

Supplemental Materials

Supplemental Table 1. Clinical information of the DDH patients carrying *LRPI* variants.

Supplementary Fig. 1. Information and radiographic features of the DDH patients carrying *LRPI* variants.

Supplementary Fig. 2. *LRPI* variants in DDH. a) Pedigrees and Sanger sequencing results of two families carrying heterozygous *LRPI* missense variants. The position of each variant is indicated by an arrow in the sequence chromatogram. (b) Amino acid alignments in different species around the missense variant. p.R1783 and p.T2129 are highly evolutionarily conserved. (c) *LRPI* variants identified in non-familial DDH patients.

Supplementary Fig. 3. Data on the *Lrp1* model mice. a) Sanger sequencing of heterozygous and homozygous *Lrp1*^{R1783W} mice their wild-type littermates (WT). b) Western blot for *Lrp1*. Hip articular tissues were isolated from heterozygous (HET) and homozygous (HOM) *Lrp1*^{R1783W} mice and *Lrp1*^{+/-} mice, and their WT littermates at age 4 weeks. WT1 and WT2 are littermates of KI and *Lrp1*^{+/-} mice, respectively. Relative protein levels were determined by a density analysis. Values are means ± SD for 3 independent experiments (n = 9). *p < 0.05; **p < 0.01; ***p < 0.0001.

Supplementary Fig. 4. Acetabulum of *Lrp1*^{R1783W} mice and their wild-type littermates at 8 weeks. Homozygous KI and heterozygous KI mice showed similar views with their WT littermates.

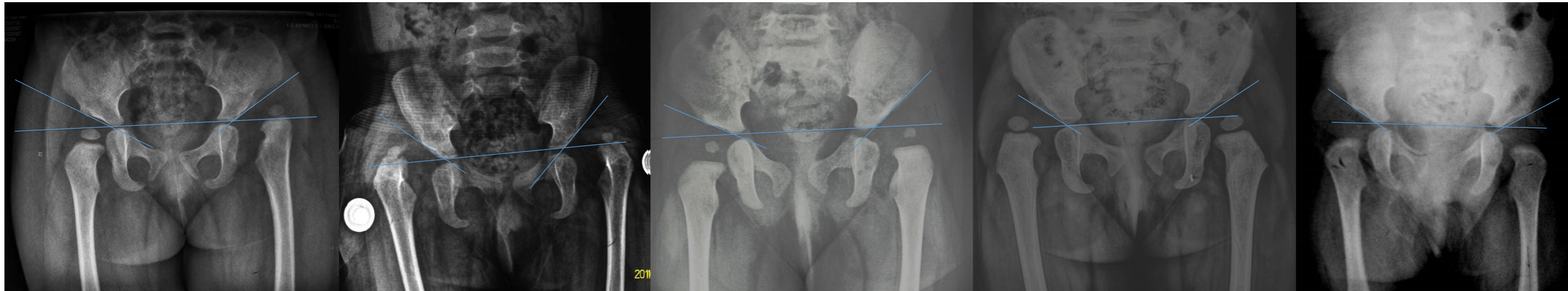
Supplementary Fig. 5. The Alizarin red staining and Alcian blue staining of ADTC5 after the chondrogenic differentiation induced with 1% ITS for 7 days. The positive results of Alcian blue staining and negative results of Alizarin red staining indicating that the cells differentiated into chondrocytes under the induction of chondrogenic differentiation medium. Scale bar for 4x: 500 μm , for 40x: 50 μm

Supplementary Fig. 6. Western-blot for levels of autophagy and β -catenin in chondrogenesis induced ADTC5 cells on day 1, 4, 7, 10, and 12.

Supplementary Fig. 7. Western-blot for levels of upstream proteins (p-GSK3 β , Lrp6, Dvl2 and GSK3 β) of β -catenin in Wnt signaling.

Supplement Table 1. Clinical information of the DDH patients carrying *LRPI* variants.

