Supplementary Table S1. Extended clinical description of LSDMCA cases

| Ref;Case Id | Mutation | Linear skin lesions | Micro- /anophthalmia | Corneal abnormalities | Other eye abnormalities | CNS abnormalities | Intellectual disabilities | Short stature | Cardiac abnormalities | Genitourinary abnormalities | Nail Dystrophy | Diaphragmatic hernia |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| [30]; case 1 | X/Y translocation (Xp22.3/Yq11.2) | + | + | + | + | + | - | + | - | - | - | - |
| [30]; case 2 | X/Y translocation (Xp22.3/Yq11.2) | + | + | + | + | + | - | + | - | + | - | - |
| [31] | 46,X,del(X) (p22.3;pter) | + | + | + | - | + | - | - | - | - | + | - |
| [32] | 46,X,del(X) (p22.2;pter) | + | + | + | + | - | - | NI | - | - | - | - |
| [33]; case 1 | 46,X,del(X) (p22.2;pter) | + | + | - | - | + | NA | NA | - | - | - | + |
| [33]; case 2 | 46,X,del(X) (p22.2;pter) | + | - | - | - | - | - | + | - | - | - | - |
| [34]; case 1 |  46,Xt(2;X) (p25.1;p22.1) | + | - | + | - | + | NI | NI | - | - | - | - |
| [34]; case 2 |  46,Xt(2;X) (p25.1;p22.1) | + | - | + | - | + | NI | NI | - | - | - | - |
| [35] | 46,X,-X, + der(X)t(X,?) (p22.3;?) | + | + | + | + | + | NI | + | + | - | - | - |
| [36]; case 1 | 46,X,del(X) (p22.11;p22.31) | + | + | + | + | + | - | + | - | - | - | - |
| [36]; case 2 | del Xp22.3-pter | + | + | + | - | + | NI | NI | + | - | + | - |
| [1]; case 1 | 46,X,del(X) (p22.2;pter) | + | + | + | + | + | + | + | - | - | - | - |
| [1]; case 2 | 46,X,del(X) (p22.2;pter) | + | - | - | + | - | - | + | - | - | - | - |
| [1];\*\*case 3  | 46,X,del(X) (p22.2;pter) | NA | NA | NA | NA | + | NA | NA | NI | NI | NA | NI |
| [1]; case 4 | Xp/Yp exchange (SRY), distal Xp monosomy | + | + | - | - | - | - | + | - | + | - | - |
| [37]; case 1 | 46,XX,t(X;Y), (p22.3;p11.2) | + | + | + | + | + | + | - | - | + | - | - |
| [37]; case 2 | 46,XX,t(X;Y), (p22.3;p11.2) | + | + | - | - | NI | NI | + | NI | - | - | - |
| [38] | 46,X,del,(X) (p22.1) | + | + | + | + | + | + | NI | + | + | - | - |
| [39] | Xp/Yp exchange (SRY), distal Xp monosomy | + | + | + | + | + | + | + | + | + | - | - |
| [40] | Xp22.3del, cryptic Yp11.2 transl | + | + | + | - | + | NI | NI | + | + | - | - |
| [15] | 45,X/46,X,r (X)(p22q21)/46,X,del(X)(p22) | + | + | + | + | + | - | + | - | - | + | - |
| [41] | 46,X,der(X),t (X:Y)(p22.13;q11.2) | - | + | + | - | - | NI | NI | + | + | - | - |
| [42] | 46,X,der(X),t (X:Y) | + | + | - | + | - | NI | NI | NI | - | - | - |
| [43] | 46,X,der(X),t(X:3) (p22.2; p22.2) | - | + | + | + | - | - | - | - | - | - | - |
| [44] | 46,X,del(X) (p22.3) | - | + | - | + | - | NI | NI | NI | - | - | - |
| [45] | 46,X,der(X),t (X:Y) (p22.13; p11.2) | - | + | - | - | - | NI | NI | + | - | - | - |
| [46] | 46,X,der(X)t(X;Y) | + | + | + | - | + | - | - | + | + | - | - |
| [47] | 46,X,del(X) (p22.3-pter) | + | + | - | - | + | + | - | - | + | - | - |
| [48] | 46,Y,inv(X)(p22.13∼22.2p22.32∼22.33)[49]/46,XY[271]Mosaic | + | - | - | - | + | NI | NI | + | - | - | - |
| [49]; case 1 | 46,X,Xt(X;Y) (p22.3;p11.3) | + | + | + | + | - | - | - | + | + | - | - |
| [49]; case 2 | 46,X,Xt(X;Y) (p22.3;p11.3) | + | + | + | + | - | - | - | + | + | - | - |
| [50] | 46,X,Xp22.3 microdel | + | + | + | - | - | - | + | + | - | - | - |
| [51]; case 1 | 46,X,der(X)t(X;Y) | + | + | + | - | - | NI | - | + | + | - | - |
| [51]; case 2 | 46,X,der(X)t(X;Y) | + | + | + | - | - | NI | - | + | + | - | - |
| [51]; case 3 | 46,X,der(X)t(X;Y)(p22.3;q11) | + | + | + | + | + | NI | - | + | - | + | - |
| [51]; case 4 | 46,X,der(X)t(X;Y)(p22.3;q11.2) | - | - | + | + | - | - | + | - | - | - | - |
| [5]; BA 389 | 46,X,del(X) (p22.22) | + | + | - | + | + | + | + | - | - | - | - |
| [5]; BA 644 | 46,X,der(X),t (X:Y)(p22.22; q11.2) | + | + | - | + | NI | NI | + | - | - | - | - |
| [5]; BA 659 | 46,X,der(X),t (X:Y)(p22.22;q25.3) | + | + | + | - | NI | + | - | - | - | - | - |
| [5]; BA 745 | 46,X,del(X)(p22.22,p22.22) | + | + | + | - | - | NI | NI | - | - | - | - |
| [52];\*\*\* | 46,X,der(X)t (X;Y)(p22.2;q11.2) | + | + | + | + | + | NA | NA | + | + | - | - |
| [53] | 46,X,del(X) (p22.2) | + | - | + | + | - | - | + | - | - | - | - |
| [54] | 46,X,del(X) (p22.2;pter) | + | + | + | + | - | + | + | - | + | - | - |
| [55];\*\*\* | 46,X,del(X) (p22.3)(3,6Mb) | + | + | - | - | + | NA | NA | + | + | - | + |
| [56] | Xp22.3 ab | + | + | - | - | + | NI | NI | + | - | - | - |
