Supplementary Figure 1:

Blood melatonin concentration of sheep in constant light. Animals were maintained in constant light at usual lights-off and given melatonin implant (square) or control implant-free (circle) treatments. Blood samples were taken at 1h30, 3h30, 6h30 and 9h30 after implant insertion.

Supplementary Figure 2:

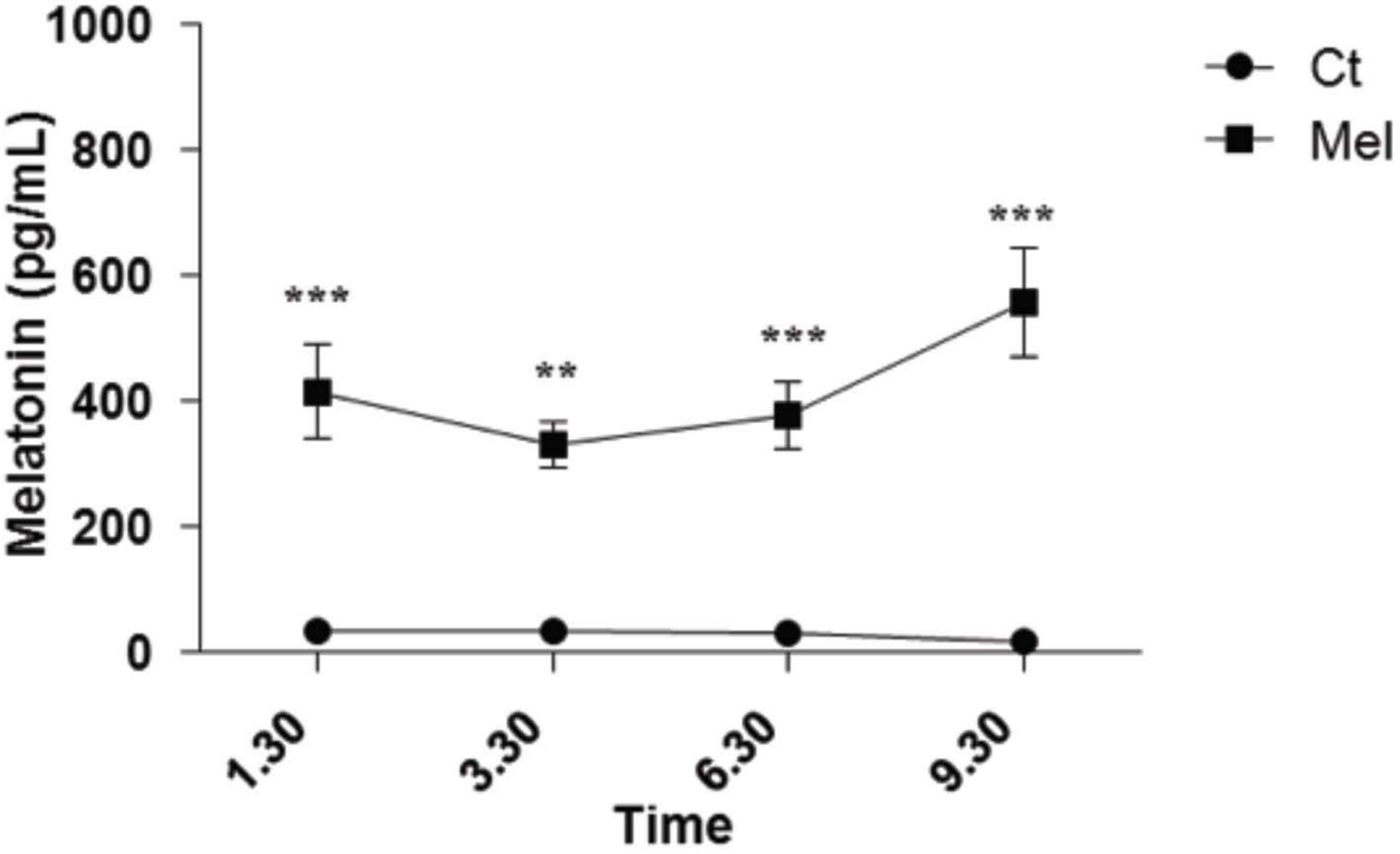
Confirmation of αNPAS4 antibody specificity. A: Alignment of the NPAS4 protein sequence with mouse, rat and human sequences. **B:** Immunohistochemistry showing comparative labelling of αNPAS4 in the ovine PT in both male and female sheep using three separate αNPAS4 antibodies (A) SAB2101623, (B) NBP1-68589 and (C) NBP-06574. Scale bars represent 50 µm.

