The DNA methylation pattern of prepubertal and pubertal Alpine goats

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INTRODUCTION

- Puberty timing is controlled by many genes and the elements coordinating this process have not yet been completely identified.
- Hypothalamus is a pivotal organ in the control of sexual maturation[1].
- There is evidence that epigenetic modifications, such as DNA methylation, play a key role in the process.
- GNRHR and Cbx7 are two key genes in the initiation of mammalian puberty [2,3].

OBJECTIVES

Highlight epigenetic differences at DNA methylation level that occur when reaching puberty in goat

METHODS

- The methylome of the hypothalamus of 10 Alpine goats, 5 at a prepubertal stage and 5 at their pubertal stage was analysed.

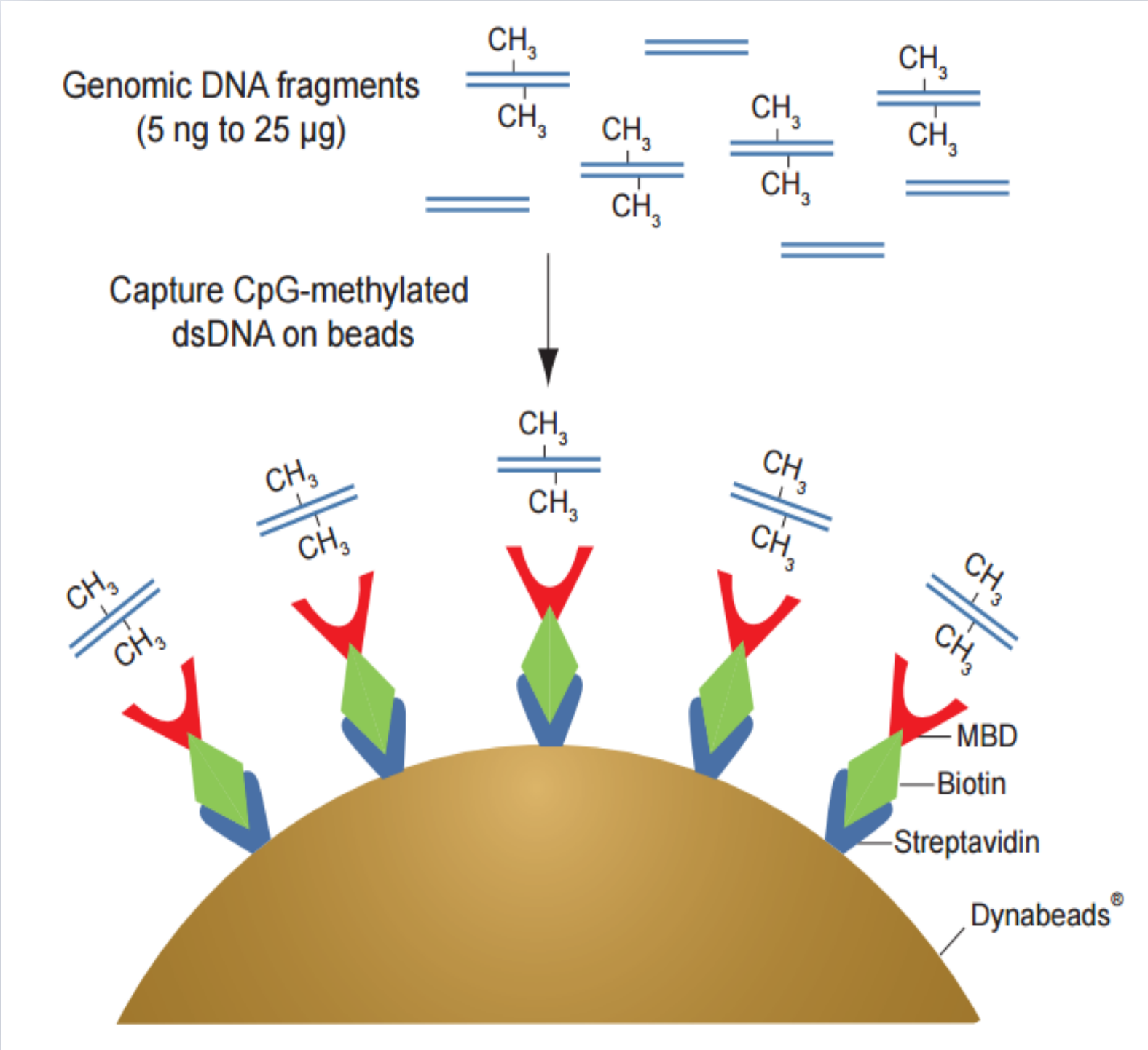

Figure 1 - MethylMiner™ Methylated DNA Enrichment Kit.

