Supplementary Table 1. PCR and primers for analysis of cat *ALX1*.

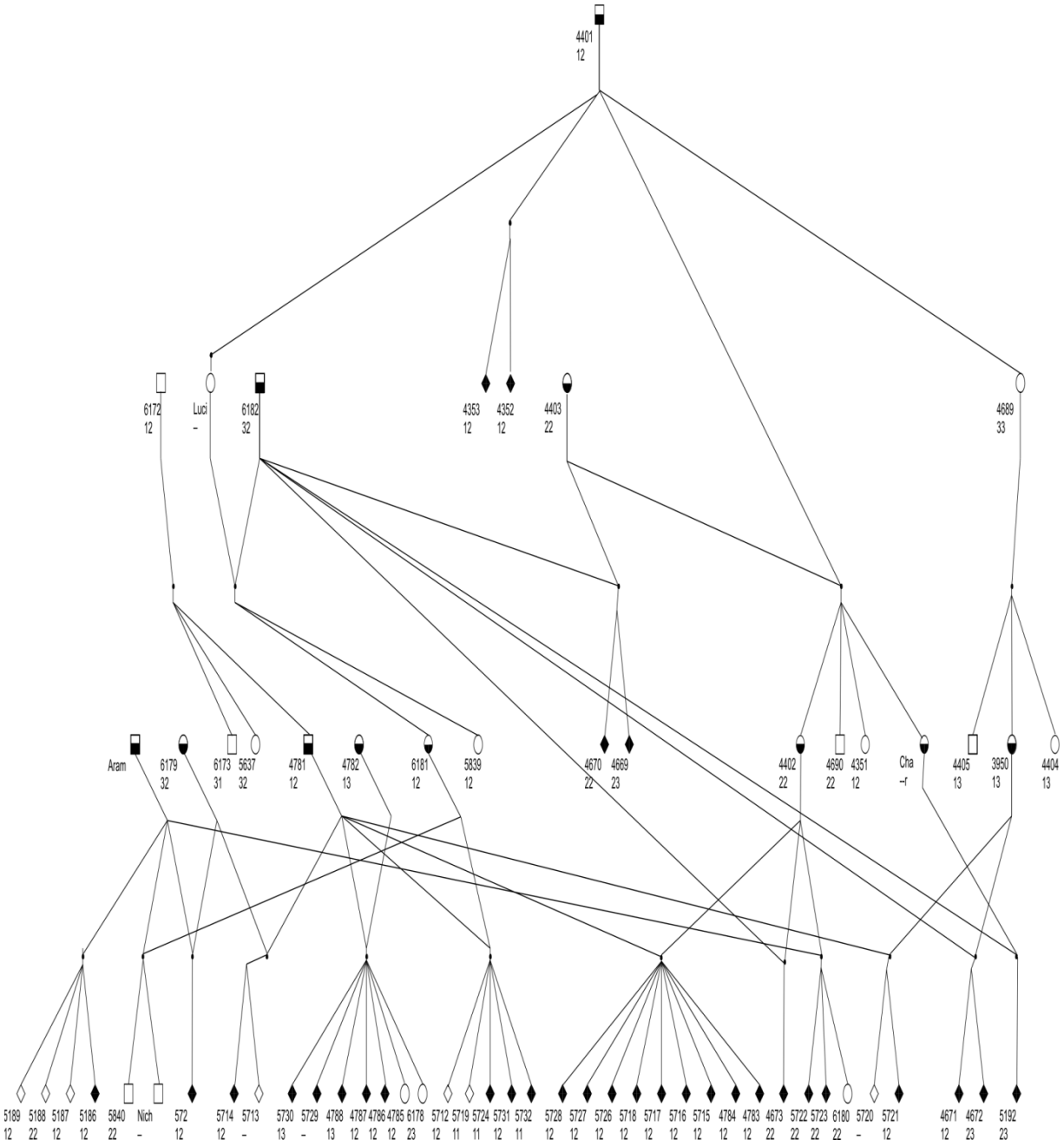
Forward	Reverse	Mg	Tm
GGACGTATTAAGGGCTCGGAGC	TAAAACGCTCGCAGTTCCACCG	1.5 mM	58 °C
AAATCATTAACAGACTGCTTTCCTGA	ATGGTTCTAGTCTTTAGTGAGAGGATCA*	2 mM	58 °C
TTAGTGATTTTGTTGACCTGGTTTGTGT	TAAAATGCTCTCCTGGCACCTGG	1.5 mM	60 °C
TAAGGGGACAAAAGTGAGAATGCG	CGTTTGTGGAGACTGATGGATGGT	1.5 mM	60 °C
Pyrosequencing			
Biotin-GAAAACCCATTACCCGGATGTAT	CTTCATTTGGCTCCTACCTGGA		
CCTGGACTCTGGCCTCCGTGA[$]			