Supplementary Figure 3:

Identification of a 58bp within the ovine *Cry1* proximal promoter essential for the NPAS4 heterodimer-dependent transcriptional activation. A: Alignment of the Cry1 313bp promoter region (positioned -216 +97 relative to TSS), highlighting position of putative CME sites and three regions of high evolutionary conservation boxed and denoted 1, 2 and 3. **B:** Schematic representation of the Cry1 313bp, 188bp (positioned -91 +97 relative to TSS) and 130bp (positioned -33 +97 relative to TSS) promoter regions. Putative CME sites represented by red bars, regions of high evolutionary conservation (orange). **C, D:** *In vitro* transfection of COS7 cells with a 188bp or 130bp fragment of the ovine *Cry1* promoter driving the expression of the luciferase gene, together with empty Myc and/or His expression vectors and vectors expressing the full length ovine NPAS4, ARNT, ARNTL and/or ARNT2. Results show relative biolumnescence (RLU) after 24h, in each group (n=4 replicates per group) normalised to control group (empty vectors), from one representative experiment out of three. Statistical differences between groups were analysed after one way ANOVA

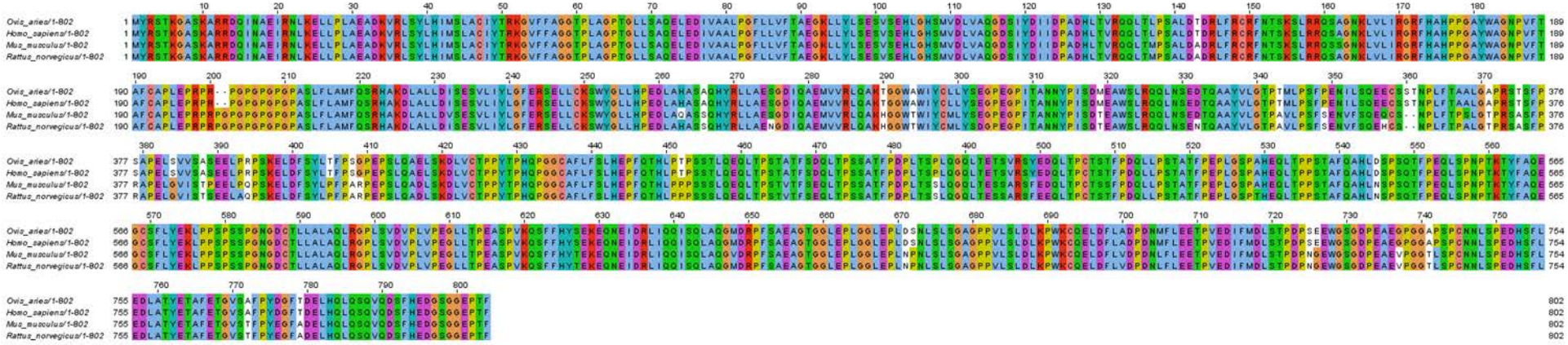
followed by Bonferroni's post hoc test (***p≤0.001, ****p≤0.0001 against control group). **E:** Schematic representation of the *Cry1* 188bp promoter region. Putative CME site shown by red bar and region of evolutionary conservation 2 in orange section. Highly conserved region 2 shown in detail through sequence alignment subsequent site-directed mutagenesis alterations are shown in yellow boxes. **F:** *In vitro* transfection of COS7 cells with the 188bp fragment of ovine *Cry1* promoter, without mutation (wild-type,WT) or with single (grey bars) or double (black bars) mutations, driving the expression of the luciferase gene, together with empty Myc and/or His expression vectors and vectors expressing the full length ovine NPAS4 and ARNT. Results show fold induction in biolumnescence (RLU) in the presence of NPAS4/ARNT compared to empty vectors (n=4 replicates per group), after 24h. Data for three technical repeats for each single or double mutation were combined to allow for comparison between groups. Statistical differences between groups were analysed after one way ANOVA followed by Bonferroni's post hoc test (*p<0.05 against WT). **G:** Alignment of Cry1 58bp sequence required for NPAS4/ARNT induction (red) with CCAAT box and WT1 consensus binding site.