Patient No.	Age	Site	Acetabulum index	
			Left	Right
2621	2 years 1 month	Bilateral	43	40
2726	1 year 5 months	Left	34	28
3193	5 months	Right	25	30
3151	4 months	Left	42	27
3211	6 months	Right	28	32
3196	8 months	Left	37	26
3161	1 year 8 months	Bilateral	30	33
3174	1 year	Right	31	41
3210	1 year 6 months	Bilateral	32	34



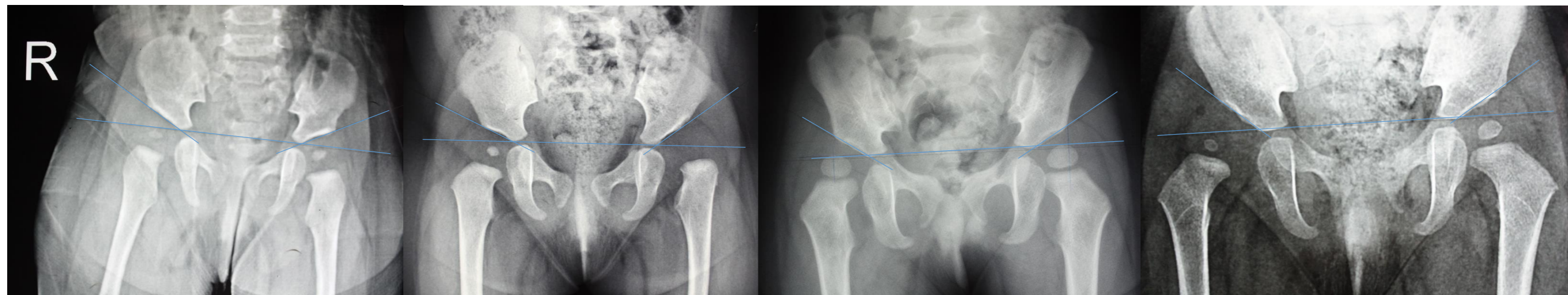
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3211