*for genotyping, this primer was labelled with FAM dye.
[$]This primer is for sequencing in the pyrosequencing reaction.

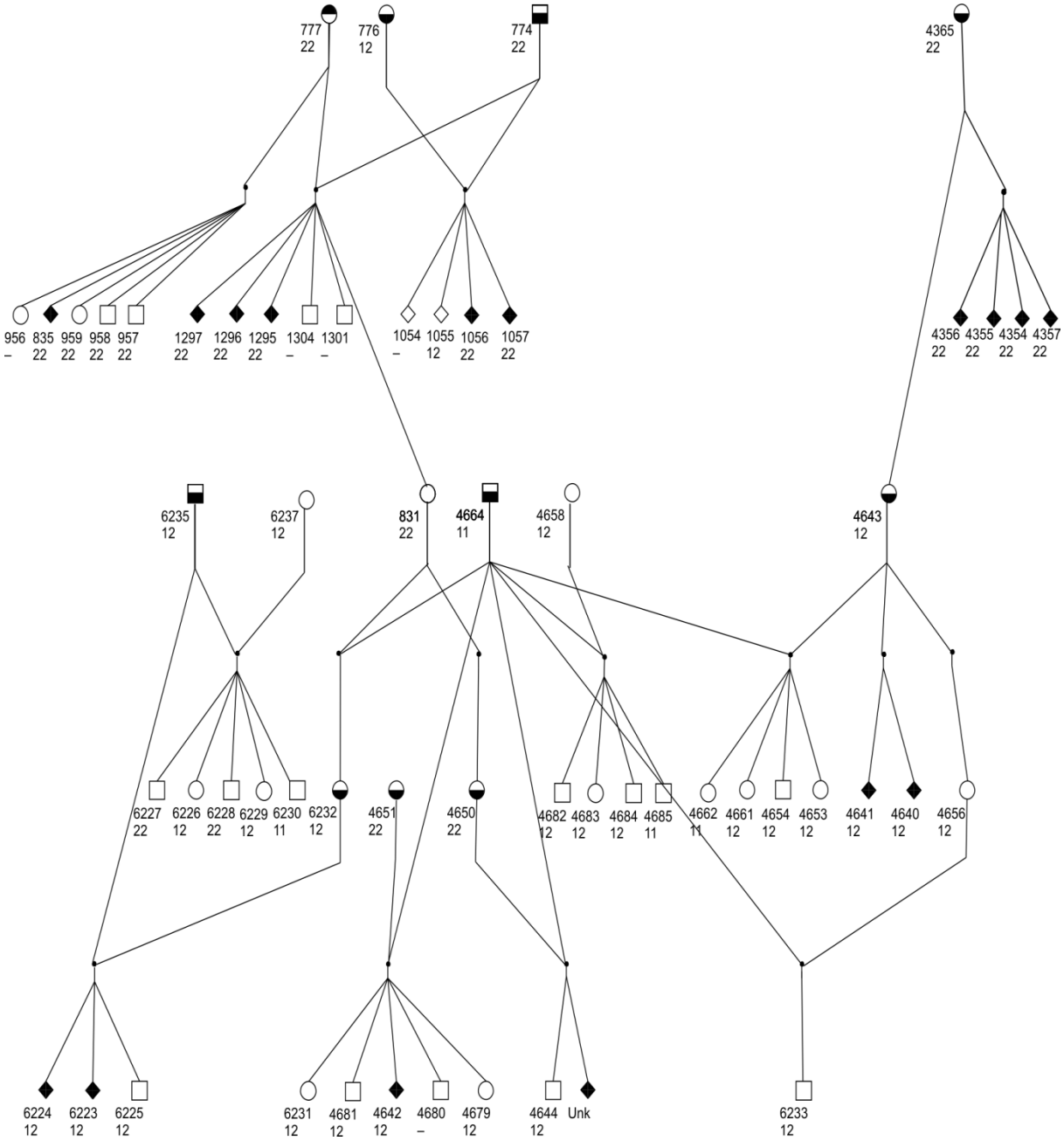
Supplementary Table 2. Consensus details homozygous regions across the affected cats.

