this Table S2, we listed genome coordinates for Figure 2.

As a reference, we included the classic 22q11.21 deletion region (Velocardiofacial/DiGeorge syndrome) (<https://decipher.sanger.ac.uk/syndrome/16#genotype/cnv/21/browser>) and the recently characterized critical region for a higher rate of autism (LCR-A to LCR-B) [4].

Case data were analyzed from Autism Genome Project (AGP) [3]. For cases with identical deletions, we grouped cases into groups G1 to G9 (column ID/Group ID).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Count | Type | Size (bp) | Chrom. | Start | Stop | ID/Group ID |
| 1 | Deletion | 2,578,170 | chr22 | 17241748 | 19819918 | 3183\_7 |
| 2 | Deletion | 2,537,993 | chr22 | 17257787 | 19795780 | 17015\_1 |
| 3 | Deletion | 327,829 | chr22 | 17060279 | 17388108 | 6246\_4 |
| 4 | Deletion | 301,170 | chr22 | 18724527 | 19025697 | 4074\_1 |
| 5 | Deletion | 294,246 | chr22 | 18719310 | 19013556 | 2288\_1 |
| 6 | Deletion | 225,582 | chr22 | 17020300 | 17245882 | 13112\_1293 |
| 7 | Deletion | 216,802 | chr22 | 18794653 | 19011455 | 5264\_4 |
| 8 | Deletion | 210,493 | chr22 | 18815204 | 19025697 | 5382\_3 |
| 9 | Deletion | 206,237 | chr22 | 17051550 | 17257787 | G1 |
| 10 | Deletion | 206,237 | chr22 | 17051550 | 17257787 |
| 11 | Deletion | 206,237 | chr22 | 17051550 | 17257787 |
| 12 | Deletion | 206,237 | chr22 | 17051550 | 17257787 |
| 13 | Deletion | 206,237 | chr22 | 17051550 | 17257787 |
| 14 | Deletion | 197,508 | chr22 | 17060279 | 17257787 | G2 |
| 15 | Deletion | 197,508 | chr22 | 17060279 | 17257787 |
| 16 | Deletion | 194,332 | chr22 | 17051550 | 17245882 | G3 |
| 17 | Deletion | 194,332 | chr22 | 17051550 | 17245882 |
| 18 | Deletion | 194,332 | chr22 | 17051550 | 17245882 |
| 19 | Deletion | 194,332 | chr22 | 17051550 | 17245882 |
| 20 | Deletion | 194,332 | chr22 | 17051550 | 17245882 |
| 21 | Deletion | 185,603 | chr22 | 17060279 | 17245882 | G4 |
| 22 | Deletion | 185,603 | chr22 | 17060279 | 17245882 |
| 23 | Deletion | 185,603 | chr22 | 17060279 | 17245882 |
| 24 | Deletion | 185,603 | chr22 | 17060279 | 17245882 |