SUPP FIGURE 1

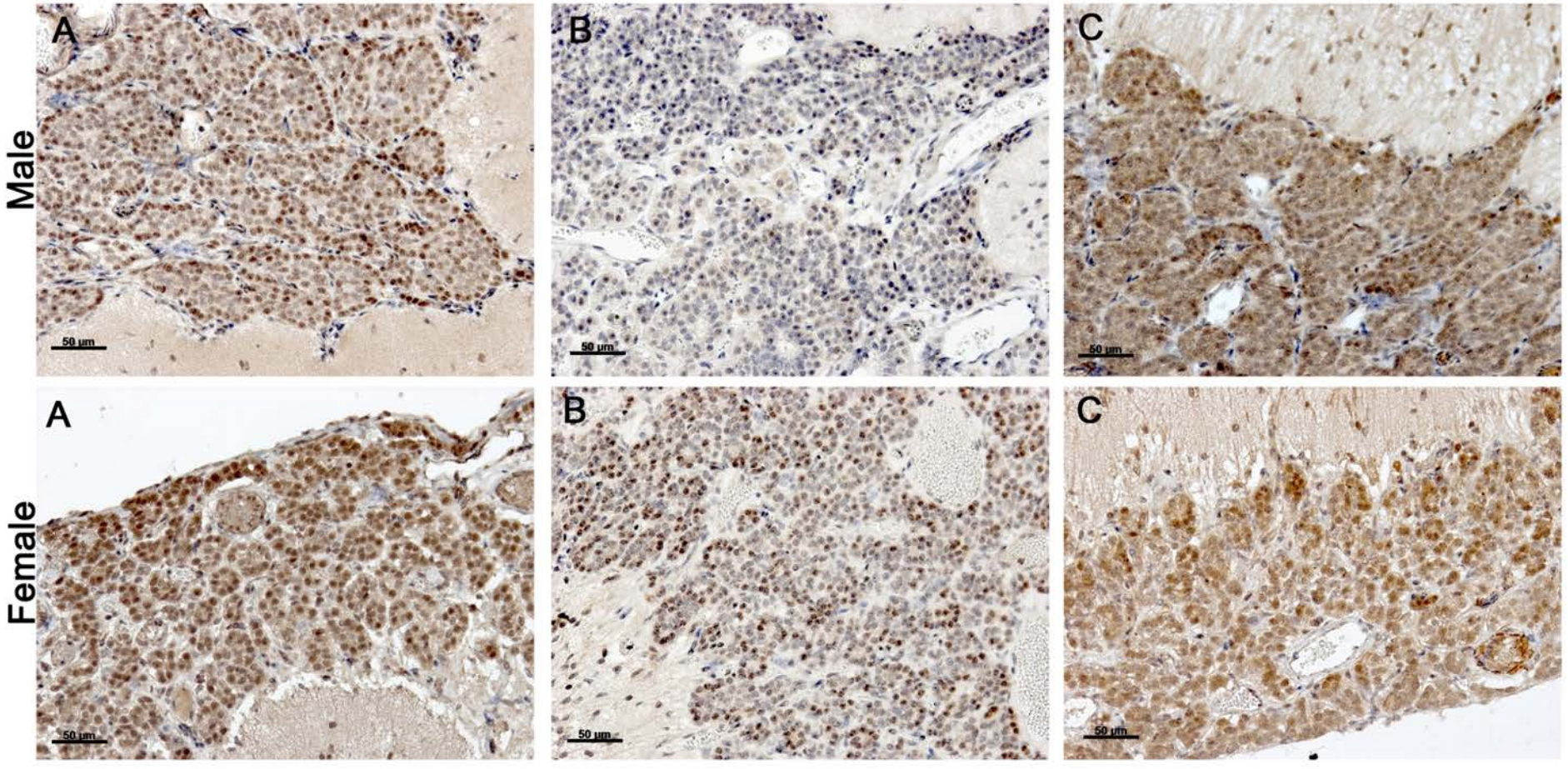


SUPP FIGURE 2

A.