Chr.	SNP1	SNP2	bp start	bp end	Kb	# SNPs	# cats
X	chrX.38990530	chrX.40531503	31154766	32362304	1207.54	26	23
X	chrX.36970662	chrX.38733350	29539864	30953514	1413.65	38	23
B4	chrB4.122309957	chrB4.129821393	106754478	112937278	6182.8	162	23
X	chrX.17358465	chrX.26762022	13769102	21616256	7847.15	201	21
D1	chrD1.29042292	chrD1.31719770	23604822	25470200	1865.38	61	21
B3	chrUn.36239579	chrB3.37818450	30716536	32150500	1433.96	38	21
D3	chrD3.10607895	chrA1.170901230	8276516	10296770	2020.25	55	20
D1	chrD1.74373646	chrD1.77044135	47727880	49998734	2270.85	69	20
B4	chrB4.133640812	chrB4.133943775	116050184	116294718	244.534	5	20
B1	chrB1.58452923	chrB1.58795359	45352082	45619806	267.724	9	20
B1	chrB1.55781749	chrB1.56493341	43293324	43849984	556.66	18	20

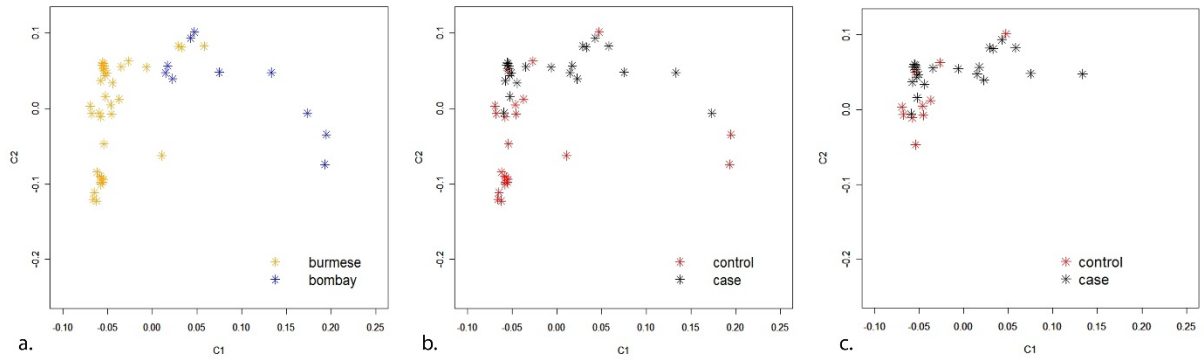
Supplementary Figures:



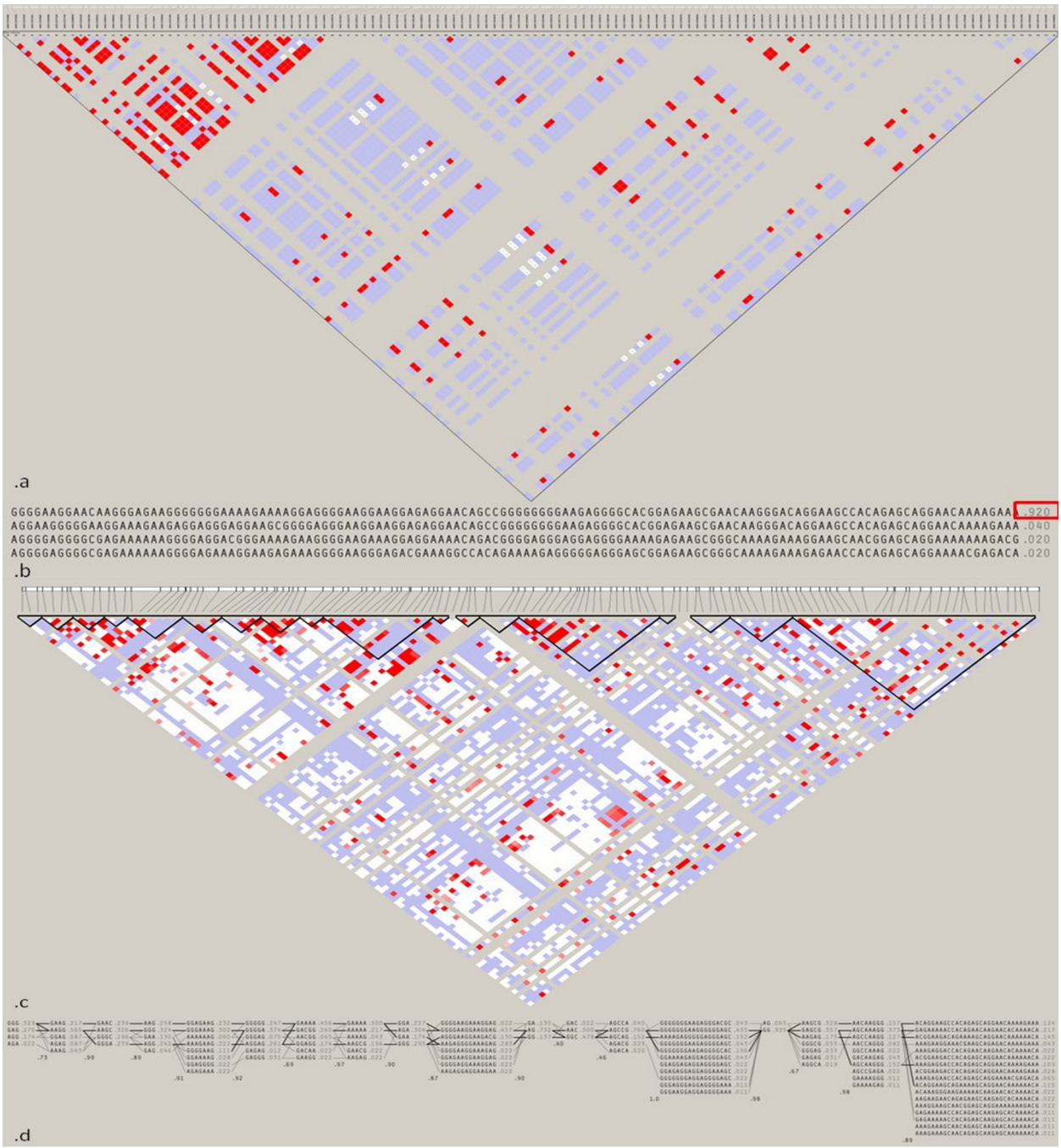
Supplementary Figure 1. Pedigree segregating for the Burmese Craniofacial Defect. Circles represent females, squares represent males, diamonds are unknown gender. Open symbols indicate phenotypically normal animals, filled symbols indicate affected cats, half-filled are obligate carriers. A small filled circle represents a "breeding node" for parental cats. Numbers under the symbols represent the laboratory sample number. Genotypes for the linked marker *FCA864* are represented below the identification numbers or names. The base pair size of the microsatellite marker was converted to a single number to distinguish the allele. No data is represented by dashes, "--".