- Methylated DNA Binding Domain sequencing (MBD-seq) (Figure 1) and NGS (Hiseq2000 Illumina) were performed.
- An average of 24.13 million of reads (range 18.00 and 30.11 million of reads) were produced per sample.

RESULTS

- The analysis highlighted an increase in methylation in the prepubertal goats. The extent of methylation had a median value (±IQR) of 12.32±10.21 Mbp of the genome for prepubertal goats, compared with 8.18±9.71 Mbp for pubertal goats.
- Significantly increased methylation was seen on 18 chromosomes in prepubertal goats. Chromosomes 2, 4 and 7 were the most highly significant differentially methylated ones (Figure 2).

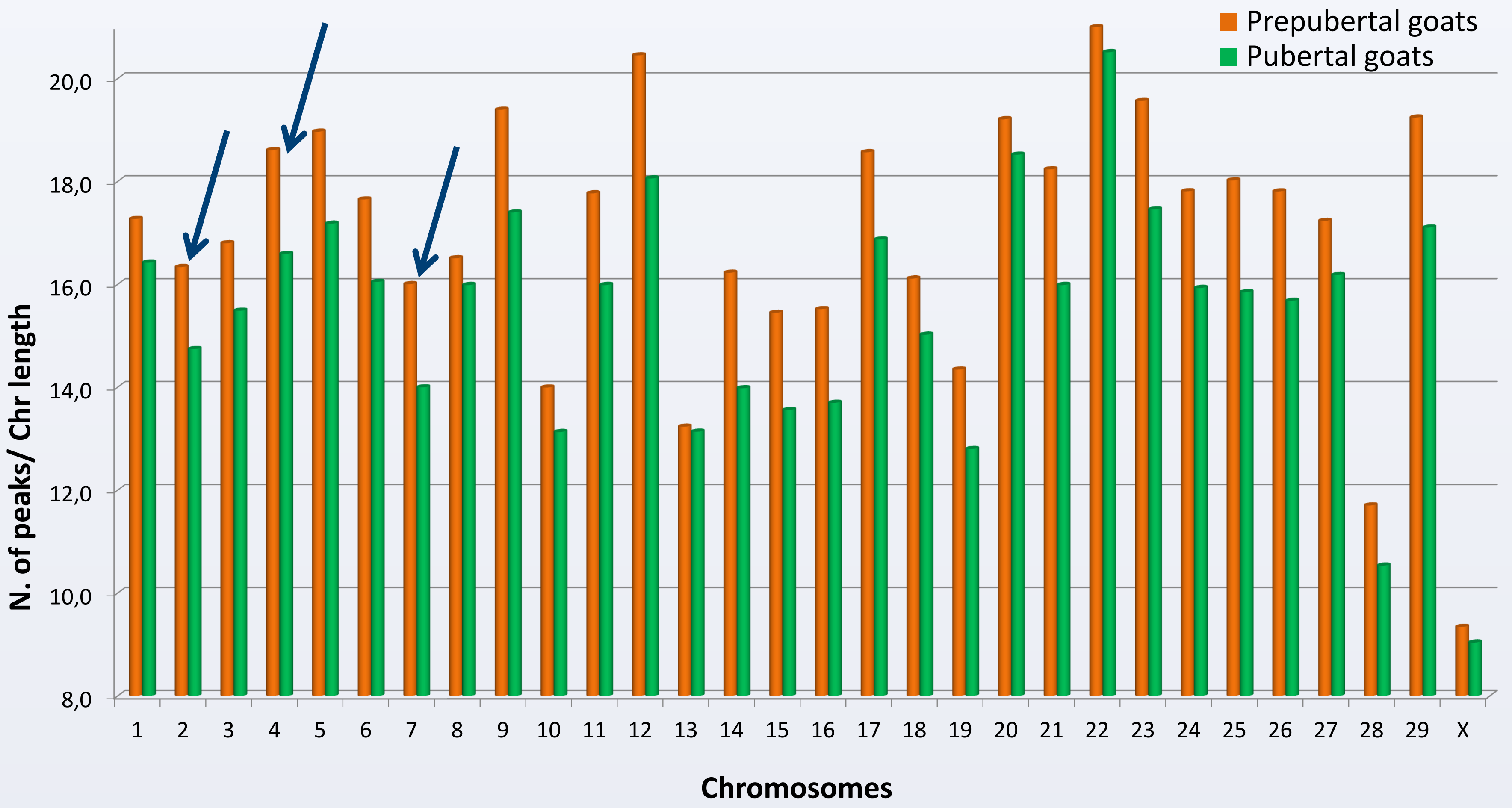

Figure 2 - *Number of methylation peaks per chromosome corrected for chromosome length in the hypothalamus of prepubertal and pubertal goats.*

- A higher methylation level (P<0.001) was observed in a small fragment of the terminal part of Cbx7 gene and of the body of the gene of GNRHR (coding for GNRH receptor) in prepubertal goats (Table 1 and Figure 3).