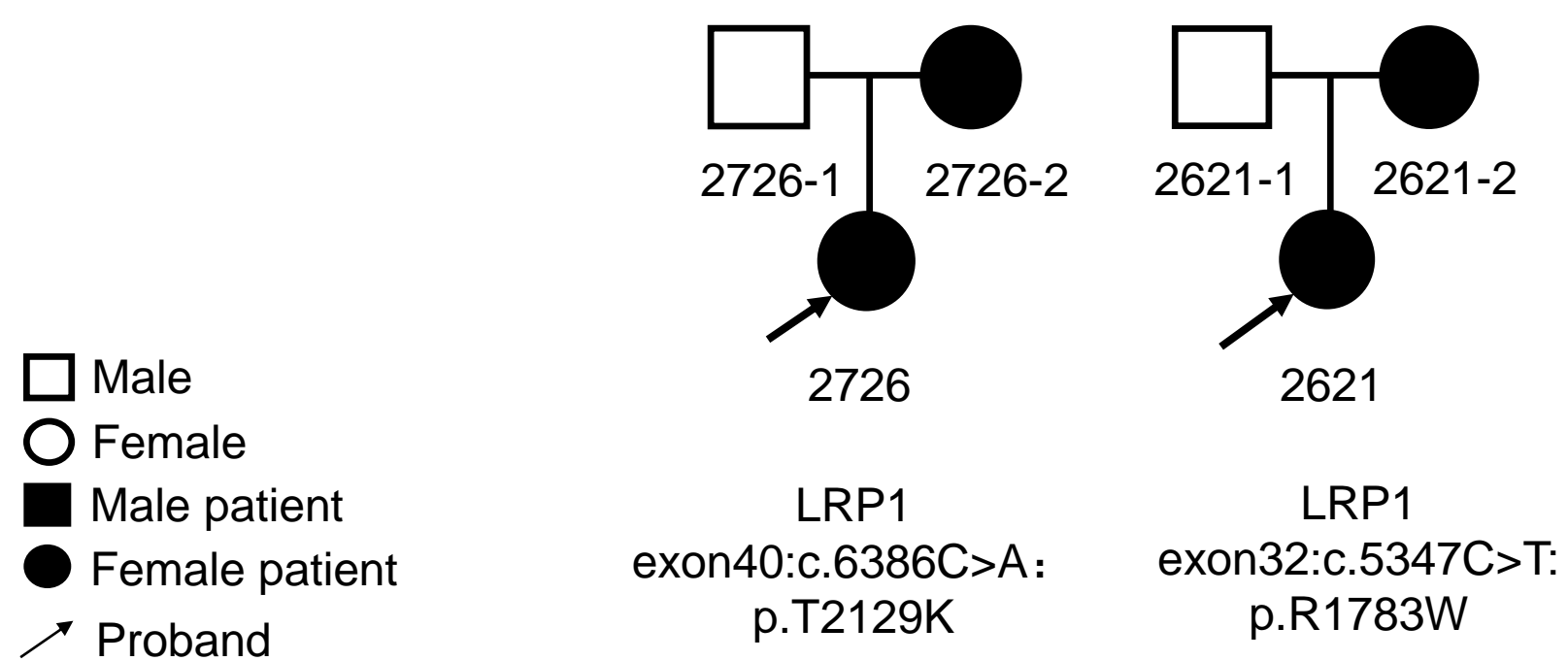


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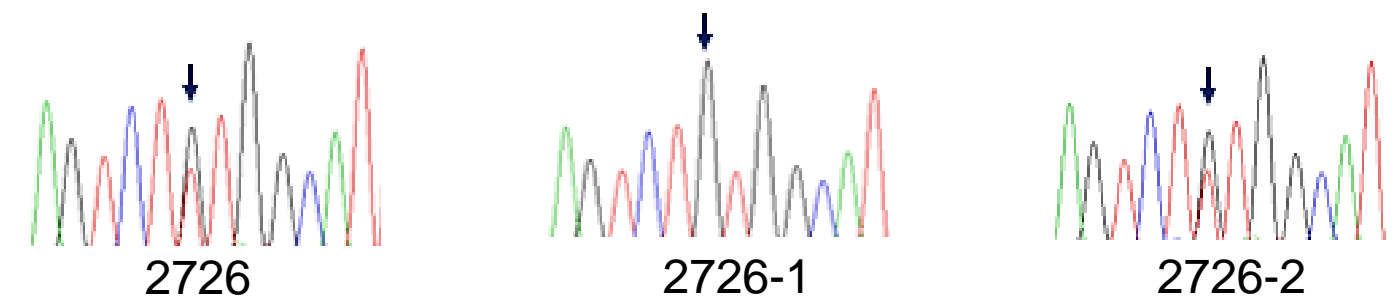
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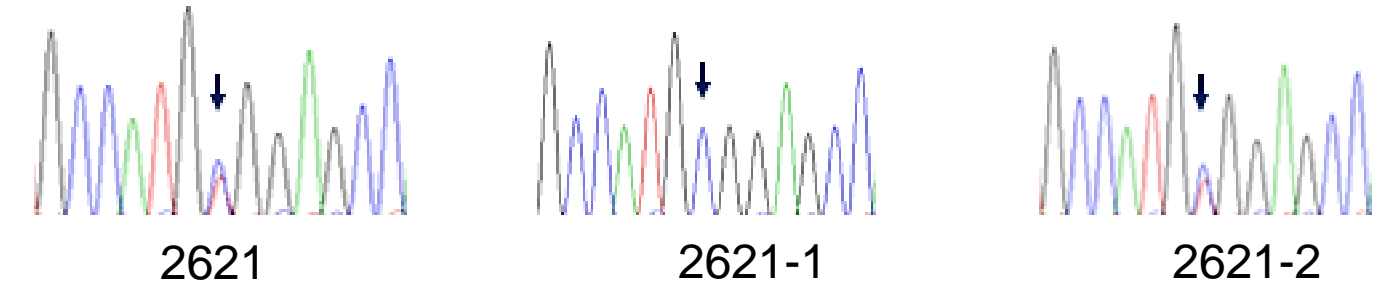
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(a)