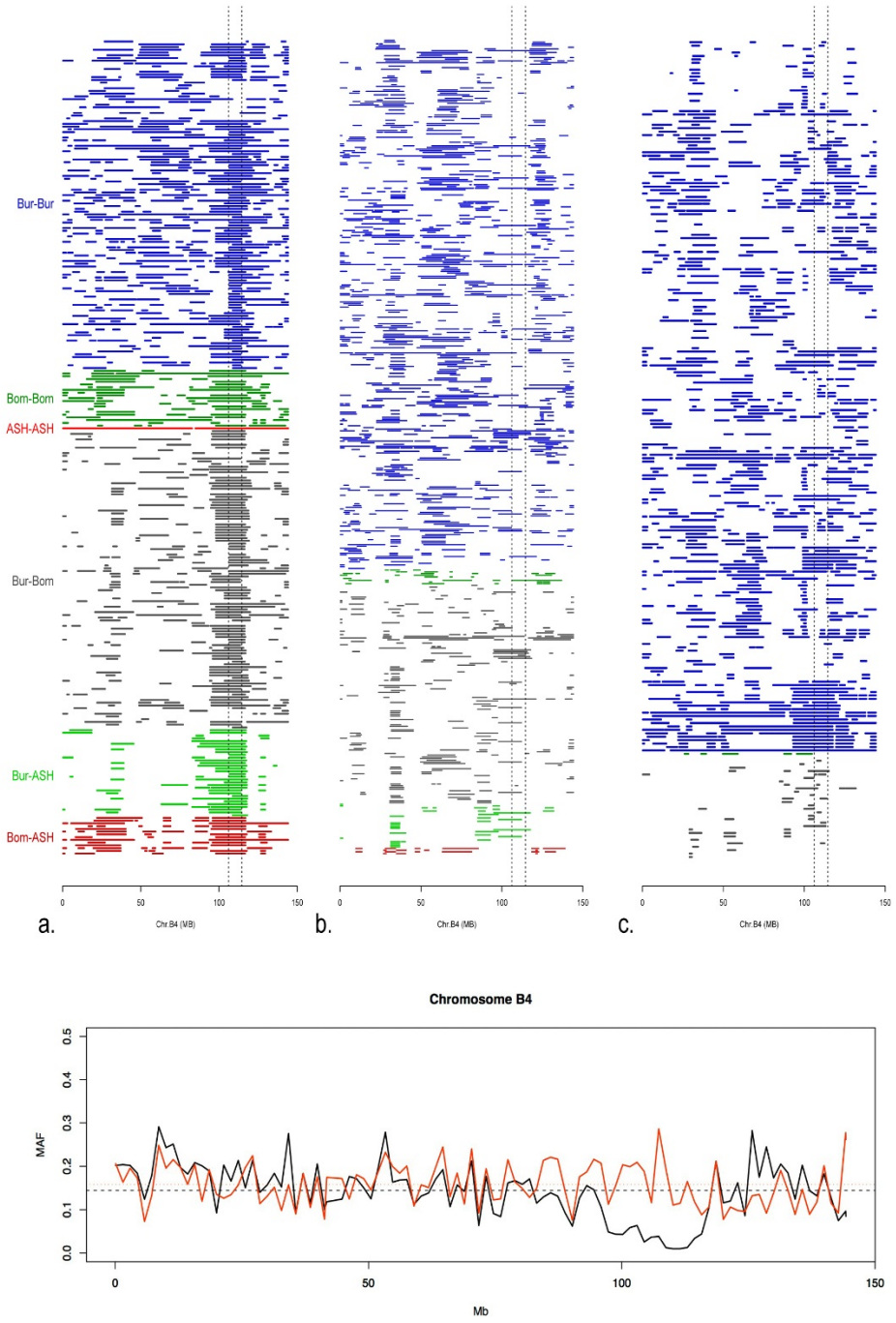
Supplementary Figure 2. Pedigree segregating for the Burmese Craniofacial Defect. Circles represent females, squares represent males, diamonds are unknown gender. Open symbols indicate phenotypically normal animals, filled symbols indicate affected cats, half-filled are obligate carriers. A small filled circle represents a “breeding node” for parental cats. Numbers under the symbols represent the laboratory sample number. Genotypes for the linked marker *FCA864* are represented below the identification numbers or names. The base pair size of the microsatellite marker was converted to a single number to distinguish the allele. No data is represented by dashes, “--”.



