Figure S1

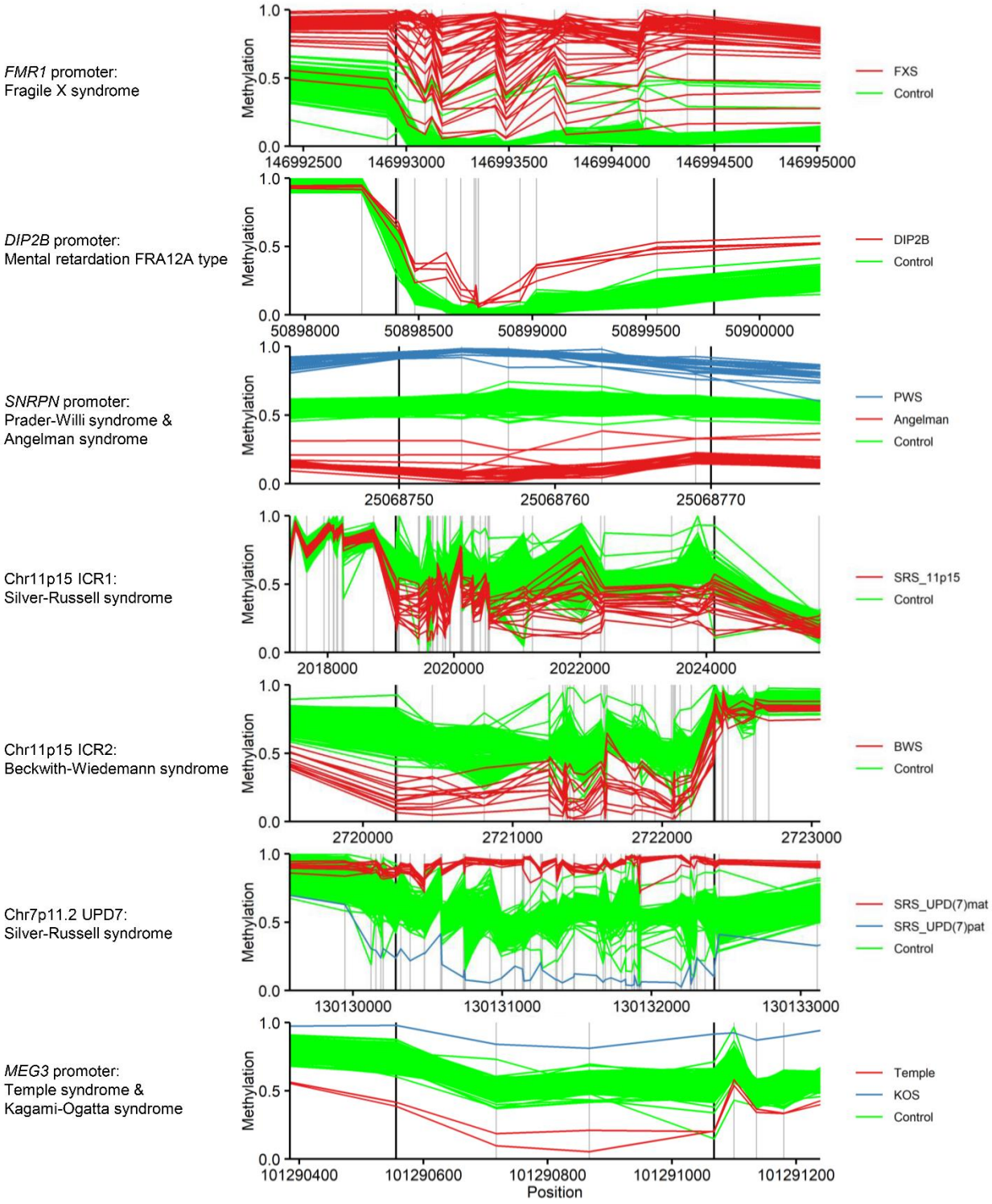
FMR1 promoter:
Fragile X syndrome
Methylation
1.0
0.5
0.0
146992500
146993000
146993500
146994000
146994500
146995000
FXS
Control
DIP2B promoter:
Mental retardation FRA12A type
Methylation
1.0
0.5
0.0
50898000
50898500
50899000
50899500
50900000
DIP2B
Control
SNRPN promoter:
Prader-Willi syndrome &
Angelman syndrome
Methylation
1.0
0.5
0.0
25068750
25068760
25068770
PWS
Angelman
Control
Chr11p15 ICR1:
Silver-Russell syndrome
Methylation
1.0
0.5
0.0
2018000
2020000
2022000
2024000
SRS_11p15
Control
Chr11p15 ICR2:
Beckwith-Wiedemann syndrome
Methylation
1.0
0.5
0.0
2720000
2721000
2722000
2723000
BWS
Control
Chr7p11.2 UPD7:
Silver-Russell syndrome
Methylation
1.0
0.5
0.0
130130000
130131000
130132000
130133000
SRS_UPD(7)mat
SRS_UPD(7)pat
Control
MEG3 promoter:
Temple syndrome &
Kagami-Ogatta syndrome
Methylation
1.0
0.5
0.0
101290400
101290600
101290800
101291000
101291200
Position
Temple
KOS
Control

