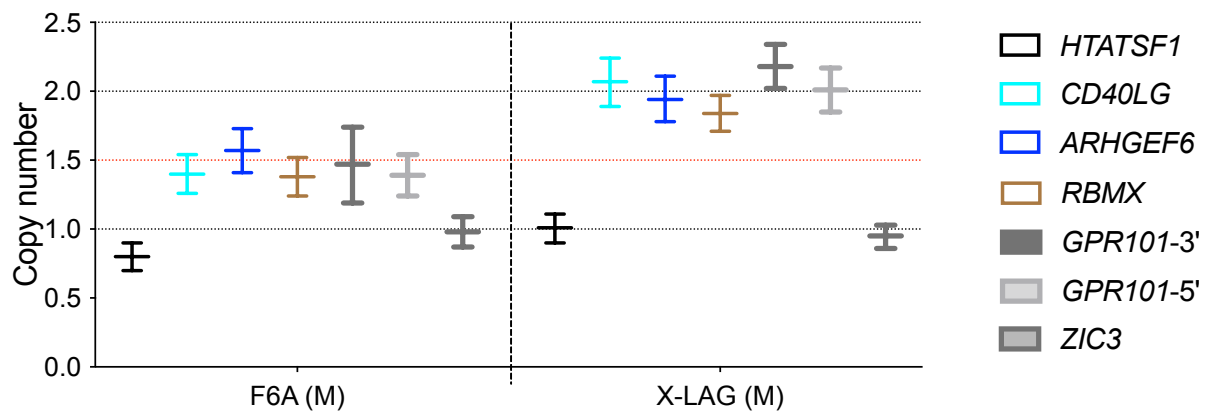




Supplementary Figure 1. Results of copy number (CN) ddPCR assays in subject F6A.

This male individual harbors a duplication that includes *GPR101* and its neighboring centromeric genes, up to *CD40LG*. As control, a typical X-LAG subject (shown here is a familial male case¹) was analyzed in the same experiment. Blood-derived DNA was used for analysis in all subjects. The calculated CN along with Poisson-based 95% confidence intervals (CN range bars) are shown for each gene. Note that two assays located at the 5' and 3' end of *GPR101* coding sequence were employed. The dotted red lines crossing the y axis at CN value 1.5 represents the threshold for duplication in male.

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Metric	H3K27AC_NP2	Input
Raw reads	43,045,289	42,202,414
Clean reads	42,557,047	41,167,271
Clean ratio	0.9744	0.9724
GC content	51.62%	46.55%
Q20 raw	98.21%	97.05%
Q30 raw	95.25%	92.63%
Q20 clean	98.60%	97.73%
Q30 clean	95.94%	93.79%
Low-quality bases	789,318	1,558,626
Too many N	5,166	56,702
Too short	182,000	454,958
Clean reads	42,557,047	41,167,271
Mapped	42,125,901 (98.99%)	37,797,207 (91.81%)
Unique mapped	41,358,993 (98.18%)	36,080,138 (95.46%)
Duplicate unique mapped	11,646,828 (28.16%)	17,149,209 (47.53%)
Unique mapped (deduplicated)	29,712,165 (69.82%)	18,930,929 (45.99%)

Supplementary Table 1. Trimming and mapping statistics for the H3K27ac ChIP-seq experiments.

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Metric	NP1	NP2
Alignment (bowtie2 to hg38)	Trimmed read pairs: 76,459,876; Concordantly aligned (1×): 52,187,074; Concordantly aligned (>1×): 21,400,016	Trimmed read pairs: 77,466,765; Concordantly aligned (1×): 55,016,947; Concordantly aligned (>1×): 18,966,136
Read pairs after quality filtering	60,453,018	62,839,370
Read pairs after deduplication	50,017,838 (82.7%)	56,119,764 (89.3%)
Mitochondrial reads (after deduplication)	729,660 (1.46%)	703,904 (1.25%)
Deduplicated read pairs after chr filtering	49,234,483 (98.4%)	55,334,073 (98.6%)
Number of peaks after filtering	110,164	57,786
Fragments in peaks (Fip)	21,616,600 (43.91%)	7,007,865 (12.66%)

17 **Supplementary Table 2.** QC metrics for the ATAC-seq experiments.

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chrX	136068349	chrX	136131892	Duplication	pituitary	F1A
chrX	136111060	chrX	136388326	Duplication	pituitary	F2A
chrX	136028815	chrX	136536734	Duplication	pituitary	F3A
chrX	136104659	chrX	136470844	Duplication	pituitary	F4A
chrX	135954223	chrX	136191468	Duplication	pituitary	F5A
chrX	135702382	chrX	136147166	Duplication	pituitary	F6A
chrX	135954223	chrX	136224319	Duplication	pituitary	F7A
chrX	135601312	chrX	136170916	Duplication	pituitary	F1
chrX	135533224	chrX	136118269	Duplication	pituitary	F2
chrX	135592293	chrX	136121710	Duplication	pituitary	F3
chrX	135619986	chrX	136173873	Duplication	pituitary	S1
chrX	135616901	chrX	136250647	Duplication	pituitary	S2
chrX	135627637	chrX	136219238	Duplication	pituitary	S5
chrX	135615580	chrX	136220614	Duplication	pituitary	S6
chrX	135598653	chrX	136293076	Duplication	pituitary	S7
chrX	135580313	chrX	136267244	Duplication	pituitary	S8
chrX	135601440	chrX	136191137	Duplication	pituitary	S9
chrX	135601430	chrX	136192229	Duplication	pituitary	S10
chrX	135602028	chrX	136259908	Duplication	pituitary	S11
chrX	135549274	chrX	136126345	Duplication	pituitary	S13
chrX	135622296	chrX	136191776	Duplication	pituitary	S14
chrX	135596446	chrX	136254970	Duplication	pituitary	S15
chrX	135533330	chrX	136123779	Duplication	pituitary	S16
chrX	135603324	chrX	136244940	Duplication	pituitary	S18
chrX	135602976	chrX	136200661	Duplication	pituitary	S19
chrX	135575594	chrX	136336458	Duplication	pituitary	S20
chrX	135589958	chrX	136206619	Duplication	pituitary	S21
chrX	135625218	chrX	136327754	Duplication	pituitary	S22
chrX	135631918	chrX	136138344	Duplication	pituitary	II
chrX	135605028	chrX	136221008	Duplication	pituitary	III
chrX	135601432	chrX	136176374	Duplication	pituitary	IV
chrX	135599808	chrX	136291833	Duplication	pituitary	V
chrX	135587056	chrX	136302873	Duplication	pituitary	VI
chrX	135605143	chrX	136187364	Duplication	pituitary	VII

Supplementary Table 3. Multiple SV analysis file.

References

- 1 Trivellin, G. *et al.* Gigantism and acromegaly due to Xq26 microduplications and GPR101 mutation. *N Engl J Med* **371**, 2363-2374 (2014).
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