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# Transgenerational epigenetics in quail: whole genome DNA methylation analysis

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The influence of the prenatal environment on the adult phenotype development is partially mediated by epigenetic phenomena. Recently, an increasing number of studies highlighted the transmission of epigenetic marks between generations following an environmental exposure. However, there is much debate about their acquired transmission beyond the exposed individuals. Recent studies revealed that non-genetic inheritance was probably present in avian species. In one of them, fertilized eggs were injected with an endocrine disruptor (genistein) and after three generations without any other injection, several traits were impacted by the ancestor treatment such as the reproduction and the behavior. Here we analyse the **DNA methylation** between **control** and **treated lines** of the **third generation**.

## 1 - Experimental design 3 - Results **WGBS** ONT **Number of CpG sites measured Methylation profile of common CpG sites** 3,783,148 common CpG 7,455,313 common CpG 5,842,679 epi+ epi-4e+06-G0 PC2 (6.37%) Non-injected Genistein <u>©</u> -0.25 -1,694,328 G1 -0.50 epiline 39,136 epiepi+ 0.2 **WGBS** -0.2 -0.2 0.2 -0.4 0.0 0.0 G2 PC1 (10.31%) PC1 (10.72%) sex ▲ F 9900 G3 M 99% WGBS CpG found in ONT (from 8,974,565 CpG in quail assembly) 8 -0.50 **→WGBS** Number of DMC epiline/sex detected -0.75 DMC epiline 17,061 ONT 0.2 0.2 0.0 PC1 (10.31%) PC1 (10.72%) PC1 : sex separation PC1: sex separation PC2: epiline separation PC3: epiline separation 2 - Methods 10000 7,608 $mCpG : 0.44 \pm 0.3$ $mCpG : 0.49 \pm 0.32$ 5,264 coverage CpG: $19.5 \pm 29.8$ coverage CpG: $39.7 \pm 31.9$ Mean methylation rate of one DMC epiline WGBS 1\_111488602 (padj=0.0246382489756093) 1 111488602 (padj=0.000495914906707243) **DNA** extraction ONT <u>a</u> 0.75 **WGBS** ONT 261,896 DMC sex epiline Whole Genome Bisulfite Sequencing Oxford Nanopore Technology epipepi+ Bisulfite conversion No bisulfite conversion 54,088 Illumina sequencing Nanopore sequencing **Heatmap of methylation rate of 10,000 DMC epiline** 20,860 Short reads Long reads WGBS epiline Megalodon epi-epi+ nf-core/ \* **CpG** sites detection CoJa 2.0 NANOPORE methylseq Greater number of DMC detected with **ONT than WGBS Distribution of CpG sites and DMC epiline Preprocessing** by genomic region Native SNP filtering from nanopore (Longshot) • CpG with coverage > 5X & < 1000X in 80% of samples **Detection of Differentially Methylated Cytosines / Regions** DMC epiline mostly (DMC / DMR) located in introns and Sequecin (in house pipeline) intergenic regions Package DSS Smaller number in promoters and exons Conclusion Similar methylation profile between WGBS and ONT Significant difference between epi-/epi+ Thousands of DMC detected between epilines Transgenerational effects of genistein on **Correlation of the metylation rate Smooth proportion of methylation by distance to TSS** methylation between WGBS and ONT (1 sample) • ONT vs WGBS: comparable results and best detection of ONT vs WGBS at: 6722689 CpGi. Correlation: 0.915 transgenerational effects from ONT data Perspectives Optimising SNP filtering and minimising false positives: • **SNP calling** with **GemBS** for WGBS data Gene Ontology (GO) analysis to be finalised: ViSEAGO Average • Exclude the genetic causes for the observed differences correlation: between epilines $0.9 \pm 0.01$ Distance to TSS 0.00 Lower methylation rate around TSS for ONT • Identification of the biological mechanisms involved **ONT** fractions