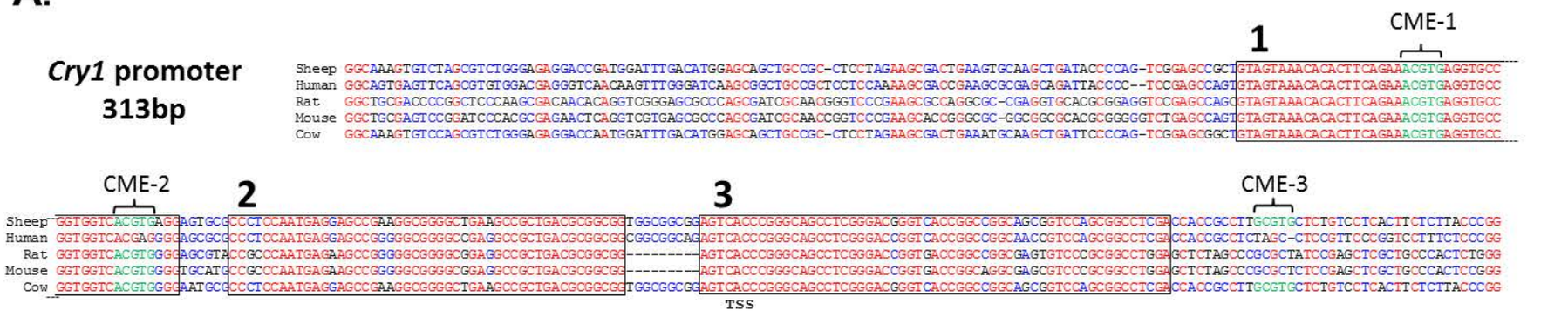


B.



SUPP FIGURE 3

A.