Gene	Fragment size (bp)	Coverage of methylation ± DS		P-Value
		Prepubertal	Pubertal	
GNRHR	115	820.5 ± 72.9	751.0 ± 63.4	<0.001*
Cbx7	390	62.8 ± 15.6	47.55 ± 12.7	<0.001*

Table 1 – *Coverage of methylation in a part of GNRHR and Cbx7 genes.*

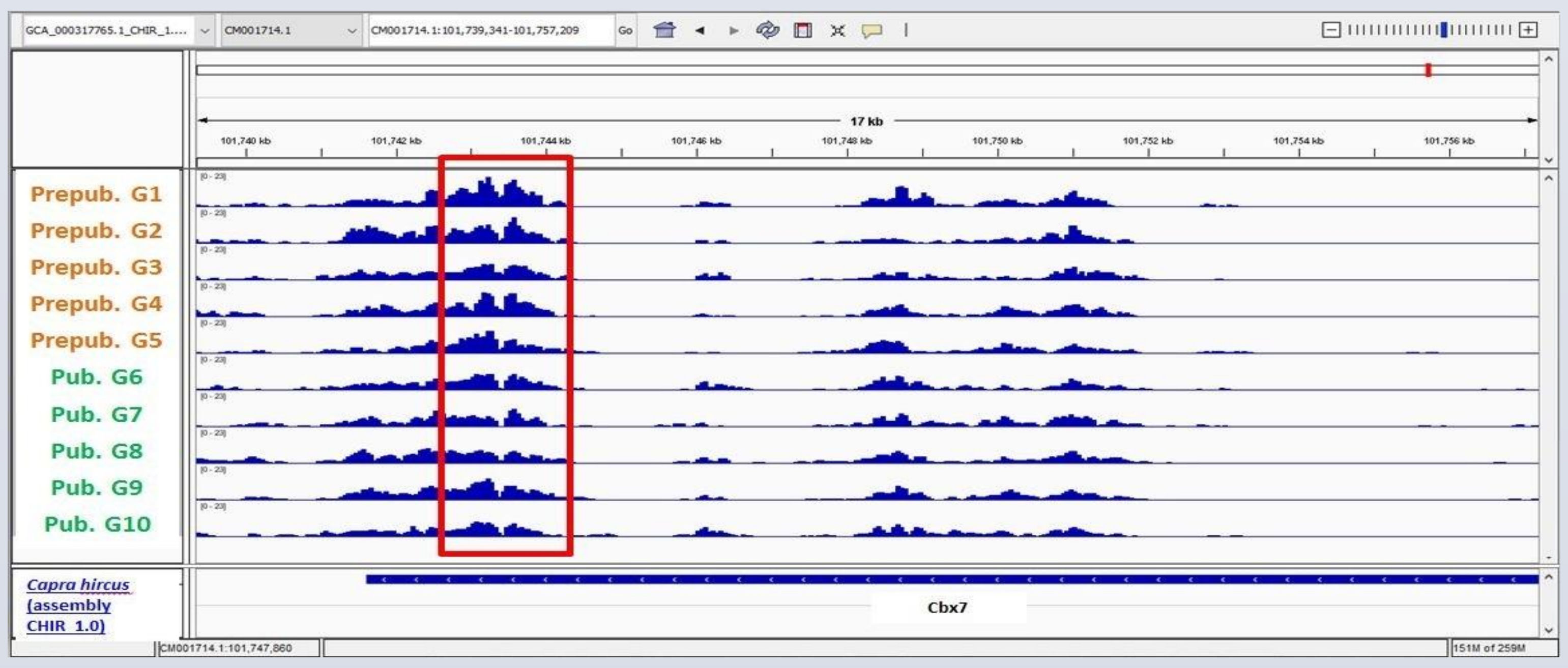

Figure 3 – *Methylation profile of Cbx7 in the hypothalamus of prepubertal and pubertal goats (IGV sofware). In the red box the methylated fragments as in Table 1.*

CONCLUSIONS

- These results confirm that female puberty in goats is associated with a modification of the DNA methylation pattern in the hypothalamus

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