

Analysis of Polycerate Mutants Reveals the Evolutionary Co-option of *HOXD1* to Determine the Number and Topology of Horns in Bovidae

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This document contains:

Supplementary Figures 1-13,

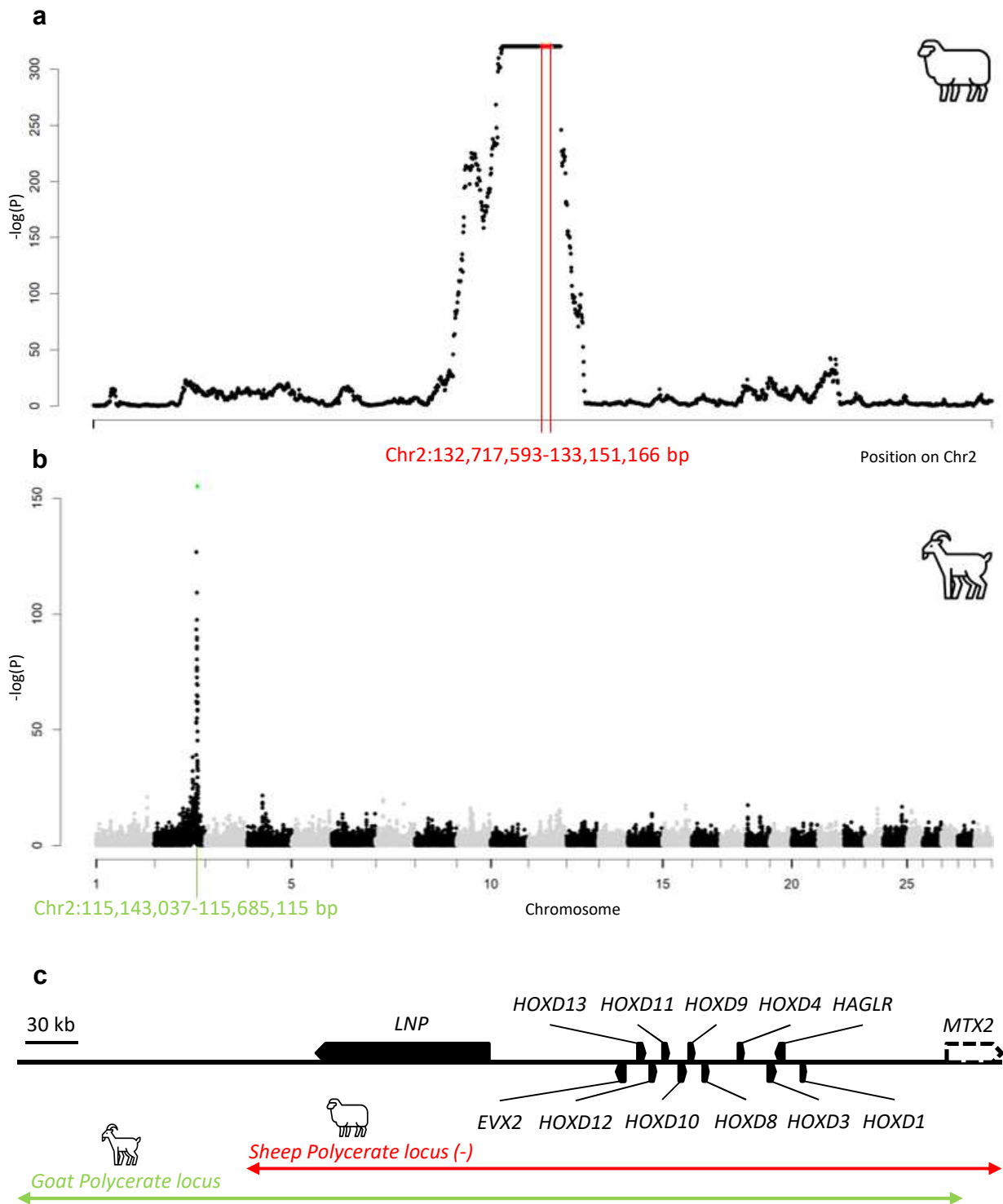
Supplementary Tables 1-16,

Supplementary Note 1,

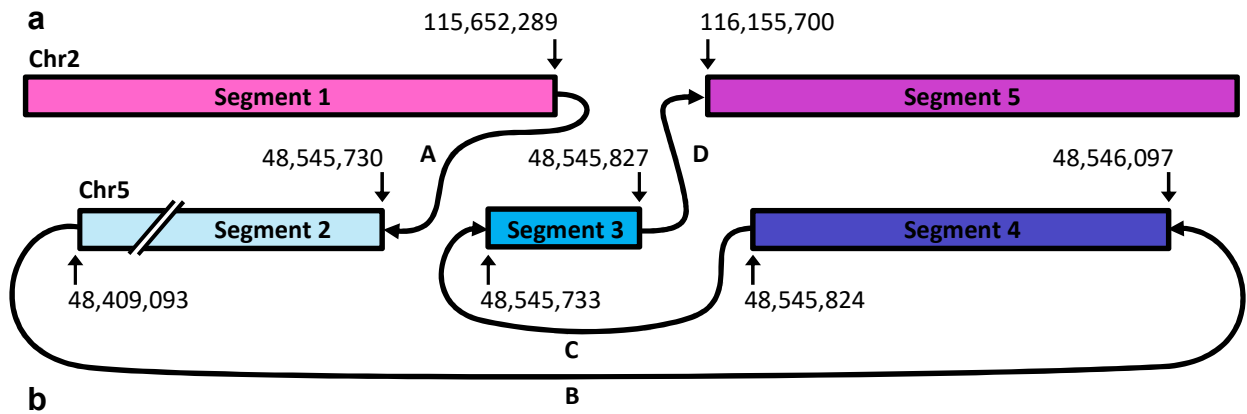
and additional references.



Supplementary Figure 1. Comparison of Pecoran headgear types. a-c) Pronghorns of *Antilocapra Americana* in adult male (a,b) and female (c) skull specimens. d,e) Antlers of a male *Capreolus capreolus*. f,g) Horns of a male *Rupicapra rupicapra*. h,i) Ossicones of a *Giraffa Camelopardalis* of unknown gender. Note the shared position of the different headgear types on the frontal bones (a, d, f, h) and the change of texture between the frontal bone and their bony core as indicated by arrows (c, e, g, i). Note also the presence of vestigial hairs (marked with arrows) after keratinization of the decidual sheath of the pronghorn in (b). Specimens MNHN-ZM-AC 1964-272, 2007-1354, 1993-280 and 1907-277 belong to the *Collection d'anatomie comparée du Muséum National d'Histoire Naturelle*, Paris, France while Mam-04525 originates from the *Collection d'anatomie du Musée Zoologique de Strasbourg*, France.

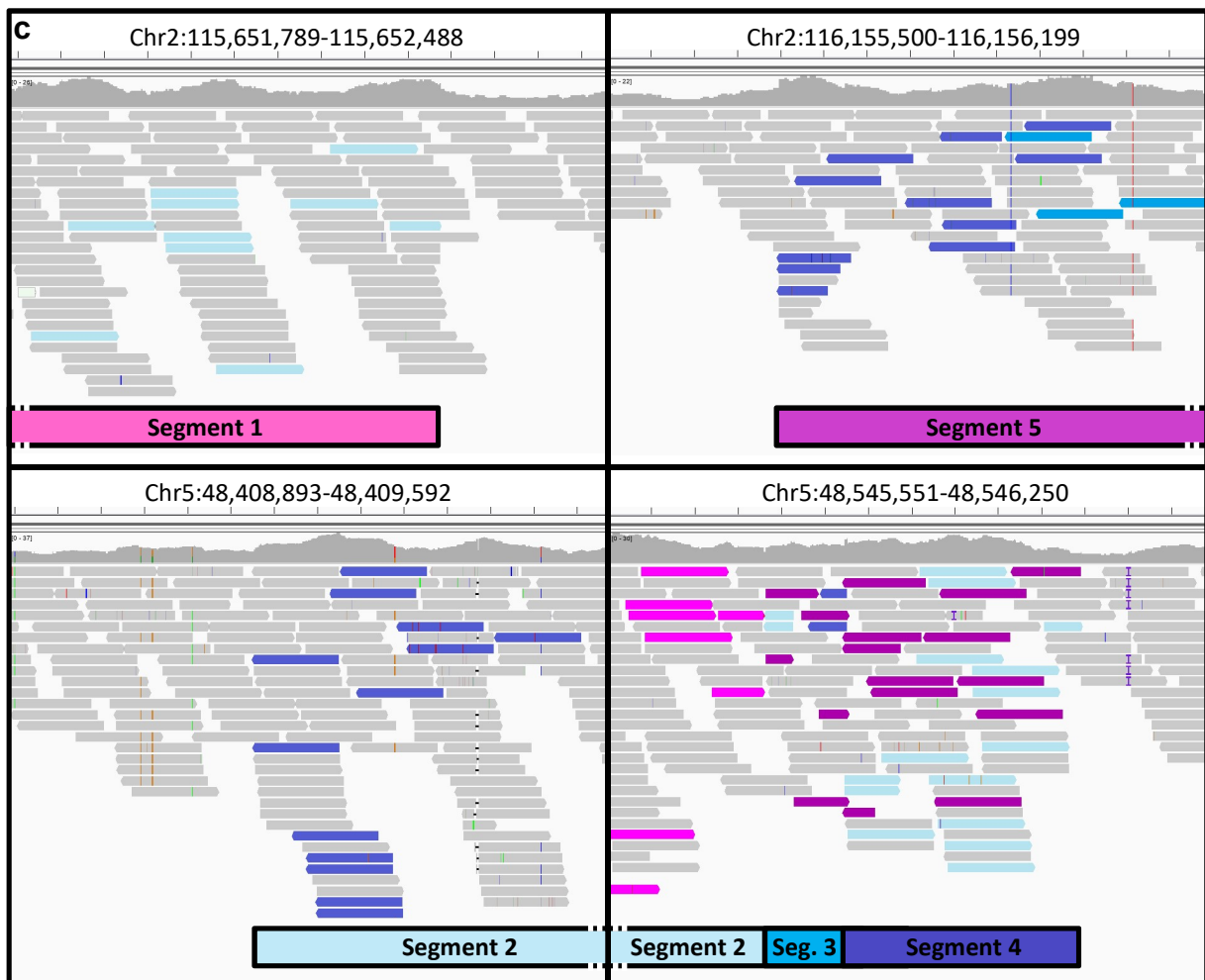


Supplementary Figure 2. Mapping of the *POLYCERATE* loci in sheep and goat. a) Identical-By-Descent (IBD) mapping of ovine *POLYCERATE* locus around the *HOXD* gene cluster and +/- 5 Mb on Chr2 (see Methods). Fisher's exact test p-values equal to zero were set to 1.0×10^{-320} ; 30 consecutive sliding windows of 50 markers corresponding to an IBD segment shared by all the polycerate sheep are highlighted in red. b) IBD mapping of caprine *POLYCERATE* locus on Chr2. One IBD segment of 10 markers shared by all the polycerate goats is highlighted in green. The intervals indicated are defined by the positions of the most proximal markers outside of the IBD segments (on Oar_v4.0 and ARS1 assemblies). c) Gene content and relative localization of the mapping intervals of the *POLYCERATE* loci in sheep (minus strand) and goat. Dashed lines indicate that a part of *MTX2* is located outside of the region displayed. Sheep and goat icons were made by "Monkik" from www.thenounproject.com.



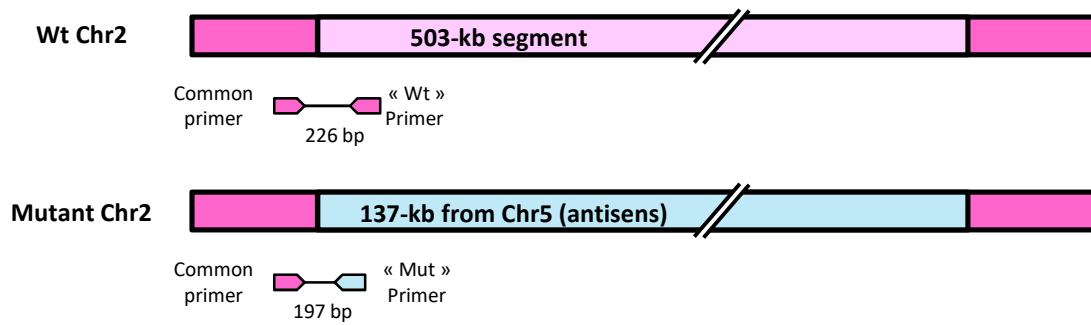
b

Fusion point A: No repeat 5'-AAGCAAATTCTTAATATTATT**GTATA**AAACTTAAATAAGTATGTAG-3' LINE (L1MC5)
Fusion point B: No repeat 5'-GCTACAGCAGAAAGTAAACCT**GCAGT**GGGCATGGGTTTGATC-3' SINE (CHRL)
Fusion point C: LINE (L1MC5) 5'-TTTAAAGACATTGAGAACA**AGC**AGGAGGGAAAGGCAACCC-3' LINE (L1MC5)
Fusion point D: LINE (L1MC5) 5'-AAAGACACACACAAAATT**GTACCT**GATTGTTACCTTTTC-3' No repeat

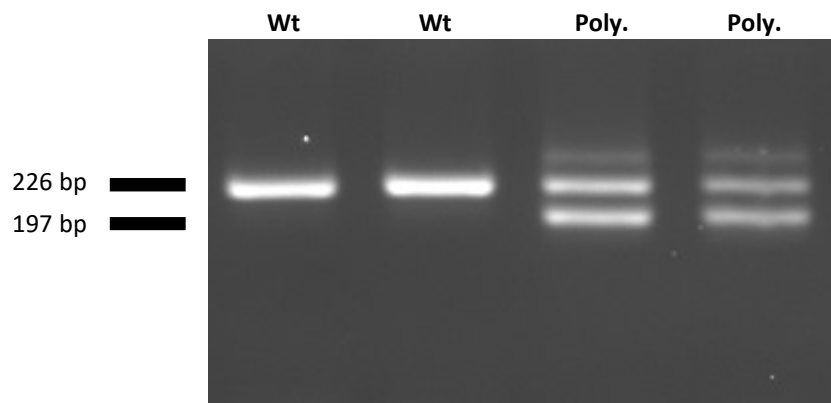


Supplementary Figure 3. Details on the large insertion-deletion at the goat *POLYCERATE* locus. a) Schematic representation of the segments involved in the translocation of 137 kb from Chr5 and the 503-kb deletion on Chr2. Fusion points are coded with letters. Positions refer to ARS1 caprine genome assembly. b) DNA sequences at the four fusion points. Nucleotides in bold highlight microhomologies between the fused segments, whereas nucleotides inserted between the breakpoints are underlined. The existence of repeated elements on each side of fusion points is indicated. c) Integrated Genome Viewer screen-captures showing aligned paired-end reads (~100-bp) around the various breakpoints. Reads from aberrantly mapping pairs are color-coded to indicate the chromosomal segment to which the other pair maps.