| 25 | Deletion | 185,603 | chr22 | 17060279 | 17245882 |
| 26 | Deletion | 185,603 | chr22 | 17060279 | 17245882 |
| 27 | Deletion | 185,603 | chr22 | 17060279 | 17245882 |
| 28 | Deletion | 171,395 | chr22 | 17074487 | 17245882 | 5264\_4 |
| 29 | Deletion | 153,319 | chr22 | 17092563 | 17245882 | 5516\_3 |
| 30 | Deletion | 150,936 | chr22 | 17051550 | 17202486 | G5 |
| 31 | Deletion | 150,936 | chr22 | 17051550 | 17202486 |
| 32 | Deletion | 149,365 | chr22 | 17108422 | 17257787 | G6 |
| 33 | Deletion | 149,365 | chr22 | 17108422 | 17257787 |
| 34 | Deletion | 146,360 | chr22 | 17241748 | 17388108 | G7 |
| 35 | Deletion | 146,360 | chr22 | 17241748 | 17388108 |
| 36 | Deletion | 146,360 | chr22 | 17241748 | 17388108 |
| 37 | Deletion | 142,226 | chr22 | 17245882 | 17388108 | 5265\_5 |
| 38 | Deletion | 142,207 | chr22 | 17060279 | 17202486 | 5388\_3 |
| 39 | Deletion | 138,876 | chr22 | 17257787 | 17396663 | 13071\_843 |
| 40 | Deletion | 137,460 | chr22 | 17108422 | 17245882 | 3029\_4 |
| 41 | Deletion | 132,045 | chr22 | 17051550 | 17183595 | 4220\_1 |
| 42 | Deletion | 130,321 | chr22 | 17257787 | 17388108 | G8 |
| 43 | Deletion | 130,321 | chr22 | 17257787 | 17388108 |
| 44 | Deletion | 130,321 | chr22 | 17257787 | 17388108 |
| 45 | Deletion | 130,321 | chr22 | 17257787 | 17388108 |
| 46 | Deletion | 130,321 | chr22 | 17257787 | 17388108 |
| 47 | Deletion | 123,316 | chr22 | 17060279 | 17183595 | 4222\_1 |
| 48 | Deletion | 120,248 | chr22 | 18751164 | 18871412 | 5432\_3 |
| 49 | Deletion | 110,386 | chr22 | 18569077 | 18679463 | G9 |
| 50 | Deletion | 110,386 | chr22 | 18569077 | 18679463 |
| 51 | Deletion | 90,508 | chr22 | 18575591 | 18666099 | 4208\_1 |
| 52 | Deletion | 46,573 | chr22 | 18317638 | 18364211 | 4288\_1 |
| 53 | Deletion | 44,554 | chr22 | 18274542 | 18319096 | 8703\_201 |
| 54 | Deletion | 29,885 | chr22 | 18409878 | 18439763 | 20033\_1227001 |
| 55 | Deletion | 14,003 | chr22 | 18323020 | 18337023 | 1240\_3 |
| 56 | Deletion | 10,514 | chr22 | 17742142 | 17752656 | 14388\_4970 |
| 57 | Deletion | 6,252 | chr22 | 18166460 | 18172712 | 14327\_4410 |