| [57] | 46,X,del(X) (p22.2;pter) | + | + | + | - | + | + | + | - | + | - | + |
| [58]; case III.3 | 46,X,del(X) (p22.2) | - | + | + | - | + | - | + | + | - | - | - |
| [58]; case II.1 | 46,X,del(X) (p22.2) | - | - | - | - | - | - | - | - | - | - | - |
| [59]; proband | 46,X,del(X) 12.9Mb ter del | + | + | + | + | + | + Autistic behaviors | + | - | - | NI | - |
| [59]; Mother | 46,X,del(X) 12.9Mb ter del | - | - | + | - | - | - | + | - | - | NI | - |
| [60]; proband | 46,X,del(X)(p22.2) 11.5Mb ter del | + | + | + | + | - | - |  NI | + | - | + | - |
| [60]; Mother | 46,X,del(X)(p22.2) 11.5Mb ter del | - | - | - | - | - | - | - | - | - | - | - |
| [29]; proband | 46,X,del(X)(p22.2) int del ~220 kb including *HCCS* | - | + | + | + | NI | - | - | - | - | NI | - |
| [29]; mother | 46,X,del(X)(p22.2) int del ~220 kb including *HCCS* | + | + | - | + | NI | - | - | - | - | NI | - |
| [13]; Patient 1; III.1 | 46,X,del(X)(p22.2p22.2), int del ~850 kb including *HCCS* | - | + | + | + | + | - | - | - | - | - | - |
| [13]; Patient 1; II.1 | 46,X,del(X)(p22.2p22.2), int del ~850 kb including *HCCS* | - | - | - | - | - | - | - | - | - | - | - |
| [13]; Patient 1; II.2 | 46,X,del(X)(p22.2p22.2), int del ~850 kb including *HCCS*  | - | - | - | - | - | - | - | - | - | - | - |
| [13]; Patient 4 | 46,X,del(X)(p22)  | + | + | + | + | + | + | + | - | - | - | - |
| [13]; Patient 5 | 46,X,del(X)(p22)  | + | + | + | - | - | + | - | - | + | - | - |
| [13]; Patient 6 | 46,X,del(X)(p22) int del ≥3 Mb including *HCCS* | + | + | + | - | - | - | - | - | - | - | - |
| [61] | 46,XX,ish del(p22.2p22.31) 3,3 Mb del mosaic | + | + | - | - | - | NI | - | + | NI | - | - |
| [62] | 46,X,del(X)(p22) | + | + | + | + | - | - | - | - | + | + | - |
| [62]; mother | 46,X,del(X)(p22) | + | - | - | - | NI | NI | NI | NI | NI | NI | NI |
| [62]; elder daughter | 46,X,del(X)(p22) | + | - | - | - | NI | NI | NI | NI | NI | NI | NI |
| [63] | 46,X,del(X)(p22.33p22.2) 11Mb del | + | + | - | - | + | - | NI | + | - | - | + |
| [64] | 46,XX,del(X)(p22.3p22.2) 11.5Mb del | + | + | + | - | + | + | + | - | + | - | - |
| [66] | Xp22.2 ter del | + | + | + | + | - | - | - | + | + | - | + |
| [67]; case 1 | Xp22 del | + | + | + | - | - | NI | NI | - | + | - | - |
| [67]; case 2 | 46,X,der(X)t (X;Y) | + | + | + | - | + | NI | NI | + | + | - | - |
| [2]; case II.7 | 8.6kb del spanning 5’*HCCS* and *MID1* | + | + | + | - | - | - | - | + | - | - | - |
| [2]; case II.1 | 8.6kb del spanning 5’ *HCCS* and *MID1* | - | - | - | + | - | - | - | - | - | - | - |
| [2]; case II.3 | 8.6kb del spanning 5’ *HCCS* and *MID1* | - | + | - | - | NI | NA | NA | - | - | - | + |
| [2]; case I.1 | 8.6kb del spanning 5’ *HCCS* and *MID1* | - | - | - | - | - | - | - | - | - | - | - |
| [2]; case MS1 | point mut *HCCS* | + | + | + | + | + | + | - | - | - | - | - |
| [2]; case MS2 | point mut *HCCS* | - | + | + | - | + | + | - | + | - | - | - |
| [14] | point mut *HCCS* | - | + | + | - | - | - | - | - | - | - | - |
| [13]; Patient 2 | point mut *HCCS* | + | + | + | + | + | NA | + | + | - | - | - |
| [13]; Patient 3 | point mut *HCCS* | - | + | + | + | NI | +a | - | - | - | - | - |
|  | TOT # cases | 56/75 | 59/75 | 50/75 | 34/75 | 40/70 | 16/50 | 24/54 | 25/70 | 21/72 | 6/69 | 5/73 |
|  | % | 75 | 79 | 67 | 45 | 57 | 32 | 44 | 36 | 29 | 9 | 7 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| [3]; case 1 | point mut *COX7B* | + | - | - | - | + | - | + | - | - | + | - |
| [3]; case 2 | point mut *COX7B* | + | - | - | - | + | + | + | + | + | - | + |
| [3]; case I.2 | point mut *COX7B* | + | - | - | + | + | + | - | + | - | - | - |
| [3]; case II.4 | point mut *COX7B* | + | - | - | + | + | +b | - | - | - | - | - |
|  | TOT # cases | 4/4 | 0/4 | 0/4 | 2/4 | 4/4 | 3/4 | 2/4 | 2/4 | 1/4 | 1/4 | 1/4  |
|  | % | 100 | 0 | 0 | 50 | 100 | 75 | 50 | 50 | 25 | 25 | 25 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
| [4]; subject 1 | point mut *NDUFB11* | + | - | - | + | - | - | NA | + | - | - | - |
| [4]; subject 2 | point mut *NDUFB11* | + | - | - | + | + | + | + | + | - | - | - |
| [4]; mother subject 2 | point mut *NDUFB11* | - | - | - | - | - | - | - | - | - | - | - |
| [4];\*\*\*\* |  | NA | - | - | - | + | NA | NA | + | NI | NA | NI |
|  |  |  |  |  |  |  |  |  |  |  |  |  |
|  | TOT # cases | 2/3 | 0/3 | 0/3 | 2/3 | 1/3 | 1/3 | 1/2 | 2/3 | 0/3 | 0/3 | 0/3 |
|  | % | 67 | 0 | 0 | 67 | 33 | 33 | 50 | 67 | 0 | 0 | 0 |