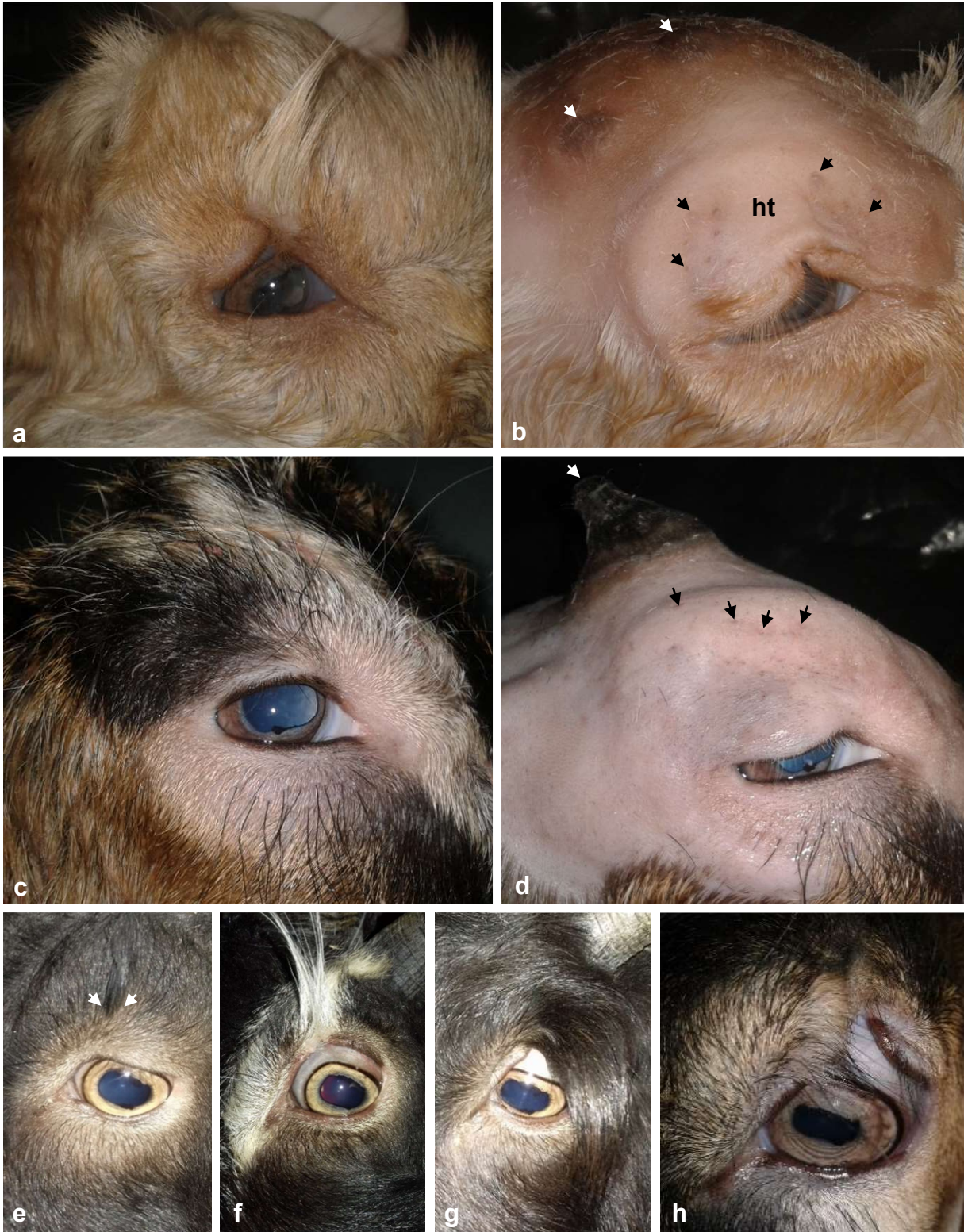
a



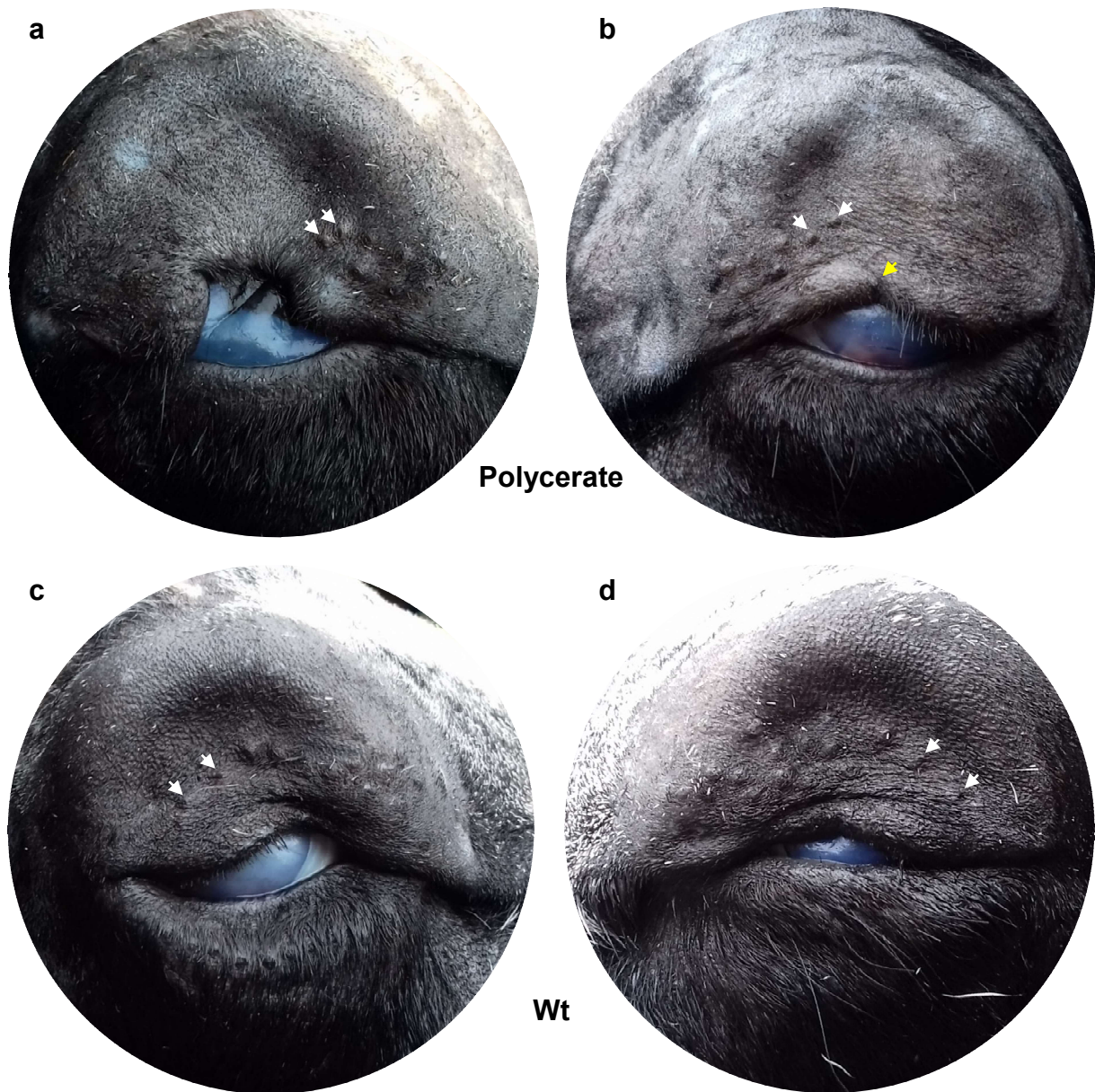
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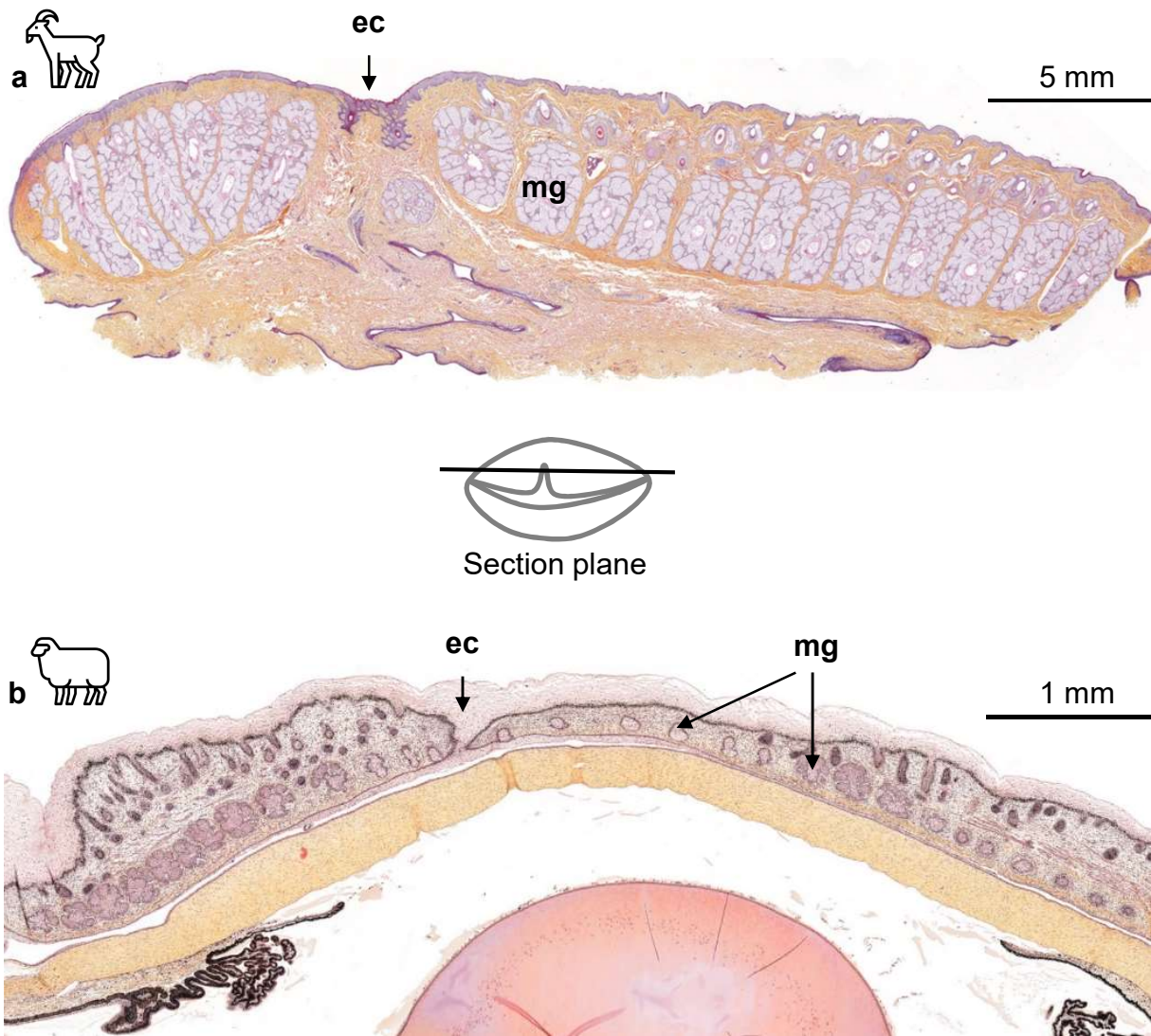
Supplementary Figure 4. Genotyping of g.115,652,290_116,155,699delins137kb in goat using PCR and electrophoresis. a) Schematic representation of the segments involved in the mutation and localization of the PCR primers on wild type (Wt) and mutant chromosomes. The coordinates of primers « Common », « Wt », and « Mut » on ARS1 genome assembly are Chr2:115,652,119-115,652,140, Chr2:115,652,323-115,652,344, and Chr5:48,545,700-48,545,722, respectively. b) Agarose gel electrophoresis of amplicons from wild type (Wt) and polycerate (Poly.) animals.