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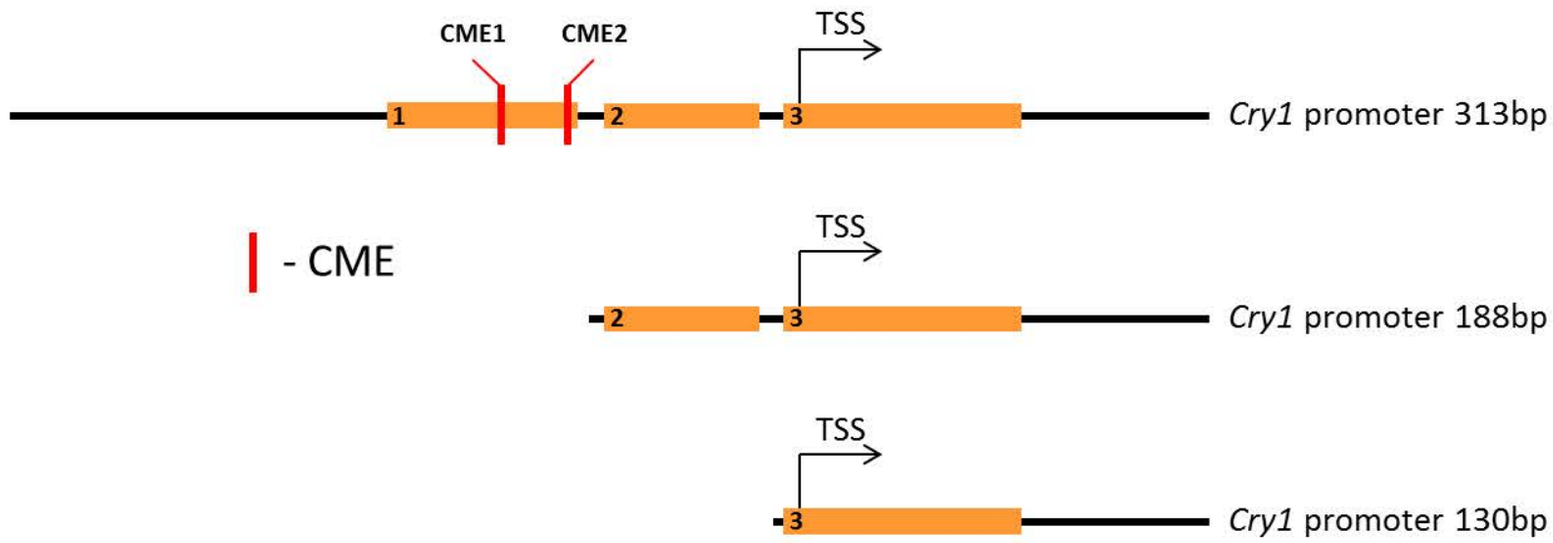
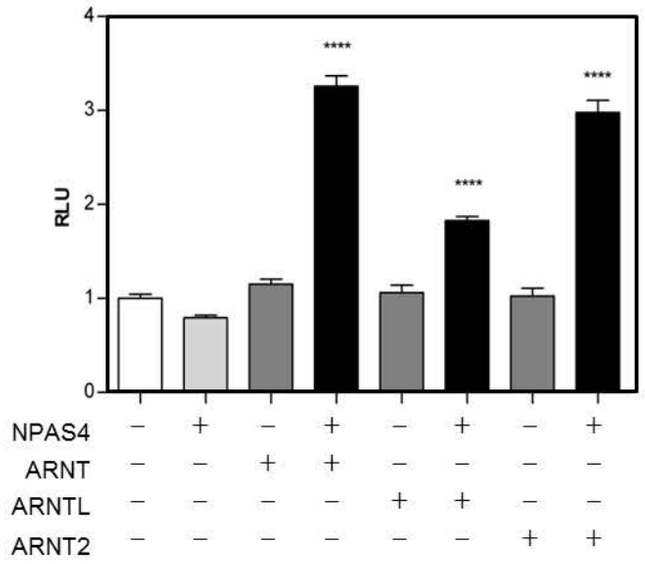
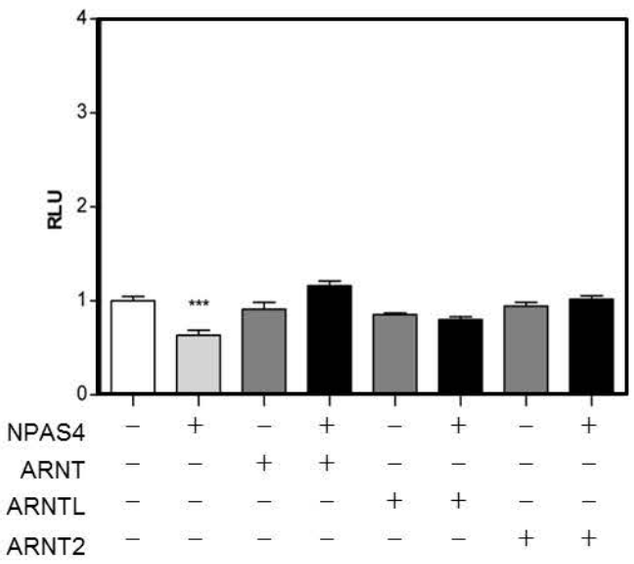