Supplementary Figure 3. Multidimensional scaling (MDS) analysis for population stratification of Burmese. Forty-six samples were plotted for principle components 1 and 2,a. represents the distribution of cases and controls, b. shows the distribution of the samples based on breed. c. The Burmese controls on the lower left of each plot were eliminated from the case-control analysis.

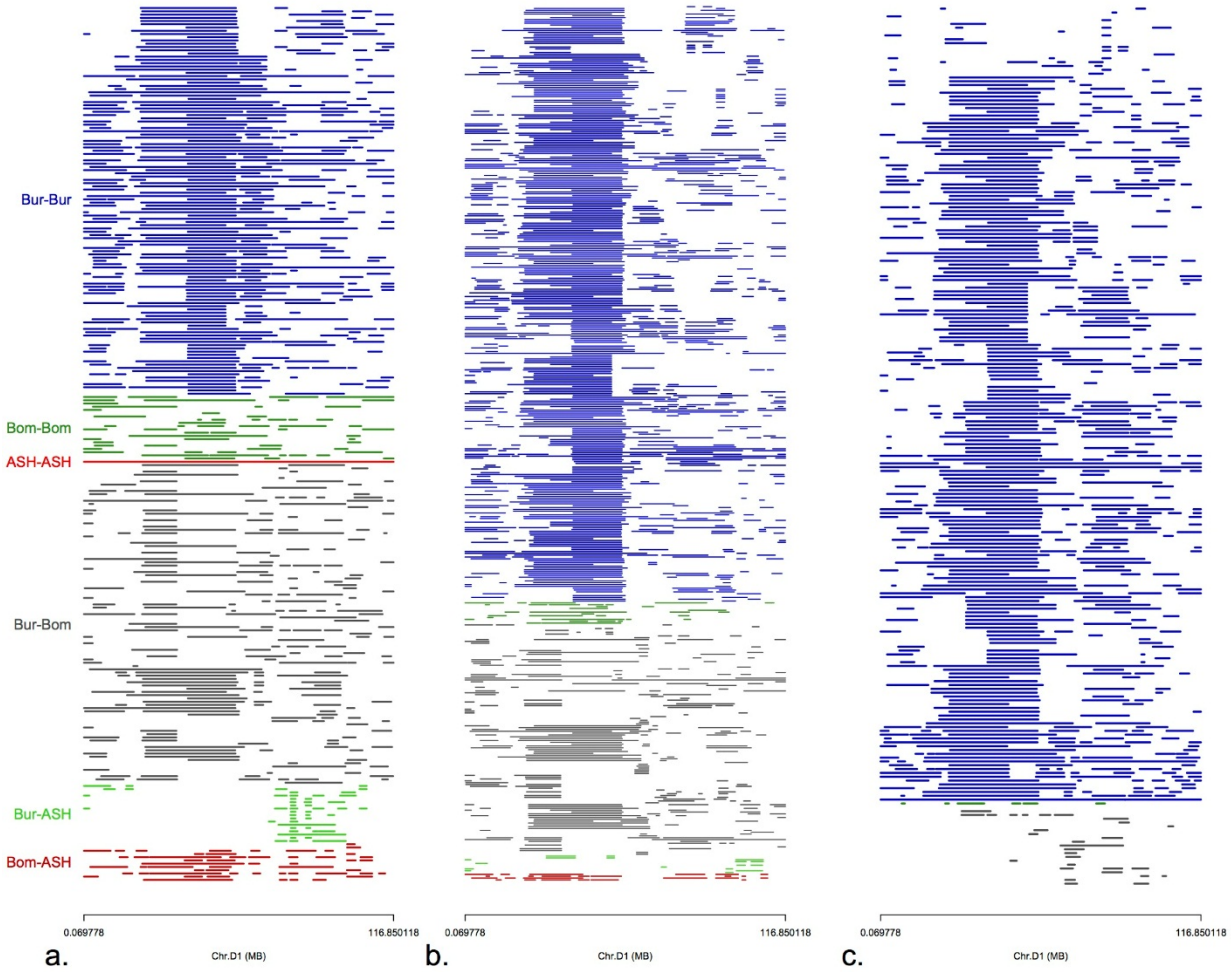


Supplementary Figure 4. Haplotype analysis of Burmese cases and controls for the craniofacial defect. Position 106,871,872 to position 111,795,156 of chromosome B4 in cases and controls. a. LD block identified by HAPLOVIEW across all the cases, spanning 4,923 Kb. b. Haplotypes sequence and frequencies across the 4,923 Kb regions. The main haplotype is squared in red and shows a frequency of 92% across cases. c. LD blocks identified by HAPLOVIEW in the correspondent region across all controls included in the study. d. Haplotypes sequence and frequencies for each identified LD block within the 4,923 Kb region in the control cats.