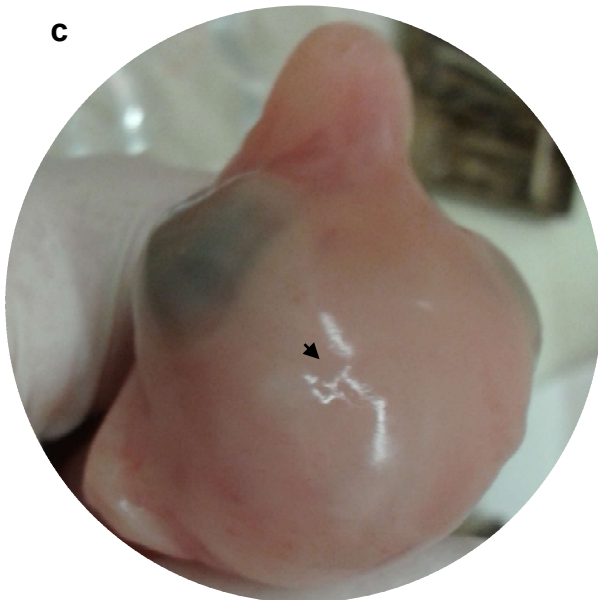
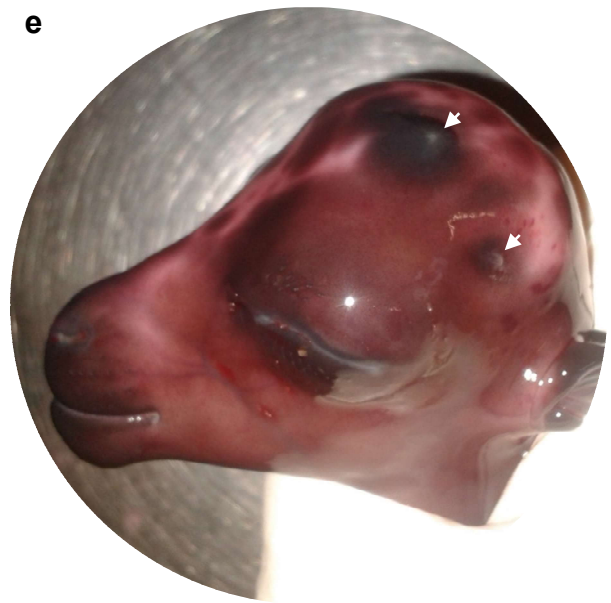
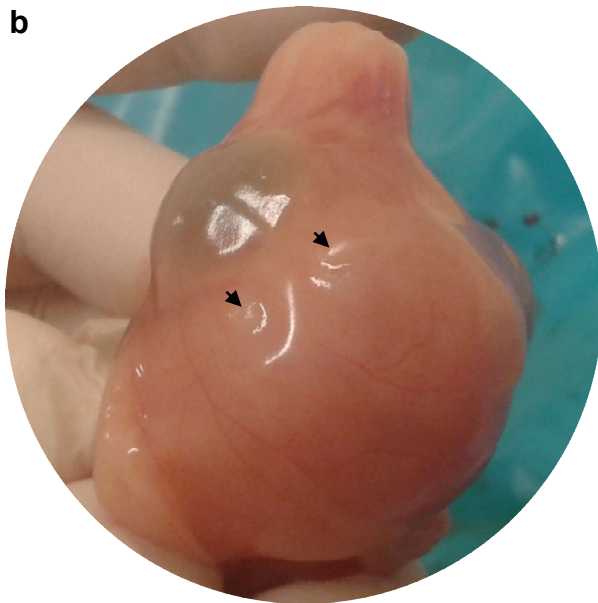
Supplementary Figure 5. Details on eyelid and eyebrow malformation in polycerate goats. Upper head of a one-week old polycerate (a, b) and a four-week old wild type (c, d) billy-goat before and after shaving. Note the splitting of the eyelid, of the two rows of vibrissae forming the eyebrow and of the horn buds (white arrows), as well as the presence of abnormally long hair forming a tuft (ht) in the polycerate individual. Black arrows point to vibrissae from the upper row of the eyebrow that are orthologous in (b) and (d). e-h) Eyelid malformation of increasing severity in adult polycerate male goats of the Provençale breed. e) absence of eyelid malformation and presence of a small hair tuft marked with arrows, f) notch in the eyelid margin and hair tuft of moderate size, g) eyelid coloboma partially hidden by a hair tuft of important size. h) Details of the eyelid in (g) after cutting the hair tuft.



Supplementary Figure 6. Details on eyelid and eyebrow malformation in polycerate sheep. Right and Left eyes of a polycerate (a, b, respectively) and a wild type (c, d, respectively) adult Jacob ewe, after shaving. Note the shortened eyebrows in the polycerate ewe as shown by the white arrows pointing to the two most posterior vibrissae. Note also the asymmetry of the eyelid defect with a large portion of the eyelid missing in (a) and only a small notch (yellow arrow) in (b). No hair tuft was observed before shaving. To our knowledge, the presence of abnormally long hair on the eyelid is only observed in polycerate goats. The white color of the cornea is due to the freezing of head samples after slaughter for conservation purpose.



Supplementary Figure 7. Histology of split upper eyelids in polycerate goats and sheep. Longitudinal section of the upper eyelid of an adult heterozygous polycerate billy-goat (a) and a heterozygous polycerate female sheep fetus at 76 dpc (b). Meibomian glands (mg) are either absent or underdeveloped in the vicinity of the eyelid coloboma (ec). Sheep and goat icons were made by “Monkik” from www.thenounproject.com.

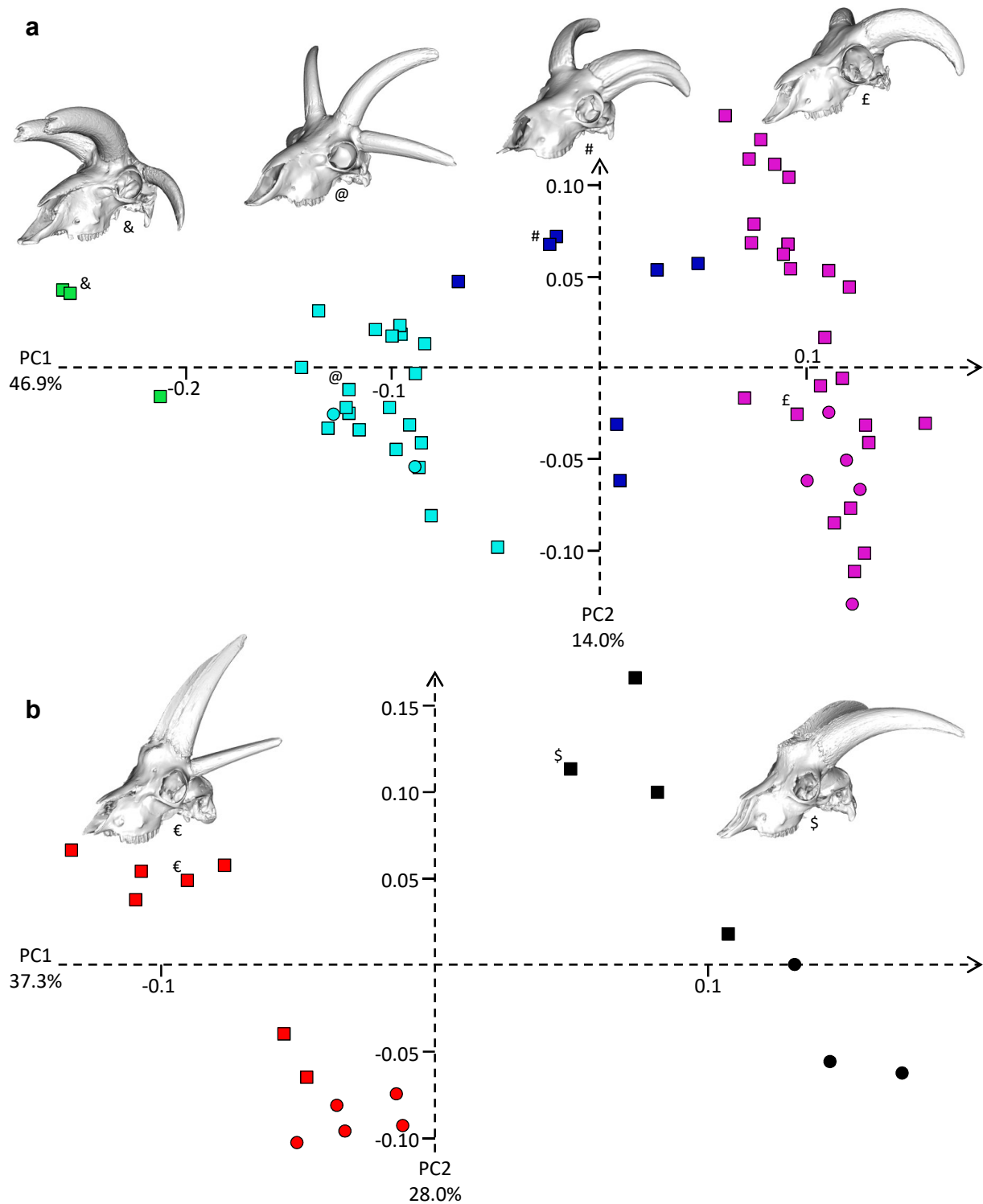


Supplementary Figure 8. Pictures of goat and sheep fetuses. a,d) General view of goat (a) and sheep (d) fetuses at 70 and 76 dpc, respectively. b, c) Head of polycerate (b) and wild type (c) goat fetuses. e, f) Head of polycerate (e) and wild type (f) sheep fetuses. Arrows indicate horn buds.

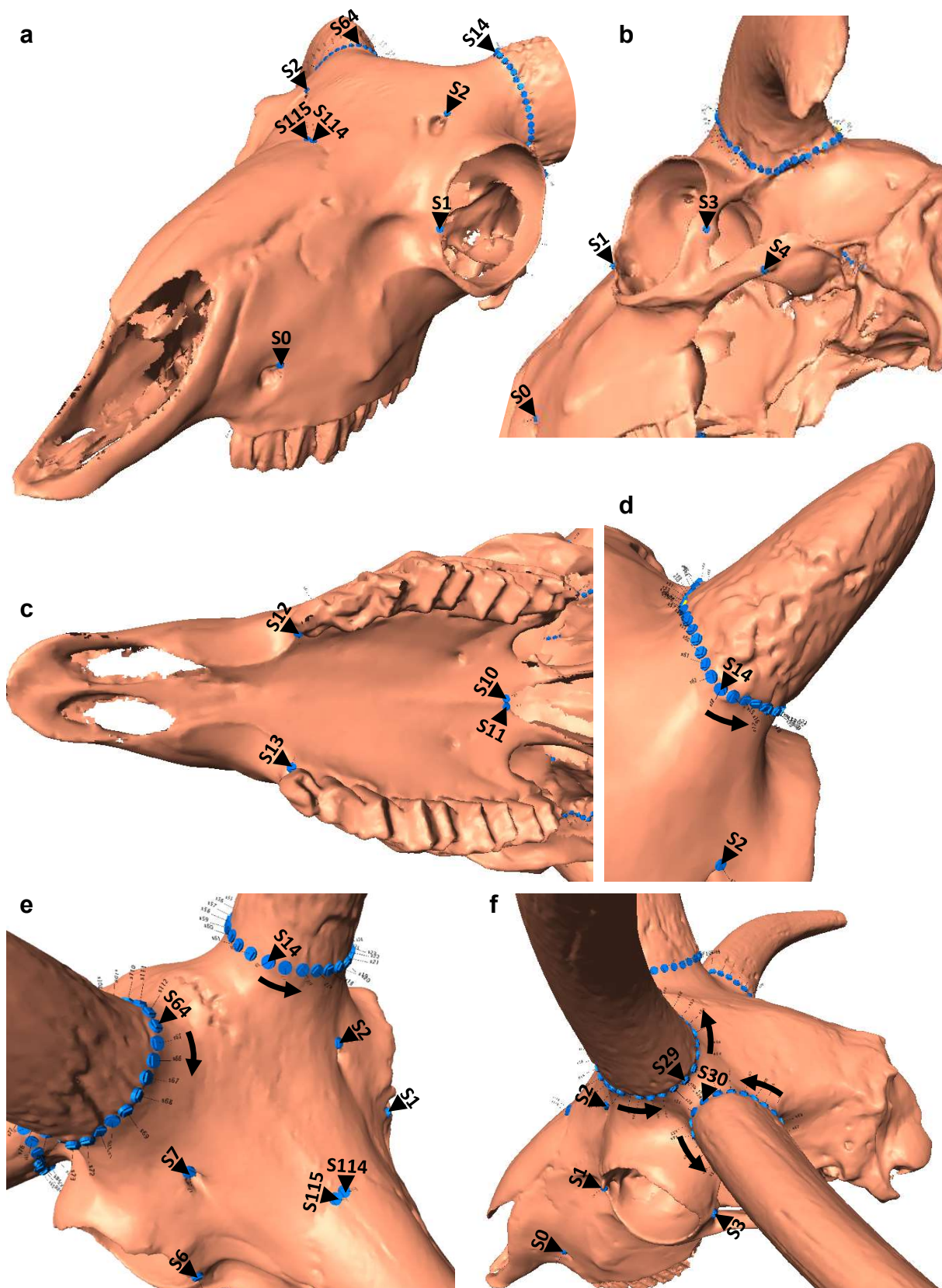
Supplementary Figure 9. cDNA (top) and amino acid (bottom) sequences for ovine wild type (Wt) and polycerate (Mut) HOXD1 alleles. Nucleotide sequences are represented in black for exon 1, red for intron 1, and blue for exon 2. Codons are labelled with alternating yellow triplets. The two nucleotides flanking the 4 bp deletion in the polycerate (Mut) allele are bolded and underlined. Boxes correspond to the RT-qPCR amplicons from intron 1 and exon 2 used for confirming intron retention. Finally, the homeobox DNA binding site of the wild type (Wt) protein is highlighted in green.