Figure S2

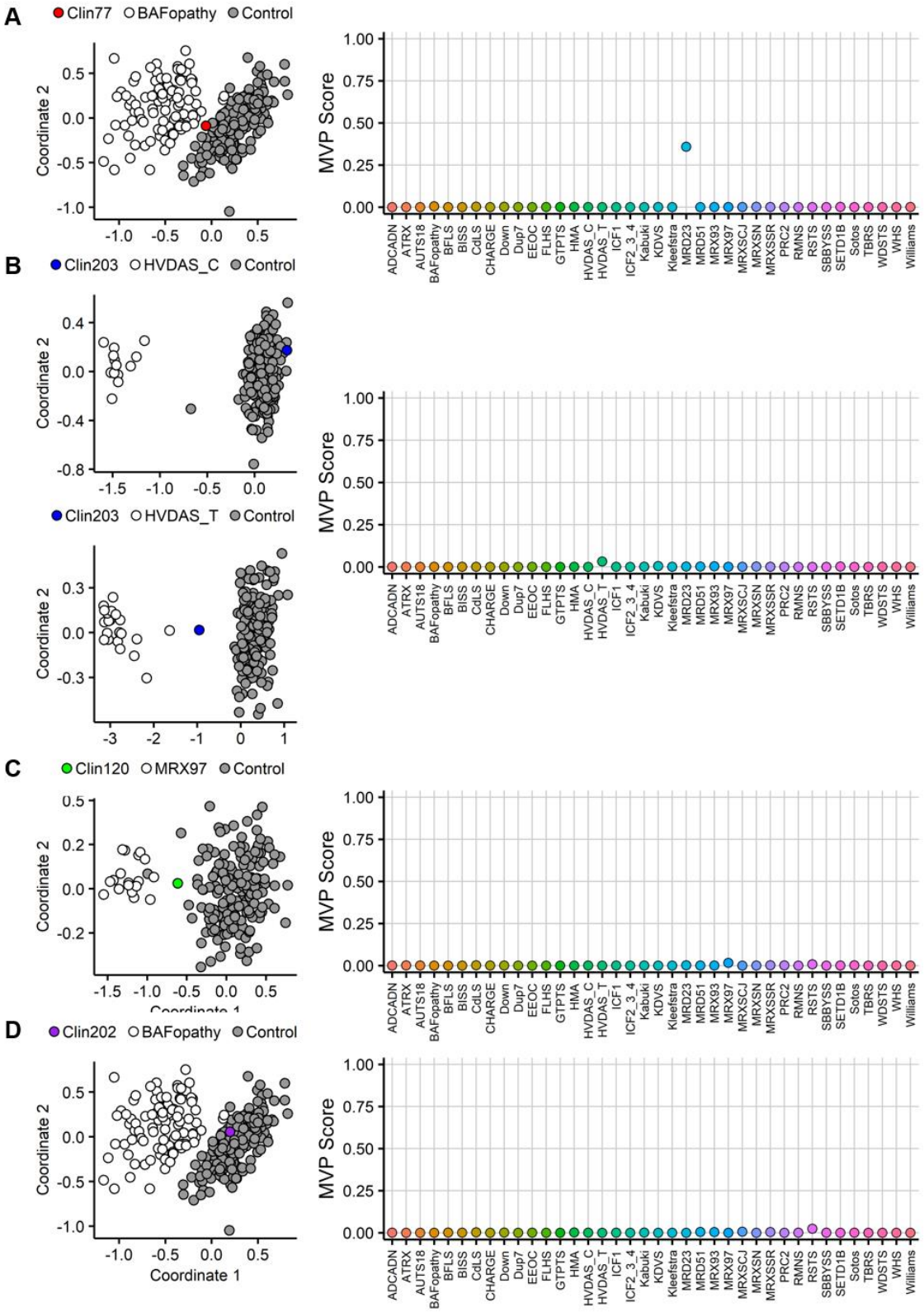
A
Clin77
BAFopathy
Control
B
Clin203
HVDAS_C
Control
Clin203
HVDAS_T
Control
C
Clin120
MRX97
Control
D
Clin202
BAFopathy
Control
Coordinate 2
Coordinate 1
MVP Score
ADCADN
ATRX
AUTS18
BAFopathy
BFLS
BISS
CdLS
CHARGE
Down
Dup7
EEOC
FLHS
GTPTS
HMA
HVDAS_C
HVDAS_T
ICF1
ICF2_3_4
Kabuki
KDVS
Kleefstra
MRD23
MRD51
MRX93
MRX97
MRXSCJ
MRXSN
MRXSSR
PRC2
RMNS
RSTS
SBBYSS
SETD1B
Sotos
TBRS
WDSTS
WHS
Williams

Table S3

Validation Cohort	Total	EpiSign Concordant
Normal Control	58	58
EpiSign Positive	123	119
Imprinting Positive	21	21
Imprinting low level mosaics (not EpiSign detectable)	9	9
Total samples	211	207

Clinical Testing Cohort	Total	EpiSign Positive	EpiSign Negative	Inconclusive
Targeted Analysis	136	48	86	2
Screening Analysis	71	9	60	2
Total Samples	207	57	146	4

Legends:

Figure S1. EpiSign DNA methylation profiles for imprinting disorders and Fragile X. Methylation levels (y-axis) are plotted against the genomic coordinates (y-axis) for subjects with the respective disorders, and control subjects. The black vertical lines indicate the borders of the region assayed for diagnostic testing, grey and black vertical lines indicate the locations of CpG probes.

Figure S2. DNA methylation (EpiSign) analysis or the inconclusive clinical cases. MDS plot and MVP score for A. Case Clin77 (ARID2:c.988_1008del, p.(Leu330_Gly336del)); B. Case Clin203 (ADNP:c.46C>G, p.(Arg16Gly); C. Case Clin120 (no genetic variant identified); and D. Case Clin202 (no genetic variant identified).