\*\*This patient was an aborted fetus with exencephaly and absence of the entire scalp skin. \*\*\*Malformed female infants died 9hs [55] and 5 days [52] after delivery. \*\*\*\*Aborted female fetus from the mother of subject 2. These cases were not considered in the total number of patients for the calculation of the percentage of occurrence of clinical signs as well as all the other patients for which that specific feature had not been studied (NI) or could not be observed (NA) because the patient was too young and so on.

NI, not investigated

NA, not applicable

amild motor delay; battention deficit disorders (ADHD)

Other Eye abnormalities: prolapsed iris, severe myopia, orbital cyst, hypopigmented and disorganized retinal pigmented epithelium, cataracts, choroidal thickening, coloboma, chorioretinopathy, glaucoma, lens abnormalities, aniridia, pale optic disk and altered visual-evoked potential.

CNS abnormalities: microcephaly, agenesis of the corpus callosum, colpocephaly, seizures, hydrocephalus, ventriculomegaly, cystic cerebral malformation.

Cardiac abnormalities: atrial and ventricular septal defect, atrio-ventricular block, histiocytoid cardiomyopathy, supraventricular tachycardia, junctional ectopic tachycardia, murmur, coarctation of the aorta, aortic stenosis/atresia and patent foramen ovale.

Genitourinary abnormalities: hypospadias, intersexual genitalia, hypoplastic genitalia, imperforate or displaced anus and polycystic ovary syndrome.

Abbreviations: Ref, reference; del, deletion; microdel, microdeletion; ter, terminal; int, interstitial; ab, abnormalities; ADHD attention deficit disorders.

Note: all references were cited in the main text and the number of the references refer to the reference list of the main text.