|  |  |
| --- | --- |
| **Count** | **Genome Browser Custom Tracks (GRCh37/hg19)** |
|  | browser position chr22:16309492-21775472 |
| track name="22q11.21 deletions" description="22q11.21 deletions" visibility=2 itemRgb="On" |
| 1 | chr22 17241748 19819918 3183\_7 0 . 17241748 19819918 34,139,34 |
| 2 | chr22 17257787 19795780 17015\_1 0 . 17257787 19795780 34,139,34 |
| 3 | chr22 17060279 17388108 6246\_4 0 . 17060279 17388108 34,139,34 |
| 4 | chr22 18724527 19025697 4074\_1 0 . 18724527 19025697 34,139,34 |
| 5 | chr22 18719310 19013556 2288\_1 0 . 18719310 19013556 34,139,34 |
| 6 | chr22 17020300 17245882 13112\_1293 0 . 17020300 17245882 34,139,34 |
| 7 | chr22 18794653 19011455 5264\_4 0 . 18794653 19011455 34,139,34 |
| 8 | chr22 18815204 19025697 5382\_3 0 . 18815204 19025697 34,139,34 |
| 9 | chr22 17051550 17257787 G1 0 . 17051550 17257787 34,139,34 |
| 10 | chr22 17060279 17257787 G2 0 . 17060279 17257787 34,139,34 |
| 11 | chr22 17051550 17245882 G3 0 . 17051550 17245882 34,139,34 |
| 12 | chr22 17060279 17245882 G4 0 . 17060279 17245882 34,139,34 |
| 13 | chr22 17074487 17245882 5264\_4 0 . 17074487 17245882 34,139,34 |
| 14 | chr22 17092563 17245882 5516\_3 0 . 17092563 17245882 34,139,34 |
| 15 | chr22 17051550 17202486 G5 0 . 17051550 17202486 34,139,34 |
| 16 | chr22 17108422 17257787 G6 0 . 17108422 17257787 34,139,34 |
| 17 | chr22 17241748 17388108 G7 0 . 17241748 17388108 34,139,34 |
| 18 | chr22 17245882 17388108 5265\_5 0 . 17245882 17388108 34,139,34 |
| 19 | chr22 17060279 17202486 5388\_3 0 . 17060279 17202486 34,139,34 |
| 20 | chr22 17257787 17396663 13071\_843 0 . 17257787 17396663 34,139,34 |
| 21 | chr22 17108422 17245882 3029\_4 0 . 17108422 17245882 34,139,34 |
| 22 | chr22 17051550 17183595 4220\_1 0 . 17051550 17183595 34,139,34 |
| 23 | chr22 17257787 17388108 G8 0 . 17257787 17388108 34,139,34 |
| 24 | chr22 17060279 17183595 4222\_1 0 . 17060279 17183595 34,139,34 |
| 25 | chr22 18751164 18871412 5432\_3 0 . 18751164 18871412 34,139,34 |
| 26 | chr22 18569077 18679463 G9 0 . 18569077 18679463 34,139,34 |
| 27 | chr22 18575591 18666099 4208\_1 0 . 18575591 18666099 34,139,34 |
| 28 | chr22 18317638 18364211 4288\_1 0 . 18317638 18364211 34,139,34 |
| 29 | chr22 18274542 18319096 8703\_201 0 . 18274542 18319096 34,139,34 |
| 30 | chr22 18409878 18439763 20033\_1227001 0 . 18409878 18439763 34,139,34 |
| 31 | chr22 18323020 18337023 1240\_3 0 . 18323020 18337023 34,139,34 |
| 32 | chr22 17742142 17752656 14388\_4970 0 . 17742142 17752656 34,139,34 |
| 33 | chr22 18166460 18172712 14327\_4410 0 . 18166460 18172712 34,139,34 |
|  |  |
|  | **LCR regions** |
|  | browser position chr22:16309492-21775472 |
| track name="LCR" description="Low Copy Number Repeat Sequences" visibility=2 itemRgb="On" |
| 1 | chr22 17276972 18600656 LCR-A\_LCR-B 0 . 17276972 18600656 0,0,0 |
| 2 | chr22 17276972 19712953 Classic\_Deletion 0 . 17276972 19712953 0,0,0 |