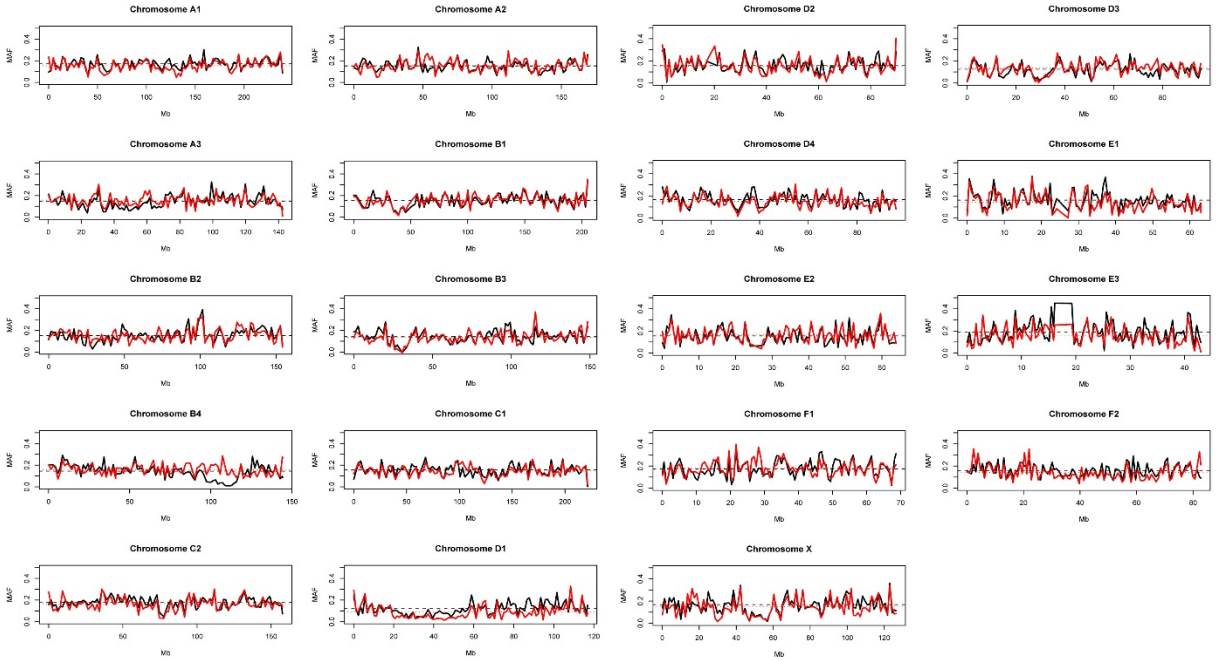


Supplementary Figure 5. **Identity by descent (IBD) and MAF analyses for chromosome B4**. The horizontal lines in the graph represent all the IBD regions (shared alleles) on chromosome B4 between all the cats included in the analysis. a. Each case is compared to all the other cases included in the analysis. Each group of comparison (breed to breed) is color-coded. Vertical black dashed lines represent a shared IDB region in common between almost all cases. b. Each case is compared to all the controls included in the study. c. Controls versus controls comparison of shared IBD. Cases versus controls and controls versus control comparisons do not show any shared IBD across all the specimens. (Bottom) Graphical representation of the MAF differences within the affected samples (black line) and the control

