GNAS is a complex imprinted locus which leads to different transcripts characterized by one specific exon 1 and shared exons 2-13, with monoallelic (XL, NES5P55) or biallelic (Gα) expression. A severe intrauterine growth retardation (IUGR) associated with placental hypotrophy has been observed in patients presenting pseudo-pseudohypoparathyroidism due to paternal GNAS mutations (1).

Given the role of placenta in fetal growth, we suspected transcriptomic alterations due to Gnas loss-of-function mutations.

**RESULTS**

XL expression was dramatically decreased in XL<sup>m+/p</sup> mice (relative quantification [RQ] versus WT: 0.20, \( P < 1.00 \times 10^{-4} \)). As expected in theory, \( \alpha \) was biallelically expressed in mice placentas, with its RQ halving in E1<sup>m+/p</sup> mice (specific to \( \alpha \)) and in E2<sup>m+/p</sup> mice (shared by the 3 other transcripts). However, XL was overexpressed in E1<sup>m+/p</sup> mice : to explain this result, we assumed there was a promoter competition between XL ‘weak’ promoter, expressing more while E1 ‘strong’ promoter is disrupted.

We showed significant variations in gene networks involved in phenotypes and pathways, such as “Prenatal growth retardation” (\( P = 3.1 \times 10^{-22} \)) and “Decreased placenta weight” (\( P = 2.4 \times 10^{-10} \)). Down-regulated transcripts such as Meg3, Mest and Igt2 have already been described in a human model of IUGR (3).

**CONCLUSIONS**

XL showed a preferential placental expression from the paternal allele.

XL and E1 promoters may compete and show an overexpression of XL in E1<sup>m+/p</sup> mice. Subtle variations of gene networks involving XL would be implicated in the pathogenesis of placental hypotrophy and IUGR associated with GNAS paternal mutation.