Table S3.

Table S3A: 4q22.1deletions (<10MB) coordinates for UCSC genome browser custom tracks (genome build GRCh37/hg19, February 2009)

Genome coordinates for Figure 3A/B are listed in this Table S3A/B.

Cases with neurodevelopmental delay, ASD, and/or other morphological phenotypes:

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| No. | Type | Size (bp) | Chrom. | Start | Stop | ID | Phenotype | Reference |
| 1 | Deletion | 67,193 | chr4 | 90791345 | 90858538 | 3521\_3 | N/A | [3] |
| 2 | Duplication | 177,945 | chr4 | 90527679 | 90705624 | CV251304 | Abnormality of the face, Intellectual disability | DECIPHER |
| 3 | Deletion | 754,432 | chr4 | 90458652 | 91213084 | VCV000146171 | Developmental delay AND/OR other significant developmental or morphological phenotypes | ClinVar |
| 4 | Deletion | 754,432 | chr4 | 90458652 | 91213084 | nsv529189 | Developmental delay AND/OR other significant developmental or morphological phenotypes | [5] |
| 5 | Deletion | 884,797 | chr4 | 90272120 | 91156917 | nsv949454 | NA | [6] |
| 6 | Deletion | 996,780 | chr4 | 90168566 | 91165346 | nsv1323206 | NA | [7] |
| 7 | Deletion | 999,006 | chr4 | 90167781 | 91166787 | nsv1012406 | NA | [8] |
| 8 | Duplication | 4,065,651 | chr4 | 88265504 | 92331155 | CV342092 | Duane anomaly, Growth delay, Hemivertebrae, Horseshoe kidney, Vertebral segmentation defect | DECIPHER |
| 9 | Deletion | 5,756,752 | chr4 | 89571443 | 95328195 | CV337659 | Global developmental delay, Joint hypermobility, pes planus | DECIPHER |
| 10 | Deletion | 6,251,589 | chr4 | 88295927 | 94547516 | CV339430 | Agenesis of corpus callosum, porencephalic cyst | DECIPHER |
| 11 | Deletion | 6,966,581 | chr4 | 90005204 | 96971785 | VCV000562945 | N/A | ClinVar |
| 12 | Deletion | 7,231,379 | chr4 | 85839771 | 93071150 | VCV000396146 | Developmental delay AND/OR other significant developmental or morphological phenotypes | ClinVar |
| 13 | Deletion | 8,344,282 | chr4 | 89891197 | 98235479 | VCV000443904 | Oculomotor apraxia Impaired social interactions  Delayed speech and language development Delayed gross motor development | ClinVar |
| 14 | Deletion | 8,523,827 | chr4 | 86370518 | 94894345 | VCV000152923 | Developmental delay AND/OR other significant developmental or morphological phenotypes | ClinVar |
| 15 | Deletion | 9,004,389 | chr4 | 82210925 | 91215314 | CV994\_2 | Broad palm, Intellectual disability, Narrow nasal bridge, Short foot, Short palm, Short philtrum, Short stature, Tapered finger, Thin lower lip vermilion | DECIPHER |

DECIPHER: <https://decipher.sanger.ac.uk/>

ClinVar: <https://www.ncbi.nlm.nih.gov/clinvar/>

|  |  |
| --- | --- |
| Count | Genome Browser Custom Tracks (GRCh37/hg19) |
|  | browser position chr4:81985657-98524436 |
| track name="SNCA - 4q22.1" description="SNCA CNV cases" visibility=2 itemRgb="On" |
| 1 | chr4 90791345 90858538 3521\_3 0 . 90791345 90858538 65,105,225 |
| 2 | chr4 90527679 90705624 CV251304 0 . 90527679 90705624 65,105,225 |
| 3 | chr4 90458652 91213084 VCV000146171 0 . 90458652 91213084 34,139,34 |
| 4 | chr4 90458652 91213084 nsv529189 0 . 90458652 91213084 34,139,34 |
| 5 | chr4 90272120 91156917 nsv949454 0 . 90272120 91156917 34,139,34 |
| 6 | chr4 90168566 91165346 nsv1323206 0 . 90168566 91165346 34,139,34 |
| 7 | chr4 90167781 91166787 nsv1012406 0 . 90167781 91166787 34,139,34 |
| 8 | chr4 88265504 92331155 CV342092 0 . 88265504 92331155 65,105,225 |
| 9 | chr4 89571443 95328195 CV337659 0 . 89571443 95328195 34,139,34 |
| 10 | chr4 88295927 94547516 CV339430 0 . 88295927 94547516 34,139,34 |
| 11 | chr4 90005204 96971785 VCV000562945 0 . 90005204 96971785 34,139,34 |
| 12 | chr4 85839771 93071150 VCV000396146 0 . 85839771 93071150 34,139,34 |
| 13 | chr4 89891197 98235479 VCV000443904 0 . 89891197 98235479 34,139,34 |
| 14 | chr4 86370518 94894345 VCV000152923 0 . 86370518 94894345 34,139,34 |
| 15 | chr4 82210925 91215314 CV994\_2 0 . 82210925 91215314 65,105,225 |

