homologous end joining process, were generated in each of the targeted CFTR loci. We also isolated single cell-derived sheep fetal fibroblast colonies by limiting dilution following transfection. The colony screening with the PCR/RFLP assay confirmed that we achieved targeted gene disruption in 10/51 (19.6%) colonies for exon 2 (5 colonies with biallelic and 5 with monoallelic CFTR gene disruption), and in 17/49 (34.7%) cell colonies for exon 11(13 with biallelic and 4 with monoallelic). In conclusion, we demonstrate that CRISPR/Cas9 is a highly efficient system for generating targeted mutations in CFTR gene in sheep fetal fibroblasts. These cells will be subsequently used for SCNT to generate sheep models of CF.

P4: *DNA Methylation and Gene Expression Levels in Hypothalamus and Ovary of Capra hircus Across the Genome*

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Hypothalamus and ovary are two key organs of the female reproduction system of mammals. Their role in controlling ovulation is well known, but the epigenetic mechanisms behind it, such as DNA methylation, remain unclear. Goats are an important source of milk, meat and fiber, especially in developing countries. Despite this, among economically relevant livestock species, they are still poorly investigated from a genomic point of view. The aim of this work is to find a relation between expression levels and methylation levels, in order to understand how methylation peaks in different gene regions affect gene expression in goat hypothalamus and ovary. Genome-wide methylated CpG detection and gene expression analysis in hypothalamus and ovary of three adult Saanen goats were performed. Animals in the study were managed according to the existing European Directive 2010/63/EU on the protection of animals used for scientific purposes. For the methylome analysis DNA binding domain sequencing (MBD-seq) with enrichment of methylated DNA fragments was performed. Gene expression was evaluated by RNA-Seq analysis. Sequencing was accomplished with Hiseq 2000 Illumina. Around 23-37 million raw sequencing reads were generated from each sample for the methylome analysis. Methylation distribution was investigated in six different genomic regions: promoter, intron, exon, downstream of gene, distal and intergenic. Matching the methylation pattern in hypothalamus and ovaries in contrast to their transcriptome allowed the identification of genomic regions in which methylation peaks most affect gene expression. Hypothalamus showed a highly significant negative correlation ($P<0.001$) between methylation peaks in promoter and in downstream regions and gene expression. A positive correlation ($P<0.001$) was observed within exons. Conversely, ovary did not show any significant consistent correlation between gene expression and methylation. This work provides evidence for a clearer understanding of the epigenetic mechanisms underlying gene regulation. A more accurate annotation of the goat genome will be necessary for a deeper insight in the role of DNA methylation in gene expression in Capra hircus, a candidate model species for other mammals.