Chr12: 57578911 LRP1: NM_002332:exon40: c.6386C>A: p.T2129K



Chr12: 57574223 LRP1: NM_002332:exon32: c.5347C>T: p.R1783W

**(b)****LRP1**

Homo sapiens XP_016874792.1

Hylobates moloch XP_032027909.1

Macaca mulatta EHH20885.1

Pan troglodytes PNI39335.1

Panthera tigris altaica XP_015392716.1

Panthera pardus XP_019310396.1

Chrysochloris asiatica XP_006859524.1

Microcebus murinus XP_012632486.1

Balaenoptera acutorostrata scammoni XP_028021545.1

Cercocebus atys XP_011918754.1

Erinaceus europaeus XP_016048840.1

Theropithecus gelada XP_025257656.1

exon32: p.R1783

.....NLDGSGLEVIDAMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

.....NLDGSGLEVIDAMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

.....NLDGSGLEVIDAMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

.....NLDGSGLEVIDAMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

.....NLDGSGLEVIDAMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

.....NLDGSGLEVIDAMRNQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

.....NLDGSGLEIIDAMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

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.....NLDGSGLEVIEMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

exon40: p.T2129

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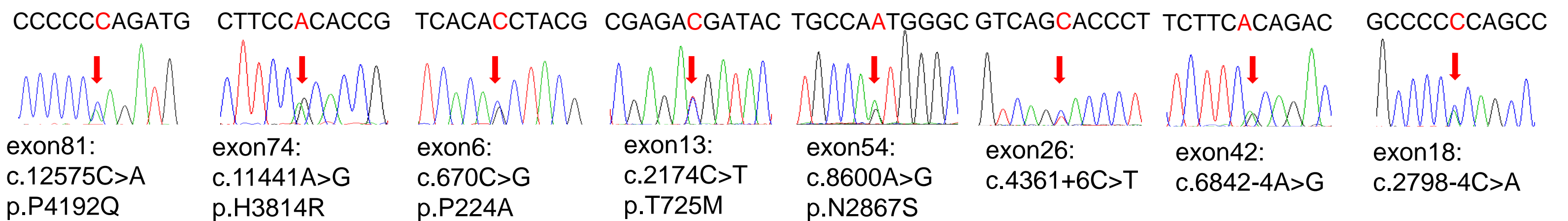
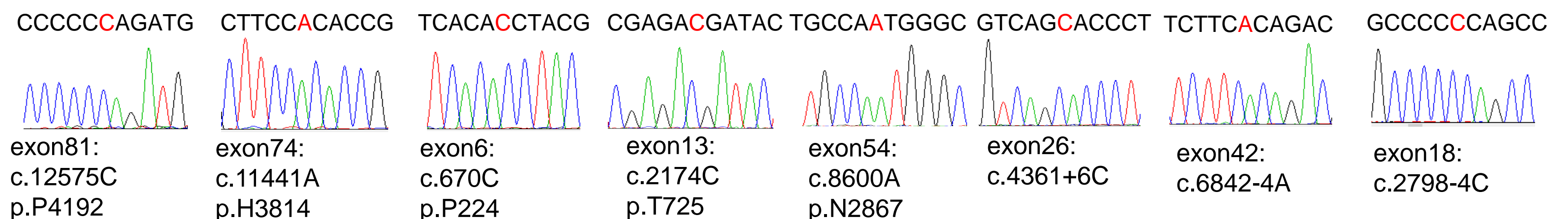