Wt	1	ATGAGCTCC TACCTCGACTACGTGTCGTGCGGCCGGGACGGCGGC GACTT GTCTGAGCTTC	60
Mut	1	ATGAGCTCC TACCTCGACTACGTGTCGTGCGGCCGGGACGGCGGC GACTT GTCTGAGCTTC	60
Wt	1	-M--S--S--Y--L--D--Y--V--S--C--G--R--D--G--G--D--L--L--S--F-	20
Mut	1	-M--S--S--Y--L--D--Y--V--S--C--G--R--D--G--G--D--L--L--S--F-	20
Wt	61	GCG CCCAAGTTCTGT CGCGCC GACGCCCGGCCCATGGTCTCTGCAG CCCGCCTT CCCCCTG	120
Mut	61	GCG CCCAAGTTCTGT CGCGCC GACGCCCGGCCCATGGTCTCTGCAG CCCGCCTT CCCCCTG	120
Wt	21	-A--P--K--F--C--R--A--D--A--R--P--M--V--L--Q--P--A--F--P--L-	40
Mut	21	-A--P--K--F--C--R--A--D--A--R--P--M--V--L--Q--P--A--F--P--L-	40
Wt	121	GGCAGCGGGC GACGGCGCGTTTGT TAGCT GCCTGCCCTGGCCGCGCGCGAGCGGGGCC	180
Mut	121	GGCAGCGGGC GACGGCGCGTTTGT TAGCT GCCTGCCCTGGCCGCGCGCGAGCGGGGCC	180
Wt	41	-G--S--G--D--G--A--F--V--S--C--L--P--L--A--A--A--R--A--G--P-	60
Mut	41	-G--S--G--D--G--A--F--V--S--C--L--P--L--A--A--A--R--A--G--P-	60
Wt	181	TCG CCCCGGCCGCCCCGGCGCAGCCT CCCCGGG CCTGCCGCGCCC GCGTAC CGCCCTGC	240
Mut	181	TCGCCCCCGGCCGCCCCGGCGCAGCCTCCCCGGG CCTGCCGCGCCC GCGTAC CGCCCTGC	240
Wt	61	-S--P--P--A--A--P--A--Q--P--P--G--P--A--A--P--A--Y--A--P--C-	80
Mut	61	-S--P--P--A--A--P--A--Q--P--P--G--P--A--A--P--A--Y--A--P--C-	80
Wt	241	CCC CTAGAGGGGGCC TACGAG CCAGGCCGCCGCACTGTCCAGGCCGGGGCGAGGACTGC	300
Mut	241	CCCCTAGAGGGGGCC TACGAGCCAGGCCGCCGCACTGTCCAGGCCGGGGCGAGGACTGC	300
Wt	81	-P--L--E--G--A--Y--E--P--G--A--A--P--V--Q--A--G--G--E--D--C-	100
Mut	81	-P--L--E--G--A--Y--E--P--G--A--A--P--V--Q--A--G--G--E--D--C-	100
Wt	301	TGC CTGCCGGGTCTGCG CCCGC TACGAGTTACCGTGC GCGCTCGGGCGGGCC GGCAGAC	360
Mut	301	TGCCTGCCGGGGTCTGCGCCCGC TACGAGTTACCGTGC GCGCTCGGGCGGGCC GGCAGAC	360
Wt	101	-C--L--P--G--S--A--P--A--Y--E--L--P--C--A--L--G--R--P--A--D-	120
Mut	101	-C--L--P--G--S--A--P--A--Y--E--L--P--C--A--L--G--R--P--A--D-	120
Wt	361	GACAGCGGGGCGCAG GTCCATTACCCGCCCCCGCCCCGGCGTCT CCCCCAAGTGT GC	420
Mut	361	GACAGCGGGGCGCAG GTCCATTACCCGCCCCCGCCCCGGCGTCT CCCCCAAGTGT GC	420
Wt	121	-D--S--G--A--H--V--H--Y--P--P--P--A--P--G--V--S--P--K--C--A-	140
Mut	121	-D--S--G--A--H--V--H--Y--P--P--P--A--P--G--V--S--P--K--C--A-	140
Wt	421	TCC CCAGCCTCCGGCCTCCCTGCCGCCTTCAGCACGTT CGAGTGGATGAAAGTGAAGAGG	480
Mut	421	TCCCAGCCTCCGGCCTCCCTGCCGCCTTCAGCACGTT CGAGTGGATGAAAGTGAAGAGG	480
Wt	141	-S--P--A--S--G--L--P--A--A--F--S--T--F--E--W--M--K--V--K--R-	160
Mut	141	-S--P--A--S--G--L--P--A--A--F--S--T--F--E--W--M--K--V--K--R-	160
Wt	481	AACGCGCCGAAGAAA AGCAATTCGCGGAGTATGGAGCCGCCACC CCCTCCAGCGCGATC	540
Mut	481	AACGCGCCGAAGAAA GTACTTGAGCCTTGACGGACGGACGCGACTGGGGTTGGGGACG	540
Wt	161	-N--A--P--K--K--S--K--F--A--E--Y--G--A--A--T--P-- S--S--A--I-	180
Mut	161	-N--A--P--K--K--S--T--*	167
Wt	541	CGCACGAATTTTCAGCACC AAGCA ACTGACAGA ACTGGAGAAGGAGTTT CATTTCAATAAG	600
Mut	541	AGCCTGCCAGCGGA ACTGAGCCGAGGGCGCGCTGCAGCGGT CCCTGTGGACGGCGGTTT	600
Wt	181	R--T--N--F--S--T--K--Q--L--T--E--L--E--K--E--F--H--F--N--K-	200
Mut			
Wt	601	TACTTAACTCGGGCCCGACGCATCGAGATAGCCA ACTCATT GCAACTGAATGACACCCAA	660
Mut	601	GGGTCTTATGGGGAACACGCGGCCCCAGGCATTATTA AACCAGGCGAATT GCATTGAGCG	660
Wt	201	Y--L--T--R--A--R--R--I--E--I--A--N--S--L--Q--L--N--D--T--Q-	220
Mut			

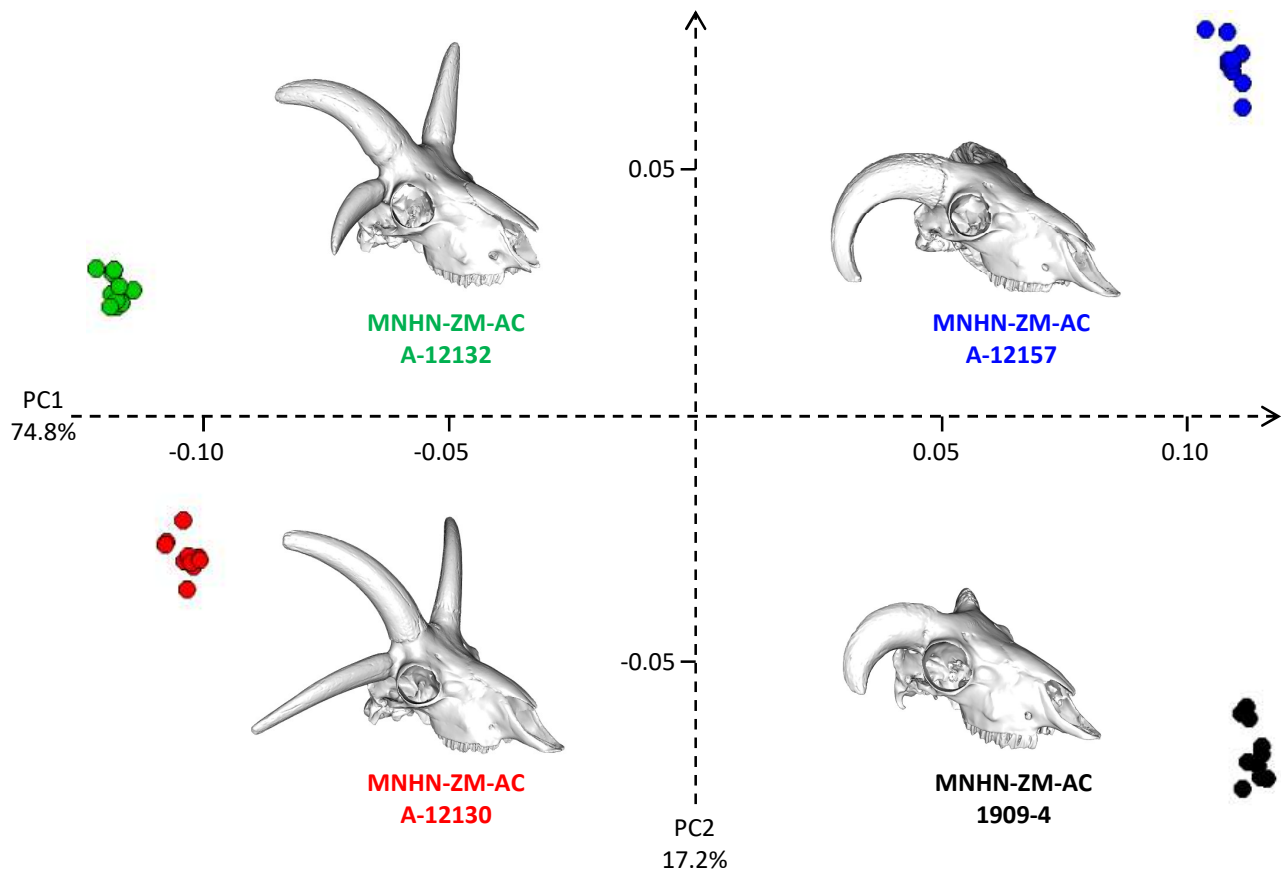
Wt	661	GTC AAAATC TGGTTCCAGAACCGCAGGATGAAACAGAAAGAAAAGGGAACGGGAAGGGCTT	720
Mut	661	TGCCCCGAATGCCAGGGGTTGAGAAAATTGCCGGAAGGAGC GCTCCGTGAAGCTTTTCTC	720
Wt	221	V--K--I--W--F--Q--N--R--R--M--K--Q--K--K--R--E-- -R--E--G--L-	240
Mut			
Wt	721	CTG CCCTCGGCCACC CCCGTGGCTTCCTTCCAGCTTCCCTCTCAGGACCGAGCCCTGCC	780
Mut	721	TTGGCACAGCTGTGTTTCGGAGGCCCAGAAGGGCCGCTCAGTAACTCTGATTCTAGTGTGG	780
Wt	241	-L--P--S--A--T--P--V--A--S--F--Q--L--P--L--S--G--P--S--P--A-	260
Mut			
Wt	781	AAG TCTGGCAAGA ACCCGGGAGCCCTCTCAGGCCCAGGAGCCATCCTGA	831
Mut	781	CCCCAAAGCTCTCCCAAGTCGCGTCTCCGTGTCATCTCGCCACGCTGACGACGCCCTGTCC	840
Wt	261	-K--S--G--K--N--P--G--S--P--S--Q--A--Q--E--P--S--*-	276
Mut			
Mut	841	TTTACGTTGCAG GGCAAATTCGCGGAGTATGGAGCCGCCACCCCCTCCAGCGC GATCCGCA	900
Wt			
Mut	901	CGAATTTTCAGCACCAAGCAACTGACAGAACTGGAGAAGGAGTTTCATTTCAATAAGTACT	960
Wt			
Mut	961	TAACTCGGGCCCGACGCATCGAGATAGCCAAC TCATTGCAACTGAATGACACCCAAGTCA	1020
Wt			
Mut	1021	AAATCTGGTTCCAGAACCGCAGGATGAAACAGAAAGAAAAGGGAACGGGAAGGGCTTCTGC	1080
Wt			
Mut	1081	CCTCGGCCACCCCGTGGCTTCCTTCCAGCTTCCCTCTCAGGACCGAGCCCTGCCAAGT	1140
Wt			
Mut	1141	CTGGCAAGAACCCGGGAGCCCTCTCAGGCCCAGGAGCCATCCTGA	1187
Wt			



Supplementary Figure 10. Intraspecific three-dimensional geometric morphometric analyses of 61 ovine (a) and 19 caprine (b) skulls. Distribution of specimens along the first two axes of the PCA. The percentages of variance explained by the two main principal components are indicated on each axis. Squares and circles represent skulls from male and female animals, respectively. a) green marks: polycerate sheep with a distance between lateral horns (dlh) larger than the distance between upper horns (duh); light blue: polycerate sheep with a $dlh \leq duh$; and blue: polycerate sheep with at least two lateral horns partially fused at their basis; purple: wild type sheep. b) red: polycerate goats; and black: wild type goats. Specimens are presented to illustrate each cluster and symbols are used to indicate their respective locations in the PCA analyses. Their respective ID in **Suppl. Table 10** are: &: Pachot_M4C_Haie; @: MNHN-ZM-AC A-12130; #: Omsr13; £: MNHN-ZM-AC A-12157; €: MNHN-ZM-AC A-12122; and \$: Bresson_M2C.



Supplementary Figure 11. Localization of selected anatomical landmarks and sliding semi-landmarks on the skulls of wild type (a-d) and polycerate (e, f) sheep. Arrows indicate the sense of the numbering of the sliding semi-landmarks around the neck of the cornual process. The definition of the whole landmarks is in Suppl. Table 11.



Supplementary Figure 12. Repeatability and reproducibility of landmark placement using PCA. A total of 116 landmarks and sliding semi-landmarks were placed ten times independently on the skulls of two polycerate and two control male sheep sampled between 1852 and 1909 in Tunisia (MNHN-ZM-AC A-12130, A12132 and 1909-4) and neighboring Algeria (MNHN-ZM-AC A12157; see **Suppl. Table 10**). The percentages of variance explained by the two main principal components are indicated on each axis. Each color corresponds to a specimen. For each skull, the inter-specimen variation on the two main axes is lower than the intra-specimen error due to differences between landmark digitalization, showing that our landmark configuration is relevant to describe shape variation within our sample.



MNHN-ZM-AC 1991-1423



MNHN-ZM-AC 1858-26



MNHN-ZM-AC 1927-18



INRAE Bresson_M4C



INRAE Pachot_M4C_Haie

Supplementary Figure 13. Comparison between the skulls of *Tetracerus quadricornis* and polycerate *Capra hircus* and *Ovis aries* individuals. a-c) skulls of males *T. quadricornis* of growing age. d, e) skulls of polycerate goat (*C. hircus* ; in mirror view) and sheep (*O. aries*) males, respectively. The ID of each specimen in the MNHN and INRAE collections is indicated on the panel. Two of the three recognized subspecies of *T. quadricornis* have additional anterior horns (Groves, 2003; Leslie and Sharma, 2009), which start to develop at 10–14 months of age in captivity (Sharma *et al.* 2005). Most male *T. quadricornis* have anterior horns $\frac{1}{4}$ to $\frac{2}{3}$ the length of their posterior horns (Sharma *et al.* 2005). Note the differences in relative placement and relative size of the anterior and posterior pairs of horns in *T. quadricornis* versus polycerate *C. hircus* and *O. aries*. Specimens MNHN-ZM-AC 1991-1423, 1858-26 and 1927-18 belong to the *Collection d'anatomie comparée du Muséum National d'Histoire Naturelle*, Paris, France while specimens Bresson_M4C and Pachot_M4C_Haie originate from the collection of INRAE UMR1313 GABI, Jouy-en-Josas, France.