samples (red line) across all the *Felis catus* chromosomes. The black line represents the MAF within the cases and is compared with the MAF within the controls for each SNP. The red dashed line represent the MAF mean for the chromosome within the cases and the black dashed line the MAF mean within the controls. Several gaps are present in the current genome assembly, thus SNPs surrounding the gaps are connected with straight lines.



Supplementary Figure 6. Identity by descent (IBD) analysis for chromosome D1. The horizontal lines in the graph represents all the IBD regions (shared alleles) on chromosome D1 between all the cats included in the analysis. a. Each case is compared to all the other cases included in the analysis. Each group of comparison (breed to breed) is color-coded. b. Each case is compared to all the controls included in the study. c. Controls versus controls comparison of shared IBD. A common IBD is shared across the majority of East Asian breeds. The trait contained in the IBD region is a phenotypic trait responsible for the Burmese point coloration, fixed within the breed and confirmed by other analysis included in this study.



Supplementary Figure 7. Full chromosomal MAF comparison within cases and controls. Graphical representation of the MAF differences within the affected samples (black line) and the control samples (red line) across all the *Felis catus* chromosomes. The black line represents the MAF within the cases and is compared with the MAF within the controls for each SNP. The red dashed line represent the MAF mean for the chromosome within the cases and the black dashed line the MAF mean within the controls. Several gaps are present in the current genome assembly, thus SNPs surrounding the gaps are connected with straight lines.

```
                1                                                          60
Wild-type       MEFLSEKFALKSPPSKNSDFYMGAGGALEHVMETLDNESFYSKASAGKCVQAFGPLPRAE
Mutant          MEFLSEKFALKSPPSKNSDFYMGAGGALEHVMETLDNESFYSKASAGKCVQAFGPLPRAE

               61                                                         120
Wild-type       HHVRLERASPCQDSGVNYGITKGEGQPLHPELNRAMDNCNSLRMSPVKGMPEKGELDELG
Mutant          HHVRLERASPCQDSGVNYGITKGEGQPLHPELNRAMDNCNSLRMSPVKGMPEKGELDELG

               121                                                        180
Wild-type       DKCDSNVSSSKKRRHRTTFTSLQLEELEKVFQKTHYPDVYVREQLALRTELTEARVQVWF
Mutant          DKCDSNVSSSKKRRHRTTFTSLQLEELEKVFQKTHYPDVYVREQLEL----TEARVQVWF

               181                                                        240
Wild-type       QNRRAKWRKRERYGQIQQAKSHFAATYDISVLPRTDSYPQIQNNLWAGNASGGSVVTSGM
Mutant          QNRRAKWRKRERYGQIQQAKSHFAATYDISVLPRTDSYPQIQNNLWAGNASGGSVVTSGM

               241                                                        300
Wild-type       LPRDTSSCMTPYSHSPRTDSSYTGFSHHQNQFSHVPLNNFFTDSLLTGATNGHAFETKPE
Mutant          LPRDTSSCMTPYSHSPRTDSSYTGFSHHQNQFSHVPLNNFFTDSLLTGATNGHAFETKPE

               301                     327
Wild-type       FERRSSSIAVLRMKAKEHTANISWAM
Mutant          FERRSSSIAVLRMKAKEHTANISWAM

Homeobox domain
OAR domain
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Supplementary Figure 8: **Protein alignment of the *Cart1* wildtype and mutated alleles**. The mutation, underlined in red, is responsible for the lack of 4 amino acids (*in silico* prediction) in the homeobox domain. In the human protein, the homeobox domain starts at position 132 and ends at position 191 of the amino acid chain. Underlined in blue is the *Cart1* OAR domain, which starts at position 306 and ends at position 319 of the Cart1 protein.