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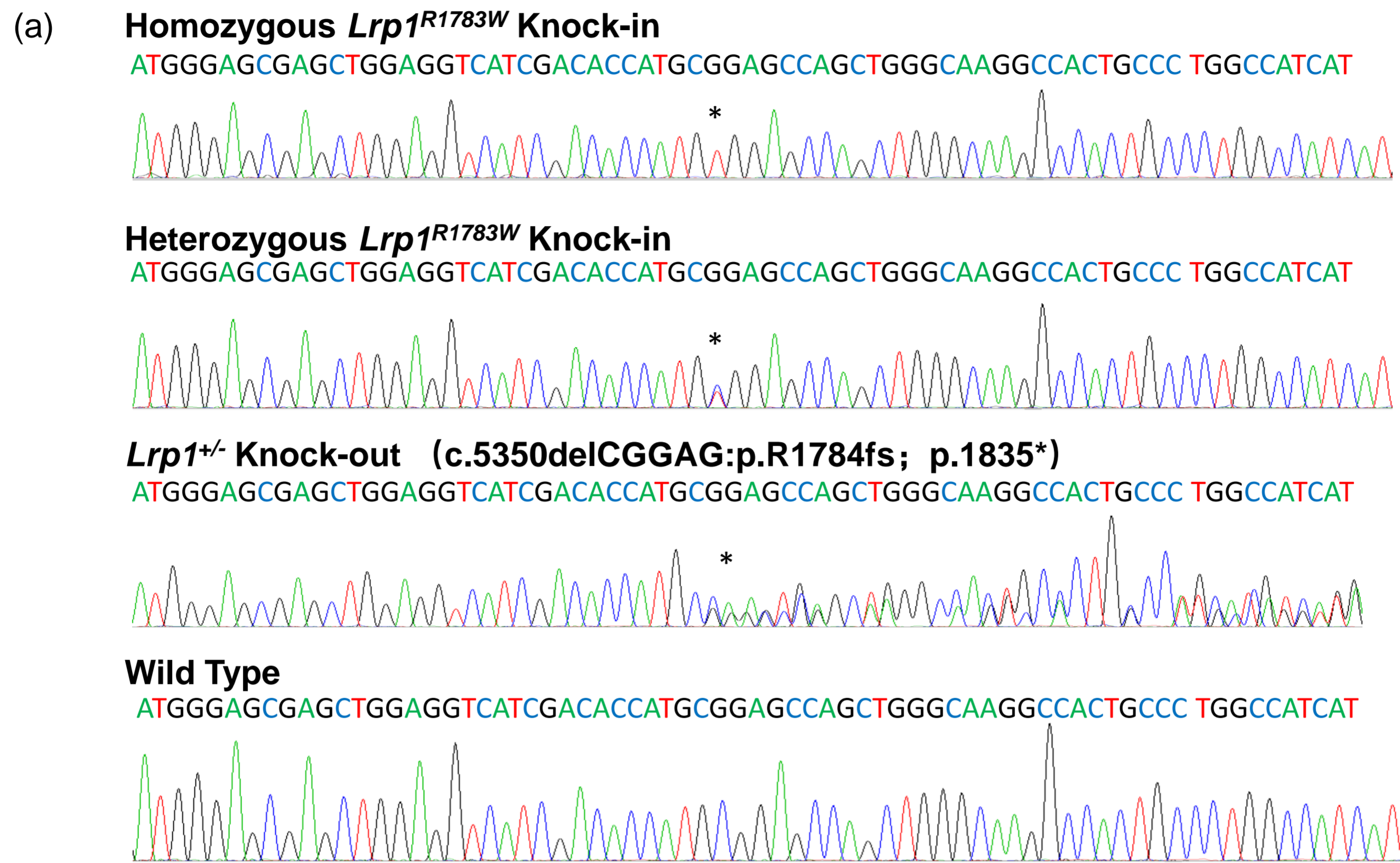
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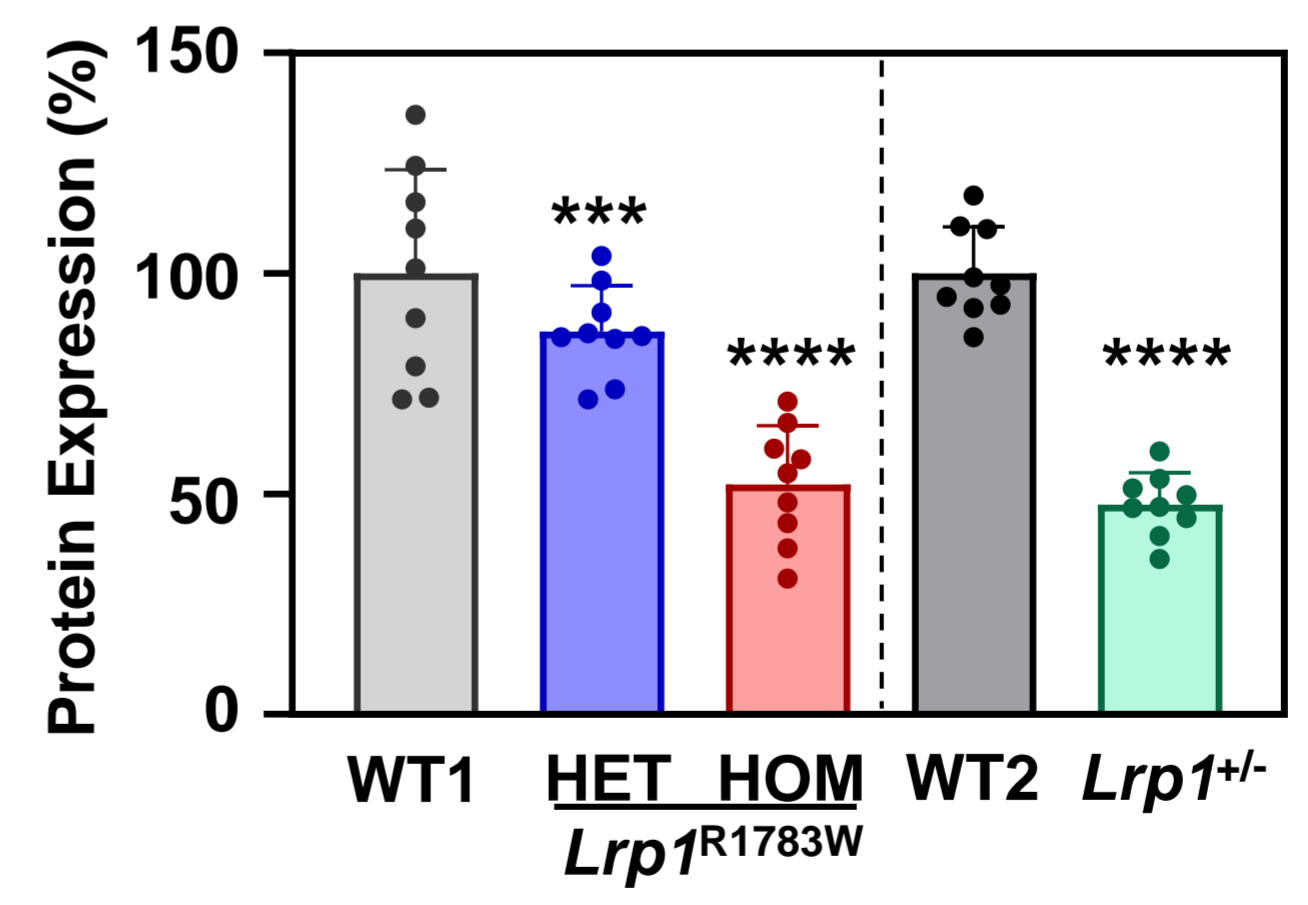
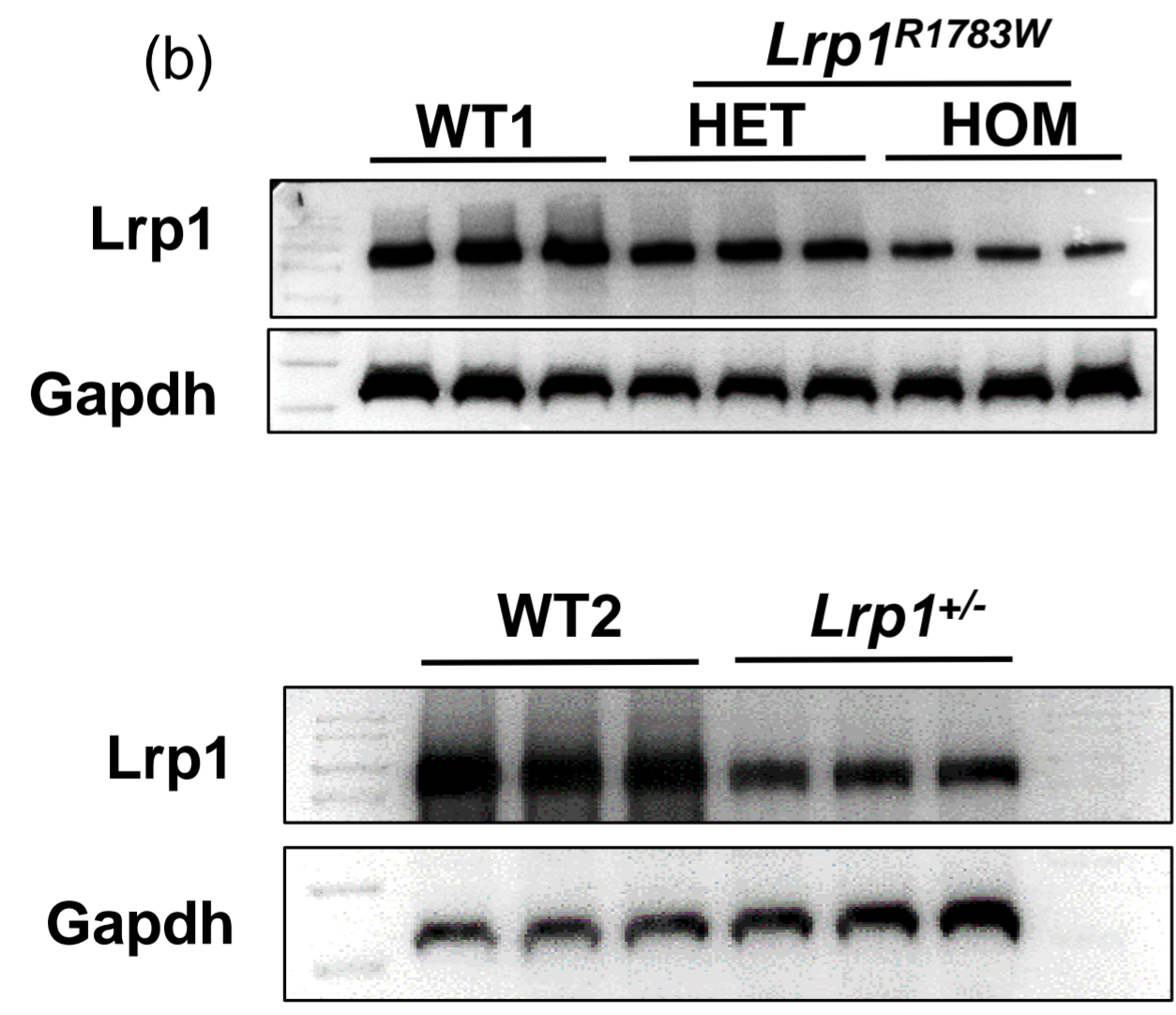
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.....NLDGSGLEVIEMRSQLGKATALAIMG.....ANGSIKRGSKDNATDSVPLRTGIGVQLK.....

(c)**LRP1 variants****Wild Type**



Lrp1-Mus musculus: NM_008512.2



***Lrp1*^{R1783W}**
HOM

WT

***Lrp1*^{R1783W}**
HET