Table S3B: Small SNCA deletions/duplication coordinates for UCSC genome browser custom tracks (genome build GRCh37/hg19, February 2009)

|  |  |
| --- | --- |
| Genome Browser Custom Tracks (GRCh37/hg19) | Reference |
| Duplications |  |
| browser position chr4:88169442-92453245 |  |
| track name=Duplications="Duplications" itemRgb=On |  |
| chr4 90791345 90858538 3521\_3 0 . 90791345 90858538 65,105,225 | Pinto et al., 2014 |
| chr4 90527679 90705624 CV251304 0 . 90527679 90705624 65,105,225 | DECIPHER |
| SNPs/SSV |  |
| browser position chr4:88169442-92453245 |  |
| track name=SNPs description="SNPs/SSVs" itemRgb=On |  |
| chr4 90678541 90678541 rs2736990 0 . 90678541 90678541 0,0,0 | Piper et at., 2018 |
| chr4 90646886 90646886 rs356165 0 . 90646886 90646886 0,0,0 | Piper et at., 2018 |
| chr4 90637601 90637601 rs356219 0 . 90637601 90637601 0,0,0 | Piper et at., 2018 |
| chr4 90757394 90757394 rs3756063 0 . 90757394 90757394 0,0,0 | Piper et at., 2018 |
| chr4 90674431 90674431 rs356168 0 . 90674431 90674431 0,0,0 | Piper et at., 2018 |
| chr4 90639515 90639515 rs11931074 0 . 90639515 90639515 0,0,0 | Piper et at., 2018 |
| chr4 90647278 90647278 rs17016074 0 . 90647278 90647278 0,0,0 | Piper et at., 2018 |
| chr4 90767039 90767305 Rep1-allele 0 . 90767039 90767305 0,0,0 | [9] |
| ECR |  |
| browser position chr4:88169442-92453245 |  |
| track name="ECR Regions" description="Evolutionarily Conserved Regions" |  |
| chr4 90614642 90614787 D1 | [10] |
| chr4 90614642 90614787 D2 | Sterling et al., 2014 |
| chr4 90629790 90630480 D3 | Sterling et al., 2014 |
| chr4 90636848 90637316 D6 | Sterling et al., 2014 |
| chr4 90659197 90659350 I2 | Sterling et al., 2014 |
| chr4 90674661 90675121 I5 | Sterling et al., 2014 |
| chr4 90675762 90675891 I6 | Sterling et al., 2014 |
| chr4 90682267 90682378 I8 | Sterling et al., 2014 |
| chr4 90721509 90721763 I12 | Sterling et al., 2014 |
| chr4 90785647 90785975 U3 | Sterling et al., 2014 |
| chr4 90789074 90789786 U4-1 | Sterling et al., 2014 |
| chr4 90791038 90791735 U4-3 | Sterling et al., 2014 |

Table S3C: SNCA deletions/duplication coordinates for UCSC genome browser custom tracks (genome build GRCh37/hg19, February 2009)

|  |
| --- |
| Genome Browser Custom Tracks (GRCh37/hg19) |
| Triplication |
| browser position chr4:85000000-98000000 |
| track name="Iowa" description="SNCA Triplication" visibility=2 itemRgb="On"  chr4 89337388 91047146  20163\_1672002 0 . 89337388  91047146  255,0,0 |
| track name="Lister" description="SNCA Triplication" visibility=2 itemRgb="On"  chr4 90302002 91143727 20163\_1672002 0 . 90302002 91143727  255,0,0 |
| Duplication |
| track name="ND40065" description="SNCA Duplication" visibility=2 itemRgb="On"  chr4 86743290 94654224 20163\_1672002 0 . 86743290 94654224 0,0,255 |

Table S4. Molecular, morphological, functional, and behavioral phenotypes in murine alpha-synuclein knockout models

