Genome-wide differential DNA methylation patterns between tropically adapted Creole cattle and their Iberian ancestors

Sevane N1, Cañón J2, Dunner S2, Martinez R3, Bruford MW1

1 School of Biosciences, Cardiff University, Cardiff, UK; 2Laboratorio de Genética, Facultad de Veterinaria, Universidad Complutense de Madrid, Madrid, Spain; 3Corporación Colombiana De Investigación Agropecuaria (Corpoica), Bogotá, Colombia

Background
Assessments of climate change impacts on agriculture predict a progressive upward trend in average temperatures over the next century, leading to decreased forage production and quality, and an increased risk of disease. Therefore, enhancing climate resilience and sustainable production for animals in harsh environments are important goals for the livestock industry. Rapid adaptation to extreme climatic conditions has already been imposed on a limited number of livestock breeds, including those exported after Columbus' arrival in the Americas.

Aim
We aimed to compare the methylomes of two tropical Creole cattle breeds and their likely Spanish ancestors belonging to three different breeds to understand the epigenetic mechanisms underlying rapid adaptation of a domestic species to a new and harsh environment.

Material & Methods
The sample comprised Colombian Creole cattle Costeño con Cuernos (CCC, n=2) and Sanmartinero (SM, n=1) breeds and Iberian samples representing the main ancestors of the Creole populations including Retinta (RET, n=1), Raza Asturiana de los Valles (RAV, n=1) and Lidia (LD, n=1) breeds. Reduced representation bisulfite sequencing (RRBS) was used to assess the differences in methylation in Creole and Spanish cattle blood samples. Bismark and MethylKit were used for data analysis. Gene ontology (GO) was analyzed with DAVID, PANTHER, WebGeStalt, and Cytoscape. Validation of RRBS data was performed with HiSeq bisulfite sequencing PCR (HiSeq-BSP).

Results
Comparison between sample groups revealed 3,639 differentially methylated CpG dinucleotides with 10X coverage (CpG10) sites using high stringency parameters (DMS10q-value < 0.01, differential methylation > 25%). Annotation of these DMS10 showed that 1,539 sites (42.3%) corresponding to 920 unique features, were overlapping or within a distance of ±100 kb from the closest transcription start site (TSS) (Figure 1).

We found a number of differentially methylated genes between Creole and Spanish samples implicated in several biological processes key for survival in harsh environments, such as immunity, energy management, heat resistance, stress response, skin and coat attributes, growth and muscle development, nervous system processes, adaptation to new feeding conditions or reproductive traits (Figure 2).

Conclusions
Our results imply that the drastic environmental changes imposed on Creole cattle have had an impact on their methylome pattern still measurable today, affecting genes implicated in important pathways for adaptation and pointing towards the epigenomic fine-tuning on the regulation of gene activity. Further work is needed to understand the relationship between epigenetic variation and rapid phenotypic response in domestic species. This is the first genome-wide map of DNA methylation at the level of single nucleotide resolution in cattle. The tissue analysed, blood, is easily accessible and reflects the immune status of individuals, thereby providing valuable data for the development of biomarkers useful for the diagnosis and monitoring of livestock health and welfare.