Supplementary Table 1. Illumina OvineHD Beadchip genotypes used for mapping the *POLYCERATE* locus in sheep. Wt: "wild type" refers to two normal horns or two scurs. "Polycerate" refers to the existence of more than two horns or scurs. *: In Greyvenstein *et al.* 2016, individual D-003 was mistakenly registered as polycerate while it has only two horns.

No	Breed or population	Country of origin of the breed	Origin of the samples	Number of animals		
				All	Wt	Polycerate
1	Jacob	UK	Kijas <i>et al.</i> 2016	130	57	73
2	Navajo-Churro	USA	Kijas <i>et al.</i> 2016	27	14	13
3	Damara	Namibia	Greyvenstein <i>et al.</i> 2016	41	16*	25*
Total				198	87	111

Supplementary Table 2. Details on individuals considered for IBD mapping of the *POLYCERATE* locus in sheep. Illumina OvineHD Beadchip genotyping data have been downloaded from the Dryad repository (datadryad.org/stash/dataset/doi:10.5061/dryad.1p7sf and datadryad.org/stash/dataset/doi:10.5061/dryad.6t34b) and phenotypic information have been obtained from the corresponding authors of the related articles: Kijas *et al.* 2016 and Greyvenstein *et al.* 2016. Breed: D.=Damara, J.=Jacob, and N.=Navajo-Churro; Ph.:Phenotype.

ID	Breed	Ph.	ID	Breed	Ph.	ID	Breed	Ph.	ID	Breed	Ph.	ID	Breed	Ph.
D-003	D.	0	H102	J.	0	H36	N.	0	H35	J.	1	H115	J.	1
D-008	D.	0	H106	J.	0	H37	N.	0	H47	J.	1	H116	J.	1
D-010	D.	0	H112	J.	0	H42	N.	0	H48	J.	1	H118	J.	1
D-011	D.	0	H114	J.	0	H43	N.	0	H50	J.	1	H121	J.	1
D-014	D.	0	H117	J.	0	H45	N.	0	H51	J.	1	H122	J.	1
D-018	D.	0	H119	J.	0	H52	N.	0	H54	J.	1	H123	J.	1
D-023	D.	0	H120	J.	0	H58	N.	0	H55	J.	1	H124	J.	1
D-076	D.	0	H125	J.	0	Black	D.	1	H57	J.	1	H131	J.	1
D-100	D.	0	H126	J.	0	Brown	D.	1	H59	J.	1	H132	J.	1
D-101	D.	0	H127	J.	0	D-004	D.	1	H61	J.	1	H133	J.	1
D-103	D.	0	H128	J.	0	D-005	D.	1	H62	J.	1	H136	J.	1
D-104	D.	0	H129	J.	0	D-013	D.	1	H64	J.	1	H138	J.	1
DD11	D.	0	H130	J.	0	DD01	D.	1	H71	J.	1	H139	J.	1
DD12	D.	0	H134	J.	0	DD02	D.	1	H72	J.	1	H143	J.	1
DD15	D.	0	H135	J.	0	DD04	D.	1	H76	J.	1	H145	J.	1
DD16	D.	0	H137	J.	0	DD05	D.	1	H77	J.	1	H146	J.	1
H7	J.	0	H140	J.	0	DD06	D.	1	H78	J.	1	H147	J.	1
H17	J.	0	H141	J.	0	DD07	D.	1	H80	J.	1	H151	J.	1
H21	J.	0	H142	J.	0	DD08	D.	1	H83	J.	1	H155	J.	1
H34	J.	0	H144	J.	0	DD09	D.	1	H87	J.	1	H158	J.	1
H40	J.	0	H148	J.	0	DD10	D.	1	H88	J.	1	H159	J.	1
H46	J.	0	H149	J.	0	DD13	D.	1	H90	J.	1	H163	J.	1
H65	J.	0	H150	J.	0	DD14	D.	1	H91	J.	1	H164	J.	1
H66	J.	0	H152	J.	0	DD17	D.	1	H92	J.	1	H167	J.	1
H67	J.	0	H153	J.	0	DD18	D.	1	H93	J.	1	H170	J.	1
H68	J.	0	H154	J.	0	DD20	D.	1	H95	J.	1	H2	N.	1
H69	J.	0	H156	J.	0	DR02	D.	1	H96	J.	1	H8	N.	1
H70	J.	0	H157	J.	0	DR03	D.	1	H97	J.	1	H10	N.	1
H73	J.	0	H160	J.	0	DR04	D.	1	H98	J.	1	H11	N.	1
H74	J.	0	H161	J.	0	DR05	D.	1	H99	J.	1	H12	N.	1
H75	J.	0	H162	J.	0	DS02	D.	1	H100	J.	1	H14	N.	1
H79	J.	0	H166	J.	0	DS03	D.	1	H103	J.	1	H28	N.	1
H81	J.	0	H169	J.	0	H5	J.	1	H104	J.	1	H31	N.	1
H82	J.	0	H1	N.	0	H13	J.	1	H105	J.	1	H38	N.	1
H84	J.	0	H4	N.	0	H16	J.	1	H107	J.	1	H44	N.	1
H85	J.	0	H9	N.	0	H20	J.	1	H108	J.	1	H56	N.	1
H86	J.	0	H15	N.	0	H22	J.	1	H109	J.	1	H60	N.	1
H89	J.	0	H24	N.	0	H26	J.	1	H110	J.	1	H63	N.	1
H94	J.	0	H29	N.	0	H27	J.	1	H111	J.	1			
H101	J.	0	H30	N.	0	H32	J.	1	H113	J.	1			

Supplementary Table 3. Details on animals phenotyped and genotyped for validating the causative mutation of the ovine *POLYCERATE* locus. Wt: "wild type" refers to two normal horns or two scurs. "Polycerate" refers to the existence of more than two horns or scurs. Wt: wild type.

No	Breed or Population	Origin of the breed	Origin of the samples	Number of animals		
				All	Wt	Polycerate
1	Hebridean	UK	Two breeders from the Netherlands	3	-	3
2	Jacob	UK	Multiple breeders from France, Switzerland and the USA	106	19	87
3	Manx Loaghtan	UK	Three breeders from the UK and the Netherlands	32	10	22
4	Ouessant admixed with Jacob	France and UK	One breeder from Paris area, France	6	4	2
5	Navajo-Churro	USA	Multiple breeders from the USA	49	32	17
6	Ovino Quadricorna	Italy	One breeder from the Province of Frosinone, Italy	16	6	10
7	Local population from Tunis area	Tunisia	Zoological Park of Tunis, Tunisia	6	2	4
8	Damara	Namibia	Three breeders from South Africa	18	12	6
Total for sheep (<i>Ovis aries</i>)				236	85	151

Supplementary Table 4. Association between the polycerate phenotype and chromosome 2 g.132,832,249_132,832,252del allele in 236 sheep. Wt: wild type; Del: deletion of four nucleotides.

Phenotype	Breed or population	Number of animals per genotype		
		Wt/Wt	Wt/Del	Del/Del
Wild type	Jacob	19	-	-
	Manx Loaghtan	10	-	-
	Ouessant admixed with Jacob	4	-	-
	Navajo-Churro	32	-	-
	Ovino Quadricorna	6	-	-
	Local population from Tunis area	2	-	-
	Damara	12	-	-
	Total for wild type animals	85	0	0
Polycerate	Hebridean	-	2	1
	Jacob	-	73	14
	Manx Loaghtan	-	17	5
	Ouessant admixed with Jacob	-	2	-
	Navajo-Churro	-	16	1
	Ovino Quadricorna	-	9	1
	Local population from Tunis area	-	3	1
	Damara	-	5	1
Total for polycerate animals	0	127	24	
Grand total	85	127	24	

Supplementary Table 5. Analysis of nucleotide sequence conservation at the *HOXD1* exon 1 –intron 1 junction in sarcopterygians and tetrapods. The 40 last nucleotides of *HOXD1* exon 1, the splice donor site of exon 1 (bolded), and 20 additional nucleotides of intron 1 are presented for 103 species and genome assemblies obtained from the Ensembl (www.ensembl.org; release 98) and UCSC (<http://genome.ucsc.edu/>) genome browser databases.

Species	Genome Assembly	Nucleotide sequence
<i>Notamacropus eugenii</i>	macEug2	TTTGAATGGATGAAAGT G AAAAGAAACGCC CCAAGAAAA GT AAGTAAACCTTAACCTTGGG
<i>Sarcophilus harrisii</i>	sarHar1	TTTGAATGGATGAAAGT G AAAAGAAACGCC CCAAGAAAA GT AAGTAAACCTTAACCTTGGG
<i>Monodelphis domestica</i>	monDom5	TTTGAATGGATGAAAGT G AAAAGGAACGCC CCAAGAAAA GT AAGTAAACCTTAACCTTGGG
<i>Vombatus ursinus</i>	bare-nosed_wombat_genome_assembly	TTTGAATGGATGAAAGT G AAAAGAAACGCC CCAAGAAAA GT AAGTAAACCTTAACCTTGGG
<i>Phascolarctos cinereus</i>	phaCin_unsw_v4.1	TTTGAATGGATGAAAGT G AAAAGAAACGCC CCAAGAAAA GT AAGTAAACCTTAACCTTGGG
<i>Octodon degus</i>	OctDeg1.0	TTTGAGTGGATGAAAGTGAAGAGGAACACCC CGAAAAAA GT GAGTACATGGACCTGGGAGG
<i>Chrysemys picta bellii</i>	chrPic1	TTCGAGTGGATGAAAGT G AAAAGAAATGCGC CCAAGAAAA GT AAGTGTGAACCTCGGCGAGG
<i>Gopherus agassizii</i>	ASM289641v1	TTCGAGTGGATGAAAGT G AAAAGAAATGCGC CCAAGAAAA GT AAGTGTGAACCTCGGCGAGG
<i>Chelonoidis abingdonii</i>	ASM359739v1	TTCGAGTGGATGAAAGT G AAAAGAAATGCGC CCAAGAAAA GT AAGTGTGAACCTCGGCAAGG
<i>Canis lupus familiaris</i>	canFam3	TTCGAGTGGATGAAAGT G AGGAGGAGCGCC CTCGAAAA GT AAGTGC GGCCGCGGGCGGG
<i>Salvator merianae</i>	HLtupMer3	TTCGAGTGGATGAAAGT G CAAGAGGAACGCAC CTCCGAAA GT AAGCAGGGCAGCCTCCGGAG
<i>Alligator mississippiensis</i>	allMis1	TTCGAGTGGATGAAGGTGAAGAGAAACGCGC CCAGGAAA GT AAGTCTCCAGCCGGGGGAGG
<i>Crocodylus porosus</i>	CroPor_comp1	TTCGACTGGATGAAGGTGAAGAGAAACGCGC CCAGGAAA GT AAGTCTCCAGCCGGGGGGT
<i>Coturnix japonica</i>	Coturnix_japonica_2.0	TTCGAGTGGATGCGGATGAAGCGGAGCACGC CAGGCAGAA GT GAGTGGGGCGGCGGGGCGCG
<i>Numida meleagris</i>	NumMel1.0	TTCGAGTGGATGCGGATGAAGCGGAGCACGC CCGGTAGAA GT GAGTGGGGCGGCGGGGCGCG
<i>Anser brachyrhynchus</i>	ASM259213v1	TTCGAGTGGATGCGAGTGAAGCGGAGCCCGC CCGGGAGAA GT GAGTGGGGCCGCGGGGCGCG
<i>Pelodiscus sinensis</i>	PelSin_1.0	TTCGAGTGGATGAAAGTGAAGCGAAACGCAC CCACGAAA GT AAGTGTAAACCTCGGGGGGC
<i>Meriones unguiculatus</i>	MunDraft-v1.0	TTCGAGTGGATGAAAGTGAAGAGGAACGCC CCAGGAAA GT AAGGAGGTGGGCGCCGGGG
<i>Dipodomys ordii</i>	dipOrd1	TTTGAATGGATGAAAGTGAAGAGGAACGCC CTAAGAAG GT AAGTACTGGGGCGTGGGGTG
<i>Ornithorhynchus anatinus</i>	ornAna2	TTCGACTGGATGAAAGT G AAAAGAAACGCGC CCAGGAAA GT AAGTAGTCTCCTCGGCGACCT
<i>Fukomys damarensis</i>	DMR_v1.0	TTCGAGTGGATGAAAGTAAAGAGGAACGCC CTAAGAAA GT AAGTACTTGGGCGAGGGGTG
<i>Microcebus murinus</i>	micMur2	TTTGAGTGGATGAAAGTGAAGAGGAACGCC CTAAGAAA GT AAGTACGTGGGCCCTCGGGCC
<i>Manis pentadactyla</i>	manPen1	TTTGAGTGGATGAAAGTGAAGAGGAACACCC CTAAGAGAA GT AAGTACTTGGGGCCCTGGACC
<i>Otolemur garnettii</i>	otoGar3	TTTGAATGGATGAAAGTGAAGAGGAATGCC CTAAGAAA GT AAGTTGTGGGCCCTTGGATGG
<i>Propithecus coquereli</i>	Pcoq_1.0	TTTGAGTGGATGAAAGTGAAGAGGAACGCCTC CTAAGAAA GT AAGTAGTGGGCCCTTGGACCG