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **α-syn KO** | **Double KO (α-β) or (α-γ)** | **Triple KO (α-β-γ)** |
| Brain architecture and neuronal morphology | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1- 14 months) | Normal [11] | Normal in α-β double KO [12] | Normal [13] |
| Old (≥24 months) | Not reported | Not reported | Normal [13] |
| Synaptic topography | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1 - 14 months) | No gross alteration on synaptic terminals, synaptic vesicles in striatum unchanged [11] | Vesicle number and size remained unchanged [12], no significant changes in presynaptic bouton area, density of vesicles (α-β double KO) [12] | 30% decreased synaptic termini [13], 28% decrease in presynaptic terminal area [13], unaltered synaptic density [13] |
| Old (≥24 months) | Not reported | Not reported | Unaltered synaptic density [13] |
| Electrophysiology | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1 - 14 months) | Not reported | Not reported | Decreased conduction velocity, excitability [13] |
| Old (≥24 months) | Not reported | Not reported | Not reported |
| Behavior | Young/adult (1 - 14 months) | Reduced learning ability, disturbance of spatial memory [14], anxiety behavior [15], no altered locomotor activity in novel environment [11] | Decrease motor performance (α-β double KO) [16] | Hyperactive in novel environments [17], decrease motor performance [16] |
| Old(≥ 24 months) | Motor coordination not impaired [18] | Not reported | Not reported |
| Midbrain dopaminergic neurons; count and morphology | Developing brain | Reduction on the dopaminergic neurons (33%) at embryonic day 13.5 [19] | Not reported | Not reported |
| Young/adult (1 - 14 months) | No difference [11] | No difference in α-β double KO [12], decrease in TH+ neurons in SNpc in α-γ KO [20] | No difference [17], no change on TH+ neurons in the SNpc [16] |
| Old (≥24 months) | Decreased of TH+ fibers in the dorsal striatum [18], decrease number of neurons [16] | Reduction of TH+ neurons in the SNpc (α-β double KO) [16] | Mild decrement [13], no change on TH+ neurons in SNpc [16] |
| Striatal dopamine | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1 - 14 months) | Reduction of striatal dopamine (18%) [11,14], attenuation of dopamine dependent locomotor response to amphetamine [11] | Not reported | Not reported |
| Old (≥24 months) | Reduction of 36.2% (24 mo)[18], around 20% decrement [16] | Reduction of 18% [12], around 25% reduction [16] (α-β double KO) | Around 30% decrease [16] |
| Survival and gross | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1 - 14 months) | Viable, fertile, and normal in size [11] | No changes on survival in α-β double KO [12] | 10% decrease survival rate [13], increased mortality (12%) by 12 months [13], unaltered overall survival rate [16] |
| Old (≥24 months) | Not reported | Not reported | Unaltered survival rate [16] |
| β-and or γ-syn | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1 - 14 months) | No changes on gross or subcellular distribution [11], increment on β-syn in midbrain [20] | 50% increase of γ synuclein in α-β double KO [12], increase of β synuclein in α-γ KO mice [20] | Not reported |
| Old (≥24 months) | Not reported | Not reported | Not reported |
| Synaptic proteins | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1 - 14 months) | Not reported | 30% increase in 14-3-3e protein and complexines in α-β double KO [12] | Increase in complexin II, synapsin IIb, and 14-3-3 β and ε isoforms [13] |
| Old (≥24 months) | Rab3a, synaptophysin, syn1 were unaltered [11] | Not reported | Decrease of complexin II, synapsin IIb [13], 14-3-3 β and ε isoforms, changes in SNARE proteins (SNAP-25) and synaptobrevin-2 [13], decrease in synaptobrevin-2 [21], increase in CSPα [21], decrease in SNARE complex [21] |
| Other dopamine metabolites and transporters | Developing brain | Not reported | Not reported | Not reported |
| Young/adult (1 - 14 months) | Not reported | DOPAC and HVA levels unchanged, unchanged levels of 5-HT [12], (in α-β double KO or α-γ KO) [20] | Not reported |
| Old (≥24 months) | Unchanged, downregulation of DAT [18] | Not reported | Unchanged [16] |
| MPTP toxicity resistance | Young/adult (1 - 14 months) | Resistance to MPTP toxicity [20] | Resistance to MPTP toxicity in (α-β double KO) [20] | Not reported |
|
| Old (≥24 months) | Not reported | Not reported | Not reported |

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