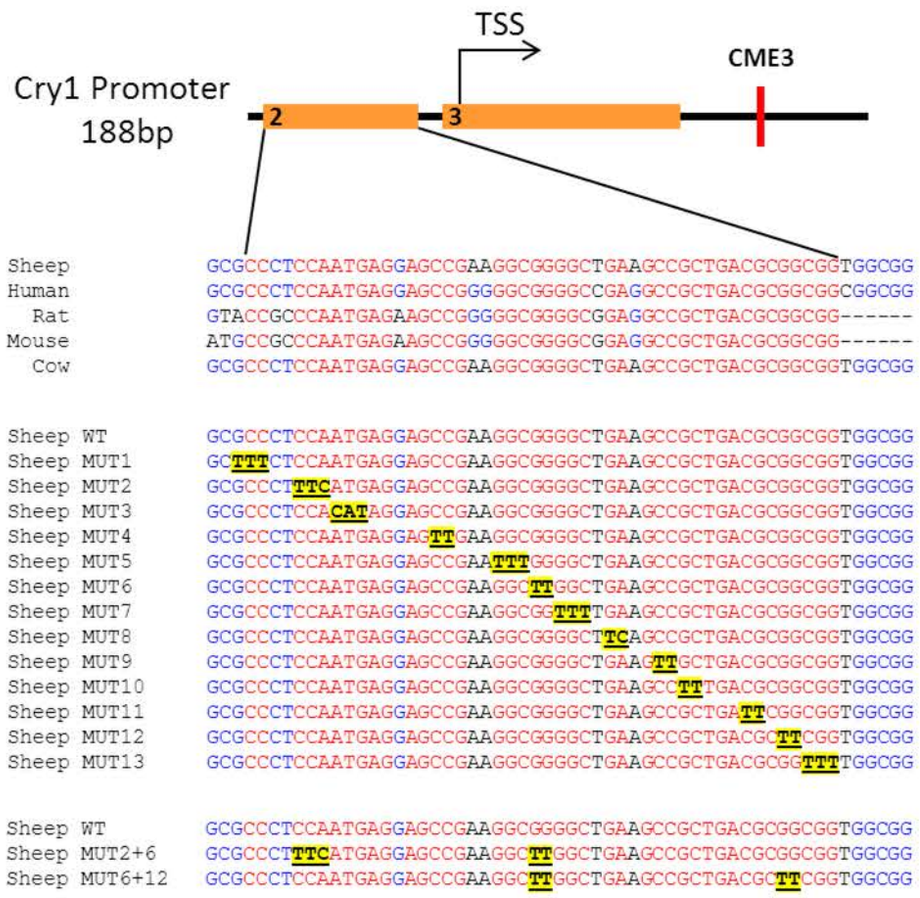
C. *Cry1* promoter 188bp



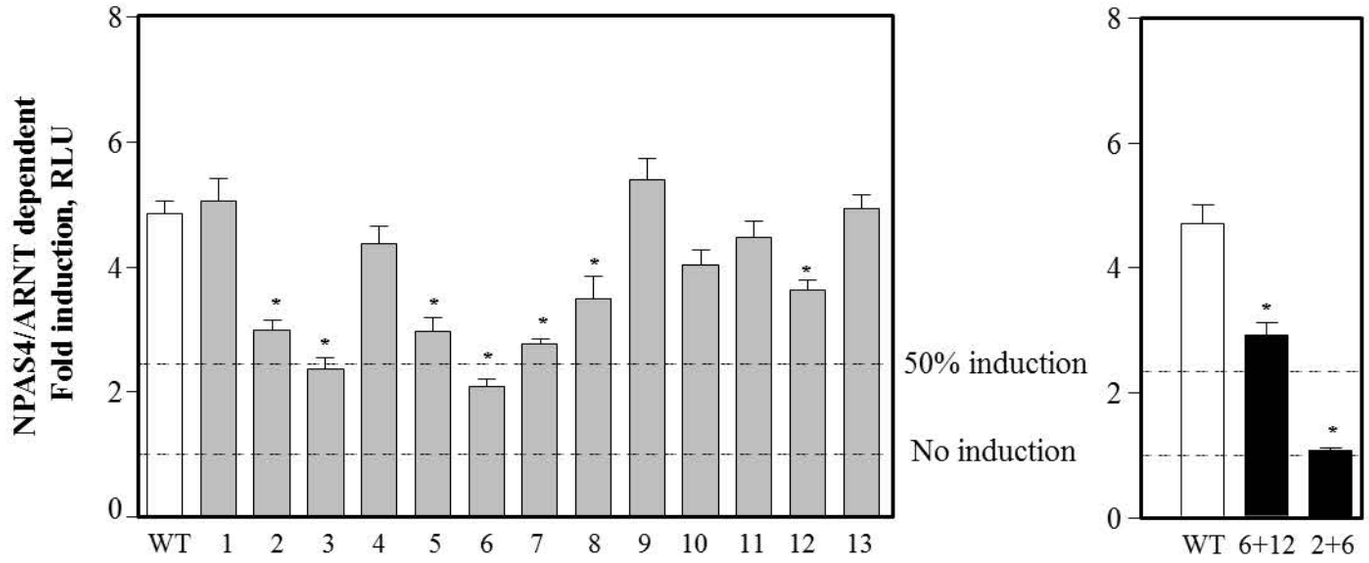
D. *Cry1* promoter 130bp



E.



F. NPAS4/ARNT dependent fold induction of the wild–type and mutated ovine *Cry1* 188bp promoter



G.

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Cry1 Essential Sequence    -86 CTCCAATGAGGAGCCGAAGGCGGGGCTGAAG -55
CCAAT Box                      --CCAATVR----------------------
WT1 Site                       -------------------GCGRGGSYGR--
```