Supplementary Table 5, continuing

Species	Genome Assembly	Nucleotide sequence
Prolemur simus	Prosim_1.0	TTTGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTCCGTGGGCCCTTGGTCCG
Mus spretus	SPRET_EiJ_v1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGGAGGTGGGCGCTGAGGG
Mus caroli	CAROLI_EIJ_v1.1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGGAGGTGGGCGCTGAGGG
Mus musculus	GRCm38.p6	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGGAGGTGGGCGCTGAGGG
Mus pahari	PAHARI_EIJ_v1.1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGGAGGTGGGCGCTGTGGG
Rattus norvegicus	rn6	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGGAGGTGGGCGCTGGGGG
Cricetulus griseus	criGriChoV2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAGGAAAA GT AAGGAGGTGGGCGCTGGAGG
Peromyscus maniculatus bairdii	HU_Pman_2.1	TTCGAGTGGATGAAAAGTCAAGAGGAACGCC CCAAGAAAA GT AAGGAGGTGGGCGCTGGAGG
Mesocricetus auratus	MesAur1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGAAGGTGGGCGCTGGAGG
Microtus ochrogaster	MicOch1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGGAGACGGACGCTGGAGG
Mus spicilegus	MUSP714	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT AAGGGGGGGGGGGCGGGGGGG
Cavia porcellus	cavPor3	TTTGAGTGGATGAAAAGTAAAGAGGAACGCC CTAAGAAAA GT AAGTACGTGGGCGCTGGGTG
Chinchilla lanigera	ChiLan1.0	TTCGAGTGGATGAAAAGTAAAGAGGAACGCC CTAAGAAAA GT AAGTACAGGGCGCTGGTGCA
Erinaceus europaeus	eriEur2	TTCGAGTGGATGAAAAGTGAAGCGCAGCGCCC CGAAGAGAA GT AAGTCGCCGGCCCCGGGGG
Nannospalax galili	S.galili_v1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC AGAAGAAAA GT AAGTGGGTGGGCGCTGAGGG
Ictidomys tridecemlineatus	speTri2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTCGCTGGGCTCTGGATG
Urocitellus parryii	ASM342692v1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTCGCTGGGCTCTGGATG
Spermophilus dauricus	ASM240643v1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTCGCTGGGCGCTGGATG
Heterocephalus glaber	hetGla2	TTCGAGTGGATGAAAAGTGAAGAGGAATGCC CTAAGAAAA GT AAGTACTTGGGTGCCGGGTG
Tupaia belangeri	tupBel1	TTTGAGTGGATGAAAAGTGAAGAGGAATGCC CTAAGAAAA GT AAGTCCCTTGGCTTCTGATGC
Ochotona princeps	ochPri3	TTCGAGTGGATGAAAAGTGAAGAGGAACGCTC CTAAGAAAA GT AAGTGAAGTAGGGTTTAGAC
Myotis lucifugus	myoLuc2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT GAGTACTCGAGTCTTGGACG
Oryctolagus cuniculus	oryCun2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CAAAGAAAA GT AAGTACTGAGCTTTGGATGC
Sus scrofa	susScr11	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CGAAGAAAA GT AAGTACTTGGGCTCTCGACG
Vicugna pacos	vicPac2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CGAAGAAAA GT AAGTACTTGGGCCCTGGACC
Tursiops truncatus	turTru2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CGAAAAAAA GT AAGTGCTTGGGCCCTTGGACG
Ovis aries	oviAri4	TTCGAGTGGATGAAAAGTGAAGAGGAACGCGC CGAAGAAAA GT AAGTACTTGGACCTTGGACG
Capra hircus	ARS1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCGC CGAAGAAAA GT AAGTACTTGGACCTTGGACG

Supplementary Table 5, continuing

Species	Genome Assembly	Nucleotide sequence
<i>Bos taurus</i>	bosTau9	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CGAAGAAAA GT AAGTACTTGGGCCCTTGGACG
<i>Bison bison bison</i>	Bison_UMD1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CAAAGAAAA GT AAGTACTTGGGCCCTTGGACG
<i>Balaenoptera acutorostrata scammoni</i>	balAcu1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CGAAGAAAA GT AAGTACTTGGGCCCTTGGACG
<i>Felis catus</i>	felCat9	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTACTTGGGCCCTTGGACG
<i>Panthera pardus</i>	PanPar1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTACTTGGGCCCTTGGACG
<i>Pteropus vampyrus</i>	pteVam1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CGAAGAAAA GT AAGTATTTGAGCCATGGACG
<i>Mustela putorius furo</i>	musFur1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAGGAAAA GT AAGTACTTGGGCCCTCGGACC
<i>Neovison vison</i>	NNQGG.v01	TTTGAGTGGATGAAAAGTGAAGAGGAACGCC CTAGGAAAA GT AAGTACTTGGGCCCTCGGACC
<i>Ailuropoda melanoleuca</i>	ailMel1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAGGAAAA GT AAGTACTTGGGCCCTCGGACC
<i>Ursus americanus</i>	ASM334442v1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAGGAAAA GT AAGTACTTGGGCCCTCGGACC
<i>Loxodonta africana</i>	loxAfr3	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTACTTGGGTCTTGGACG
<i>Trichechus manatus latirostris</i>	triMan1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTACTTGGGCCCTTGGACG
<i>Procavia capensis</i>	proCap1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCG CTAAGAAAA GT AAGTATTTGGGCCCTTGGACA
<i>Dasypus novemcinctus</i>	dasNov3	TTCGAGTGGATGAAAAGTGAAGAGGAGCGCCT CTAGGAAAA GT AAGTGTGGGCCCTTAGACAG
<i>Equus caballus</i>	equCab3	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT GAGTACTTGGGCCGTGGATG
<i>Equus asinus asinus</i>	ASM303372v1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CCAAGAAAA GT GAGTACTTGGGCCGTGGATG
<i>Galeopterus variegatus</i>	galVar1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTACTTGGGCCGTGGATG
<i>Castor canadensis</i>	C.can_genome_v1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTACGCAGGCGTTGGATG
<i>Callithrix jacchus</i>	calJac3	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTCCCGGGCCCTTGGATG
<i>Cebus capucinus imitator</i>	Cebus_imitator-1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTCCCGGGCCCTTGGATG
<i>Saimiri boliviensis boliviensis</i>	saiBol1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCTC CTAAGAAAA GT AAGTCCCGGGCCCTTGGATG
<i>Aotus nancymaae</i>	Anan_2.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CTAAGAAAA GT AAGTCCCGGGCCCTTGGATG
<i>Homo sapiens</i>	hg38	TTCGAGTGGATGAAAAGTGAAGAGGAATGCCT CTAAGAAA GT AAGTCCCGGGCCCTTGGATG
<i>Gorilla gorilla gorilla</i>	gorGor5	TTCGAGTGGATGAAAAGTGAAGAGGAATGCCT CTAAGAAA GT AAGTCCCGGGCCCTTGGATG
<i>Pongo abelii</i>	ponAbe3	TTCGAGTGGATGAAAAGTGAAGAGGAATGCCT CTAAGAAA GT AAGTCCCGGGCCCTTGGATG
<i>Pan troglodytes</i>	panTro6	TTCGAGTGGATGAAAAGTGAAGAGGAATGCCT CTAAGAAA GT AAGTCCCGGGCCCTTGGATA
<i>Pan paniscus</i>	panPan2	TTCGAGTGGATGAAAAGTGAAGAGGAATGCCT CTAAGAAA GT AAGTCCCGGGCCCTTGGATA
<i>Nomascus leucogenys</i>	nomLeu3	TTCGAGTGGATGAAAAGTGAAGAGGAATGCCT CTAAGAAA GT AAGTCCCGGGTCCCTTGGATG

Supplementary Table 5, continuing

Species	Genome Assembly	Nucleotide sequence
Cercocebus atys	Caty_1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Ptilocolobus tephrosceles	ASM277652v2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Theropithecus gelada	Tgel_1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Mandrillus leucophaeus	Mleu.le_1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Rhinopithecus bieti	ASM169854v1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Colobus angolensis palliatus	Cang.pa_1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Rhinopithecus roxellana	rhiRox1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Nasalis larvatus	nasLar1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Chlorocebus sabaesus	chlSab2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATG
Macaca fascicularis	Macaca_fascicularis_5.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATGG
Macaca mulatta	Mmul_10	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATGG
Macaca nemestrina	Mnem_1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCGGGCCTTGGATGG
Papio anubis	papAnu4	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCAGGCCTTGGATG
Papio hamadryas	papHam1	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCT CTAAGAAAA GT AAGTCCGCAGGCCTTGGATG
Sorex araneus	sorAra2	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCTC CGAAGAAAA GT AAGTACTTGGCCCGTGGACT
Jaculus jaculus	JacJac1.0	TTCGAGTGGATGAAAAGTGAAGAGGAACGCC CGAGGAAAA GT GAGTGGTGGCGATGGATGG
Thamnophis sirtalis	thaSir1	TTCGACTGGATGAAAAGTCAAGAGGAACGCAC CCCCAAAA GT AAGTGCCGGGGCCTTGGTCAA
Notechis scutatus	TS10Xv2-PRI	TTCGAGTGGATGAAAAGTGAAGAGGAACGCCTC TCCAGAAAA GT AAGTGCAGGGCTTCGTGCGGC
Xenopus tropicalis	xenTro9	TTTGATTGGATGAAAAGTAAAAGGAACCCAC CTAAGAAAA GT AAGTCCCGCCAGCTTGATA
Xenopus laevis	xenLae2	TTTGATTGGATGAAAAGTAAAAGGAACCCCTC CTAAGAAAA GT AAGTTTTTATTAGCGCGAAA
Latimeria chalumnae	LatChal1	TTCGATTGGATGAAAGTTAAAAGAAATCCTC CCAAAA GT AAGTCTCGGTACAACAATAA
Nanorana parkeri	nanPar1	TTTGATTGGATGAAAAGTAAAACGGAACGCCTC CTAAGAAAA GT AAGTACAAAGAGATCCCATT
Conservation		** ** * * * * * * * * * * * * * * * * ** **

Supplementary Table 6. Illumina GoatSNP50 BeadChip genotypes generated for mapping the *POLYCERATE* locus in goat. Wt : "wild type" refers to the presence of two normal horns while "polycerate" refers to the existence of more than two horns. a: in these admixed populations the polycerate phenotype originates from local ancestry.

No	Breed or population	Origin of the breed	Origin of the samples	Number of animals		
				All	Wt	Polycerate
1	Local population of Massif Central admixed with African dwarf goat ^a	France	One breeder from the St Etienne area, France	1	-	1
2	Local population of Normandy admixed with Nubian goat ^a	France	Parc Animalier du Beauquet Marais, Normandy, France	5	2	3
3	Provençale	France	One breeder from Moustiers-Sainte-Marie, France	44	31	14
4	Provençale crossbred with Alpine and Saanen	France	UCEA Bressonvilliers, INRAE experimental farm, France	16	11	5
5	Rove admixed with Provençale	France	One breeder from Moustiers-Sainte-Marie, France	3	-	3
6	Population from the German Alps admixed with other breeds ^a	Germany	Tierpark Hamm, North Rhine-Westphalia and one breeder from Asendorf, Lower Saxony, Germany	5	2	3
7	Local population	Italy	One breeder from the Osimo locality, Italy	8	4	4
8	Local population	Macedonia	Two breeders from Radovis and Strumica municipalities, Macedonia	3	1	2
Total				86	51	35

Supplementary Table 7. Informatin on candidate variants for polyceraty in goat and primers used for genotyping. Genotyping was done by PCR and Sanger sequencing on a panel of 5 case-control pairs for all the variants except g.115,652,290_116,155,699delins137kb. For the latter, the genotyping was done on a panel of 77 case and 355 control animals by PCR and electrophoresis, using two primers specific of the wild type (Wt) and mutant (Mut) alleles, respectively and one primer in common. The expected size of the wild type and mutant amplicons are 226 and 197 bp respectively (see Supplementary Fig. 4). Positions refer to ARS1 goat genome assembly. Conservation : "Yes" indicates that the variant affects at least one nucleotide located within a constrained element among 103 eutherian mammals genomes according to Ensembl (www.ensembl.org; release 98) EPO-Low-Coverage track and that this nucleotide is entirely conserved among the 103 species. Genotyping : "Eliminated" refers to variants for which the derived allele was not perfectly associated with polyceraty in the panel studied. *) Despite five trials with distinct primer pairs we failed to genotype these variants because of lack of PCR amplification or amplification of multiple segments. Therefore these variants are considered as retained by default. NC: not communicated. Cons. : conservation.

Variant	Primer sequences	Cons.	Genotyping
g.115,143,545G>A	CCTTGGCTTGCCTGAATCTC CCAGCCGTATCACAGTCAGA	No	Eliminated
g.115,166,967_115,166,968insT	CGGGAGCAAAGCCTACATG CTGGAGATGGACGGTCATGA CCCGGTTTGATTCTAGGTT	No	Eliminated
g.115,186,815G>A	CTTGCAAGATCCTCCGTTTC	No	Eliminated
g.115,213,759G>C	CCTGGCTTGGAGAATTTTGA TGAAGGAACAAGGCTGACCT	No	Retained
g.115,221,938C>T	ATCACAGCGCTATGAGGGTT ACCCTTATTGTGAAATAGGCAGA	No	Retained
g.115,223,871_115,223,871insA	ACTCCAGTAAGTGCAGTCTTCA AGAAAGGAGGCAGCTGTTCT	No	Eliminated
g.115,232,184T>C	CCTGCAGTGTTATTTGGGCA GGCATACATGTGTCAGGCTG	No	Retained
g.115,269,955A>G	TCAGTGCTCAGCCTTCTTCA GTGCCACAACAGCTATCTTCT	No	Retained
g.115,283,205G>A	GCCTGTTTACAGAGAATGCCTG TTCTCCCTTCTGGCTCTGTG	No	Eliminated
g.115,285,788C>T	AAGGGCTGCTGTGTCACTAT AATCAACAGTCTCGGCTCCA	No	Eliminated
g.115,319,352A>G	TGAACAAATCCATCAGATGAGTC TCCCTTTCTTTGTTTCAGCA	No	Eliminated
g.115,337,441C>T	TCGTGTCCAGTCCTAAGCAT GCCATTGACGGATTGAGGAA	No	Retained
g.115,343,411del*	NC	No	Retained by default
g.115,349,841G>T	TTACAAGCCCAACAGTAACTC ATGGGCCGTGTGGGATCA	No	Eliminated
g.115,378,261G>A	TCCTTGTTTCATAATGAGTACT ATAATTTGACCAAAGTCAATGCA	No	Retained
g.115,393,837A>G	GTCTCAGTTCAAATGGCGGA GTCCCTTTGTCAGATCCCCA	No	Retained
g.115,401,255C>A	ACTTGGAAATGCAGAGACAGC TTCCCGTTTGATCTTTCCGC	No	Retained
g.115,406,825A>T	CGCTAACTTCGAAACACTTTGAC CCCAGCGTCCTAAGTGAAC	No	Eliminated
g.115,409,283A>G	GTCCACAACCAGTCAACACC AATCTTCCCTCCCCAGTCAC	No	Retained
g.115,417,698C>A	CTGGGGAAAGGTGTTATGGGT TGGGAATCTTTGAGGGCCAT	No	Eliminated

Supplementary Table 7, continued

Variant	Primer sequences	Cons.	Genotyping
g.115,422,038T>G	GGAGTCTAGAACCCTGAACCC TCTCCAGCCGTTATCCCTTC	No	Eliminated
g.115,459,737A>G	GGCCTGAGATCCTGTGGTAA CCCTGCGCTATTCAGTAGGA	No	Eliminated
g.115,462,622del	GGCAGCTATAGAATACACTGTGC TGCCATTCTTGTAGGTCCGT	No	Eliminated
g.115,465,345T>A	TAGCACCATGACACCACACT CCTCCATACACAACACAGCG	No	Eliminated
g.115,474,151A>C	CCATTGCTTTTCTGTGCCCT GGGAAAGCTTGGACACGTTT	No	Eliminated
g.115,560,482T>A*	NC	No	Retained by default
g.115,566,277G>A	ATCAGTGTGACAATTGCCCG AGATTTCCAGCACACTCCGA	No	Retained
g.115,570,129_115,570,130 delinsCG	TCTTTGCTTTCCCCTTCCCA CCAGTCAGTACCCACCACAT	No	Eliminated
g.115,620,572A>C	GTTGTATGCGCTGACCTGAG TCCTAGCCAAGTGATCCTGG	No	Eliminated
g.115,621,441C>T	AAGGGCAGTGGACAACATCA AACTCCAAGGTCTCTGTGC	No	Eliminated
g.115,629,515G>T	CTGGGTCTTGGGCTCTTTA GTCGCCGTGAGATTCAGTTC	No	Retained
g.115,639,463G>C*	NC	No	Retained by default
g.115,643,117C>T	TTCTGTCCCCTGCATGTCTT GGCTTACATTGTCCCCTGG	No	Eliminated
g.115,644,117T>A*	NC	No	Retained by default
g.115,646,033T>C	GAACAACAAGAACGTGGGCT TTGGCTGGAGAGTTGGATTT	No	Eliminated
g.115,652,290_116,155,699 delins137kb	CTTTCAAAGCAGTGTAATAGGA(Wt) GCATGTCTACATACTTATTTAAG(Mut) AGATATAACAAGAGCAAGACTG(Common)	Yes	Retained

Supplementary Table 8. Details on wild type and polycerate goats phenotyped and genotyped for candidate mutations. Wt: "wild type" refers to the presence of two normal horns while "polycerate" refers to the existence of more than two horns. a: In these admixed populations the polycerate phenotype originates from local ancestry. The whole panel was genotyped for mutation g.115,652,290_116,155,699delins137kb while numbers between brackets refer to individuals genotyped for the other candidate mutations detailed in **Suppl. table 7**.

No	Breed or population	Origin of the breed	Origin of the samples	Number of animals		
				All	Wt	Polycerate
1	Alpine	France	Multiple breeders from France	30	30	-
2	Corse	France	Multiple breeders from France	30	30	-
3	Local population of Massif Central admixed with African dwarf goat ^a	France	One breeder from the St Etienne area, France	5	-	5
4	Local population of Normandy admixed with Nubian goat ^a	France	Parc Animalier du Beauquet Marais, Normandy, France	7 (2)	2 (1)	5 (1)
5	Poitevine	France	Multiple breeders from France	30	30	-
6	Provençale	France	One breeder from Moustiers-Sainte-Marie, France	76 (2)	45 (1)	31 (1)
7	Provençale admixed with Alpine and Saanen	France	UCEA Bressonvilliers, INRAE experimental farm, France	16	11	5
8	Pyrénéenne	France	Multiple breeders from France	30	30	-
9	Rove admixed with Provençale	France	One breeder from Moustiers-Sainte-Marie, France	4	-	4
10	Population from the German Alps admixed with other breeds ^a	Germany	Tierpark Hamm, North Rhine-Westphalia and one breeder from Asendorf, Lower Saxony, Germany	20 (2)	9 (1)	11 (1)
11	Appenzell	Switzerland	Multiple breeders from the canton of Appenzell, Switzerland	5	5	-
12	Booted goat	Switzerland	Multiple breeders from the canton of St. Gallen, Switzerland	10	10	-
13	Capra grigia	Switzerland	Multiple breeders from the canton of Ticino, Switzerland	10	10	-
14	Grisons striped	Switzerland	Multiple breeders from the canton of Grisons, Switzerland	10	10	-
15	Nera verzasca	Switzerland	Multiple breeders from the canton of Ticino, Switzerland	10	10	-
16	Peacock goat	Switzerland	Multiple breeders from the canton of St. Gallen, Switzerland	10	10	-
17	Saanen	Switzerland	Multiple breeders from France	30	30	-

Supplementary Table 8, continued

No	Breed or population	Origin of the breed	Origin of the samples	Number of animals		
				All	Wt	Polycerate
18	Toggenburg	Switzerland	Multiple breeders from the canton of St. Gallen, Switzerland	10	10	-
19	Valais blackneck	Switzerland	Multiple breeders from the canton of Valais, Switzerland	10	10	-
20	Local population	Italy	One breeder from the Osimo locality, Italy	23 (2)	10 (1)	13 (1)
21	Local population	Croatia	Four breeders from the Benkovac municipality, Croatia	22	22	-
22	Local population	Macedonia	Two breeders from Radovis and Strumica municipalities, Macedonia	7 (2)	4 (1)	3 (1)
23	Angora	Turkey	Multiple breeders from France and Germany	17	17	-
24	Boer	South Africa	Multiple breeders from Switzerland	10	10	-
Total				432 (10)	355 (5)	77 (5)

Supplementary Table 9. Association between the polycerate phenotype and chromosome 2 g.115,652,290_116,155,699delins137kb in 432 goats. Wt: wild type; Indel: deletion of 503 kb and insertion of 137 kb. a: In these admixed populations the polycerate phenotype originates from local ancestry.

Phenotype	Breed/Population	Number of animals per genotype		
		Wt/Wt	Wt/Indel	Indel/Indel
Wild type	Alpine	30	-	-
	Corse	30	-	-
	Local population of Normandy admixed with Nubian goat ^a	2	-	-
	Poitevine	30	-	-
	Provençale	45	-	-
	Provençale admixed with Alpine and Saanen	11	-	-
	Pyrénéenne	30	-	-
	Population from the German Alps admixed with other breeds ^a	9	-	-
	Appenzell	5	-	-
	Booted goat	10	-	-
	Capra grigia	10	-	-
	Grisons striped	10	-	-
	Nera verzasca	10	-	-
	Peacock goat	10	-	-
	Saanen	30	-	-
	Toggenburg	10	-	-
	Valais blackneck	10	-	-
	Local population from Italy	10	-	-
	Local population from Croatia	22	-	-
	Local population from Macedonia	4	-	-
Angora	17	-	-	
Boer	10	-	-	
Total for wild type animals		355	0	0
Polycerate	Local population of Massif Central admixed with African dwarf goat ^a	-	5	-
	Local population of Normandy admixed with Nubian goat ^a	-	5	-
	Provençale	-	31	-
	Provençale admixed with Alpine and Saanen	-	5	-
	Rove admixed with Provençale	-	4	-
	Population from the German Alps admixed with other breeds ^a	-	11	-
	Local population from Italy	-	13	-
	Local population from Macedonia	-	3	-
Total for polycerate animals		0	77	0
Grand total		355	77	0

Supplementary Table 10. Details on caprine and ovine skull specimens considered in the morphometric analyses. “ID” corresponds to the reference of the skull in its collection of origin. ENVA: Musée Fragonard, Ecole Nationale Vétérinaire de Maisons-Alfort, France; Halle: Domestic Animal Collections from the Central Natural Science Collections, Martin Luther University Halle-Wittenberg, Halle, Germany; INRAE: collection of INRAE UMR1313 GABI, Jouy-en-Josas, France; MNHN-ZM-AC: Collection d’anatomie comparée du Muséum National d’Histoire Naturelle, Paris, France; MZS: collection d’anatomie du Musée Zoologique de Strasbourg, France; ONIRIS: collection d’anatomie d’ONIRIS, Nantes, France. The horn formula provides information on the number and localisation of the horns on the left and right sides of the skulls, respectively, separated by a “;”. Each “1” designate a horn while brackets indicate fusions between the bases of neighbouring horns. Year: Year of death or of entry in the collection. Juv.: juvenile individuals have between 6 and 12 months of age approximately. Ad.: Adult. Scan: method used for the digitization of the skull, with A: Artec Eva structured-light scanner, B: Breuckmann StereoScan structured light scanner, and P: photogrammetry (see Methods). ND: missing information.

Phenotype, sex & species	Collection-ID	Scan	Horn formula	Breed or population	Year	Age
Polycerate male sheep	MNHN-ZM-AC-1845-266	B	(111);11	ND	1845	Ad.
	ENVA A-IV-N23	B	11;11	Jacob	1903	Ad.
	ENVA A-IV-N25	B	11;11	Jacob	1903	Ad.
	MNHN-ZM-AC-A-12126	B	11;11	Local population from Tunis, Tunisia	1884	Ad.
	MNHN-ZM-AC-A-12127	B	11;11		1884	Ad.
	MNHN-ZM-AC-A-12128	B	11;11		1884	Ad.
	MNHN-ZM-AC-A-12130	B	11;11		1884	Ad.
	MNHN-ZM-AC-A-12131	B	11;11		1884	Ad.
	MNHN-ZM-AC-A-12132	B	11;11		1884	Ad.
	MNHN-ZM-AC-A-12133	B	11;11		1884	Ad.
	MNHN-ZM-AC-A-12195	B	11;111		1902	Ad.
	MNHN-ZM-AC-A-12196	B	11;11		1902	Ad.
	MNHN-ZM-AC-ae781	B	11;11		ND	ND
	MZS-Mam-03721	B	11;11	Local population from Erzurum, Turkey	1910	Ad.
	MZS-Mam-01566	B	11;11	Unknown	1907	Ad.
	MZS-Az15	B	11;11	Jacob	2001	Ad.
	MZS-Ovi015	B	11;11	Jacob	2003	Juv.
	INRAE-Pachot M4C Haie	B	11;11	Jacob	2017	Ad.
	Halle-Ofswi1	A	11;11	Indian fat-tailed	1882	Ad.
	Halle-Ofswi3	A	11;(11)	Indian fat-tailed	1885	Ad.
	Halle-Ofswi8	A	11;(11)	Indian fat-tailed	1888	Ad.
	Halle-Ofswi9	P	11;11	Indian fat-tailed	1888	Juv.
	Halle-Oprs1	A	11;11	Persian	1899	Juv.
	Halle-Osom72	A	11;11	Somali	ND	Ad.
	Halle-Opru1	A	11;11	Local population from Peru	1883	Ad.
	Halle-Omsr13	A	(111);11	Local population from Masuria, Poland	1894	Ad.
	Halle-Opmm1	A	11;11	Pommeranian sheep	1909	Ad.
	Halle-O20b	A	11;11	German sheep	1888	Ad.
	Halle-Omf183	A	(11);(11)	Mufflon cross	1889	Ad.
	Halle-Our53	P	(11);(11)	Urial x Rambouillet	1891	Juv.
Polycerate female sheep	INRAE-Pachot F4C	B	11;11	Jacob	2017	Ad.
	Halle-Ojak2	A	11;11	Jacob	1995	Ad.

Supplementary Table 10, continued

Phenotype, sex & species	Collection-ID	Scan	Horn formula	Breed or population	Year	Age
Wild type male sheep	MNHN-ZM-AC-1909-4	B	1;1	Local population from Tunis, Tunisia	1909	Ad.
	MNHN-ZM-AC-1904-200	B	1;1	ND	1904	Ad.
	MNHN-ZM-AC-1945-88	B	1;1	Corsican mouflon	1945	Ad.
	MNHN-ZM-AC-2000-438	B	1;1	Corsican mouflon	1989	Ad.
	MNHN-ZM-AC-A-12151	B	1;1	Corsican mouflon	ND	Ad.
	MNHN-ZM-AC-A-12157	B	1;1	Local population from Algeria	1852	Ad.
	MNHN-ZM-AC-A-12177	B	1;1	Scottish blackface	1891	Ad.
	MNHN-ZM-AC-A-12187	B	1;1	Local population from Gascony, France	1902	Ad.
	MNHN-ZM-AC-A-12188	B	1;1	Local population from France	ND	Ad.
	MNHN-ZM-AC-A-12193	B	1;1	Local population from France	1884	Ad.
	MNHN-ZM-AC-A-12194	B	1;1	Local population from the Morvan Massif, France	1884	Ad.
	MNHN-ZM-AC-Astrakan2	B	1;1	Astrakhan	ND	Ad.
	ONIRIS-ENVN_Ouessant	B	1;1	Ouessant	1990	Ad.
	Halle-Ofswi7	A	1;1	Indian fat-tailed	1886	Ad.
	Halle-Okar22	A	1;1	Karakul	1923	Ad.
	Halle-Omf116	A	1;1	Mouflon cross	1888	Ad.
	Halle-Omf138	A	1;1	Mouflon cross	1887	Ad.
	Halle-Omsr15	A	1;1	Mauritian	1895	Ad.
	Halle-Ongr11	A	1;1	Negretti	1882	Ad.
	Halle-Orbag288	A	1;1	Rambouillet x Argali	1906	Ad.
Halle-Osh10	A	1;1	Shetland	1904	Ad.	
Halle-Osom71	A	1;1	Somali	1924	Ad.	
Halle-Okar153	A	1;1	Karakul	1930	Ad.	
MNHN-ZM-AC-A-12173	B	1;1	Astrakhan	1884	Ad.	
Wild type female sheep	MNHN-ZM-AC-A-12179	B	1;1	Local population from Iceland	1891	Ad.
	MNHN-ZM-AC-A-12224	B	1;1	Local population from Mycenae, Greece	1887	Ad.
	INRAE-Pachot_F2C	B	1;1	Jacob	2017	Ad.
	MNHN-ZM-AC-A-12172	B	1;1	Astrakhan	1884	Ad.
	Halle-O14	A	1;1	Local population from Germany	1899	Ad.

Supplementary Table 10, continued

Phenotype, sex & species	Collection-ID	Scan	Horn formula	Breed or population	Year	Age
Polycerate male goats	MNHN-ZM-AC-1875-630	B	11;11	ND	1875	Ad.
	MNHN-ZM-AC-1906-141	B	11;11	ND	1906	Ad.
	MNHN-ZM-AC-A-12122	B	11;11	ND	1884	Ad.
	INRAE-Bresson_M4C	B	11;11	Provençale X Alpine	2017	Ad.
	MZS-Mam-03727	B	11;11	Unknown, animal raised in the Zoological Garden of Strasbourg	1896	Ad.
	Halle-Csom3	P	11;11	Somali x German spotted goat	1913	Juv.
	Halle-CSom2	A	11;11	Somali x German spotted goat	1914	Ad.
Polycerate female goats	Halle-C10	A	11;11	German white goat	2013	Ad.
	Halle-C11	A	11;11	German spotted goat	2013	Ad.
	Halle-CohneNr10	A	11;11	German goat	ND	Juv.
	MNHN-ZM-AC-A12124	B	11;11	ND	<1884	Ad.
	Halle-Cbz40	P	11;11	crossbreed#: Bezoar multicross	1991	Juv.
Wild type male goats	MNHN-ZM-AC-1884-2144	B	1;1	ND	1884	Ad.
	MNHN-ZM-AC-1905-276	B	1;1	ND	1905	Ad.
	INRAE-Bresson_M2C	B	1;1	Provençale X Saanen, France	2017	Ad.
	ONIRIS-ENVN_PIS	B	1;1	Saanen	1990	Ad.
Wild type female goats	Halle-C15	A	1;1	House goat, Germany	ND	Ad.
	Halle-C16	A	1;1	House goat, Germany	ND	Ad.
	Halle-C19	A	1;1	House goat, Germany	ND	Ad.

Supplementary Table 11. Definition and designation on each side of the skull of the anatomical landmarks and sliding semi-landmarks used in the analyses. Landmarks placement is illustrated in **Suppl. Fig. 11**.

Landmarks		Definition
left	right	
s0	s5	Most dorsal point of the <i>Foramen infraorbitale</i>
s1	s6	<i>Processus lacrimalis caudalis</i> (Process on Margo supraorbitalis of the lacrimal bone)
s2	s7	Most dorsal point of the lateral <i>Foramen supraorbitale</i>
s3	s8	Most caudal point of the fronto-zygomatic suture (<i>sutura frontozygomatica</i>)
s4	s9	Caudo-lateral point of the temporo-zygomatic suture (<i>sutura temporozygomatica</i>)
s10	s11	Most caudal point of the horizontal plate (<i>lamina horizontalis</i>) of the palatine bone
s12	s13	Most caudal point of the <i>Margo interalveolaris</i> , connection with the first premolar tooth
s14	s64	Neck of the cornual process (<i>collum processus cornualis</i>)
s15 to s63	S65 to s113	<p>Points s15-s63 (resp. s65-s113) were placed round the suture line between the <i>processus cornualis</i> and the frontal bone, starting with point s14 (resp. s64) and turning in a dextral rotation (resp. sinister rotation) from the orbit and towards the back of the skull. Point s63 (resp. s113) overlays with point s14 (resp. s64) to close the loop.</p> <p>When the animal had four separated horns, landmarks were positioned for the two horns located on the same side as follows: the frontal half circle of the upper horn was made between landmarks s14 (resp. s64) and s29 (resp. s79) ; the latter being ventral on the upper horn and closest to the lower horn. Then landmark s30 (resp. s80) was placed just opposite, on the lower horn (at the most dorsal level of it). Landmarks s31 (resp. s81) to s50 (resp. s100) were positioned on the lower horn, turning forward and downward, then coming back up. Landmark s50 (resp. s100) was set to landmark s30 (resp. s80) to close the loop. Then Landmark s51 (resp. s81) was positioned on landmark s29 (resp. s79) of the upper horn and the last half circle was completed on the caudal part of the upper horn with landmarks s51 (resp. s101) to s63 (resp. s113).</p>
s114	s115	Most medial point of the fronto-nasal suture (<i>sutura frontonasalis</i>)

Supplementary Table 12. List of four-horned polycerate male sheep genotyped for the causative mutation and phenotyped for the distance between the lateral horns on the left side (dlhl) and for the distance between the upper horns (duh).

No	Breed or population	Heterozygous Polycerate		Homozygous Polycerate		Total
		DIhl ≤ duh	DIhl > duh	DIhl ≤ duh	DIhl > duh	
1	Jacob	11	-	1	6	18
2	Manx Loaghtan	2	-	-	4	6
3	Ouessant admixed with Jacob	2	-	-	-	2
4	Ovino Quadricorna	2	-	-	1	3
Total		17	0	1	11	29

Supplementary Table 13. Details on whole genome sequences considered in the present study. Ovine and caprine control individuals collected for the present analyses originate from all around the world. a) 401 individuals from the original dataset were not considered : one Navajo-Churro and two Tibetan animals with unknown phenotypes were eliminated because of the occurrence of polycerate animals in these breeds, as well as 398 animals of unknown or composite breeds. b) These animals belong to the Chinese Sishui Fur sheep breed.

Species	NCBI Bioproject or url	File format	Nb of cases	Nb of controls
Goat	www.goatgenome.org/vargoats_data_access.html	VCF	-	1160
	PRJEB39341	FASTQ	1	-
Total for goat			1	1160
Sheep	PRJEB6025	VCF	-	180
	PRJEB6495	VCF	-	14
	PRJEB9911	FASTQ	-	3
	PRJEB14098	FASTQ	-	7
	PRJEB14418	FASTQ	-	24
	PRJEB15642	VCF	-	10
	PRJEB23437	VCF	-	99
	PRJEB31241	VCF	-	535 ^a
	PRJEB31930	FASTQ	-	6
	PRJEB32110	FASTQ	-	26
	PRJEB35553	FASTQ	-	2
	PRJEB35682	FASTQ	-	20
	PRJEB37460	FASTQ	-	3
	PRJNA624020	FASTQ	10 ^b	250
PRJEB39341	FASTQ	1	-	
Total for sheep			11	1179

Supplementary Table 14. Information on transgenic mouse strains and details on PCR primers used for genotyping purpose. Mut: amplicon encompassing Chr2 g.74,768,587_75,133,794del (mutant allele) ; Wt: segment encompassing the proximal breakpoint of Chr2 g.74,768,587_75,133,794del (wild type allele).

Name of the strain	Name in original publication	Reference	Primer sequences
<i>Hoxd1^{Lac}</i>	<i>Hoxd1^{tm1Ddu}</i>	Zákány <i>et al.</i> , 2001	GAGTTTCTCTTTGCTGTAATGAAGAGCT TCACATTCTCCACGGGCAAGCC
BAC ^{<i>HoxD</i>}	TgBAC ^{<i>HoxD</i>}	Schep <i>et al.</i> , 2016	ACAGCTGCCTCTGTGGCCTC ATTACGCCAGCTGGCGAAAGGG
BAC ^{<i>Mtx2</i>}	-	This work	ACAGCTGCCTCTGTGGCCTC ATTACGCCAGCTGGCGAAAGGG
<i>HoxD^{Del(151kb)lac}</i>	Del(tpSB2-attP)	Andrey <i>et al.</i> , 2013	ACTAGCCAGATCCAATGGACC CTATTACGCCAGCTGGCGAAAGG
<i>HoxD^{Del(365kb)}</i>	-	This work	GCCTGCACCTATGCAGTTTGAAAGG CTCACAGAGTTCCTTAAACACTCCGAG (Mut) CTGTTGAGTACATCCTATCATCAGGAGC CTCAAAGTTGGGAGAAAGCAACAGTGC (Wt)

Supplementary Table 15. Details on PCR primers used for confirming the nucleotide sequence at the fusion points of variant g.115,652,290_116,155,699delins137kb. See Supplementary Fig. 3 for a scheme of the segments involved in the mutation and the corresponding fusion points identified with letters A to D.

Fusion point	Primer sequences
A	GTTTAAAAGGTGGGGGAAGG/GTTTCAGGCATGCAACACAG
B,C,D	CATCCTGCAGCCTGTGAGTA/GGTGTCATCCCCTGTCTCAG

Supplementary Table 16. Details on primers used for quantitative RT-PCR analyses.

Species	Name of gene and primer pairs	Primer sequences	Amplicon size in bp
Sheep	OAR_HOXD1_exon2	GTTGGCTATCTCGATGCGTC GATCCGCACGAATTTCAAGCA	100
Sheep	OAR_HOXD1_intron1	GCTCCTTCGGCAATTTTCT CGGTTTGGGTCTTATGGGGA	107
Goat	CHI_HOXD1_exon2	CCCTTCCCGTTCCCTTTTCT GACGCATCGAGATAGCCAAC	101
Sheep	OAR_HPRT1	GCCACCCATCTCCTTCATCA TGCTGAGGATTTGGAGAAGGT	94
Goat	CHI_HPRT1	TGGACTAATTATGGACAGGACCG TATAGCCCCCCTTGAGCACA	101
Sheep	OAR_H2AFZ	TAAAGCGTATTACCCCTCGTCA CACCACCAGCAATTGTAGCC	90
Goat	CHI_H2AFZ	GCGTATTACCCCTCGTCACTTG CAGCAATTGTAGCCTTGATGAGA	80
Both	GAPDH	CACTACCATGGAGAAGGCTGG GTGGTTCACGCCATCACA	106
Both	YWHAZ	GGAGCCCGTAGGTCATCTTG CTCGAGCCATCTGCTGTTTTT	85
Both	RPLP0	TCTCCTTCGGGCTGGTCAT AGGAAGCGGGAATGCAGAGT	100

Supplementary Note 1

Absence of homozygous mutants at variant g.115,652,290_116,155,699delins137kb amongst 77 polycerate goats.

Despite a continuous selection for polyceraty in most of the sampled herds, homozygous mutants were never observed amongst 77 polycerate animals for variant g.115,652,290_116,155,699delins137kb. Based on breeders' records, 14 of these goats were born from two polycerate parents while the other individuals were born from wild type x polycerate mating or from unknown sire with polycerate dam (i.e. when several mature males of different phenotypes are present in the same herd). Assuming that all the parents were heterozygous for variant g.115,652,290_116,155,699delins137kb, a Mendelian transmission would have generated 33% (i.e. $25\% / (50\% + 25\%)$) of homozygous mutant animals amongst the 14 polycerate goats born from polycerate parents. Considering a binomial law with parameters $n=14$ and $p=0.33$, the probability of not observing any homozygote is: 3.4×10^{-3} .

This strong presumption of homozygous lethality was supported by the analysis of a 365-kb deletion in mouse (g.74,768,587_75,133,794del on Chr2; murine genome assembly mm10), largely overlapping the orthologous 503-kb genomic segment absent in polycerate goats (g.115,652,290_116,155,699delins137kb on Chr2; **Fig. 1** of this note). Genotyping this variant at birth, in 42 animals derived from heterozygous parents did not identify any homozygous condition for the mutant allele, while at least 25% were expected (binomial $p=5.7 \times 10^{-6}$ with parameters $n=42$ and $p=0.25$; **Table 1** of this note).

Mtx2 is the only protein-coding gene affected by the two deletions and morpholino knockdown of this gene in zebrafish is lethal at gastrulation (Wilkins et al. 2008). Altogether, these results indicate that the lack of *Mtx2* causes early embryonic death, which explains the absence of live homozygous mutants amongst the caprine and murine panels studied.

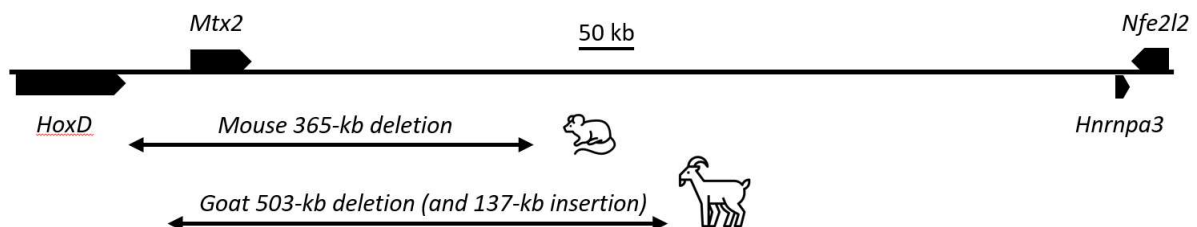


Fig. 1 of Suppl. Note 1. Details on the 365-kb deletion encompassing *Mtx2* in mouse. Murine and caprine orthologous segments of chromosome 2 with relative localizations of mouse g.74,768,587_75,133,794del and goat g.115,652,290_116,155,699delins137kb variants. Mouse and goat icons were made by "Monkik" from www.thenounproject.com.

Number of animals per genotype			
Wt/Wt	Wt/Del	Del/Del	Total
12	30	0	42

Table 1 of Suppl. Note 1. Results of the genotyping at birth of 42 mice born from mating between animals that were heterozygous for a 365-kb deletion encompassing *Mtx2*.

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