TAPS for Multimodal Epigenomic Profiling in Livestock A Comparison with ONT, WGBS, and EM-Seq

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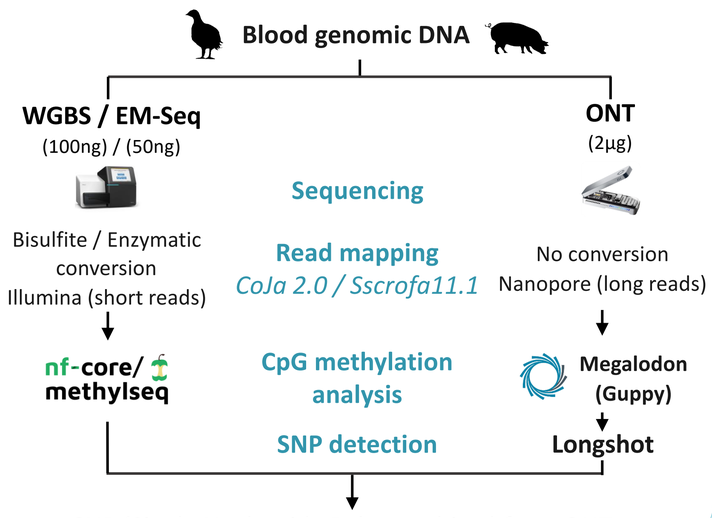
Introduction

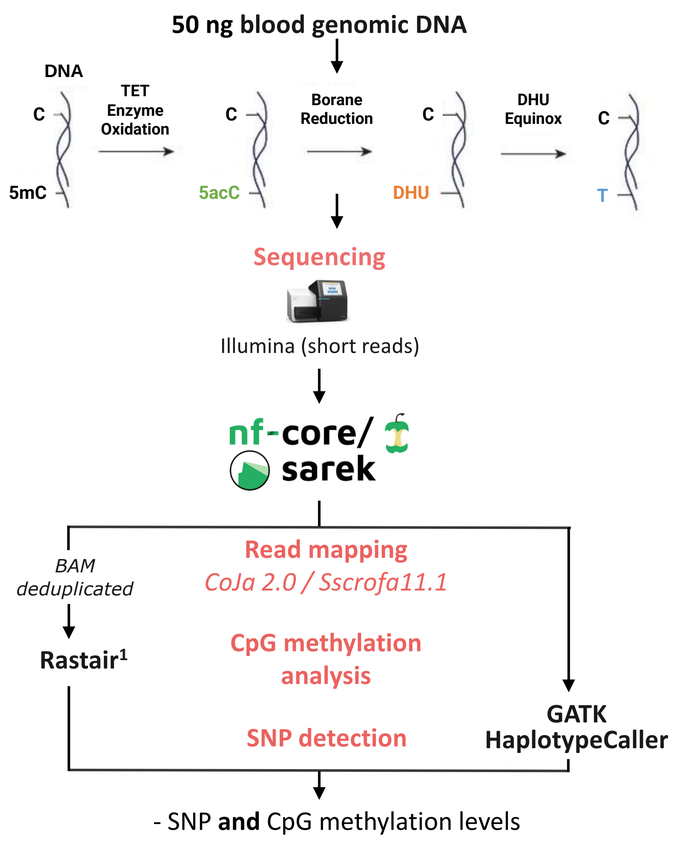
Genetic and genomic selection advances have significantly optimized livestock performance over the past decades. However, genetics accounts for only a portion of the observed phenotypic variability, while much of this variability—often attributed to environmental factors—remains inaccessible to genetic approaches. One of the questions in breeding today is thus whether integrating epigenetic markers into prediction models could improve their accuracy or even whether epigenetics should be included in genetic evaluation models for breeding candidates. The availability of a large-scale epigenotyping tool is crucial for answering this question and eventually implementing epigenotyping in animal breeding. Here we evaluated CpG methylation detection using an advanced prototype of TAPS (TET-assisted pyridine borane sequencing) against existing data from Whole Genome Bisulfite Sequencing (WGBS), EM-seq (Enzymatic Methyl-seq), and ONT (Oxford Nanopore Technology) in two farm species: pigs (*Sus scrofa*) and quails (*Coturnix japonica*).

Standard methods



- SNP (Single Nucleotide Polymorphism) from ONT
- CpG methylation levels from ONT / WGBS / EM-Seq

TAPS



- SNP **and** CpG methylation levels

- Reduces low-quality reads to enhance sequence economy.
- Speeds up analysis using standard mapping tools.
- Minimizes DNA damage relative to bisulfite for better recovery.

1 - developed at Ludwig Cancer Research by Benjamin Schuster-Böckler's lab

Conclusion

This pilot study provides very encouraging results for the use of TAPS in epi/genotyping analyses in farm animals, with robust sequencing and mapping metrics and comparable CpG methylation profiles and SNP genotypes between all technologies.

Available data sets / TAPS results

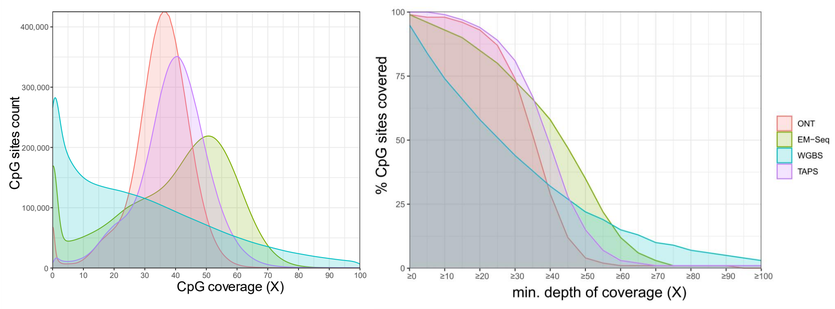
		WGBS	EM-Seq	ONT	MicroArray	TAPS
Sus scrofa	Sample 1	ND	148 Gb	192 Gb	650 k Array	287 Gb*
	Sample 2	238 Gb	ND	152 Gb	650 k Array	269 Gb*
Coturnix japonica	Sample 1	119 Gb	ND	55 Gb	ND	94 Gb*
	Sample 2	283 Gb	90 Gb	65 Gb	ND	94 Gb*

*3 replicates

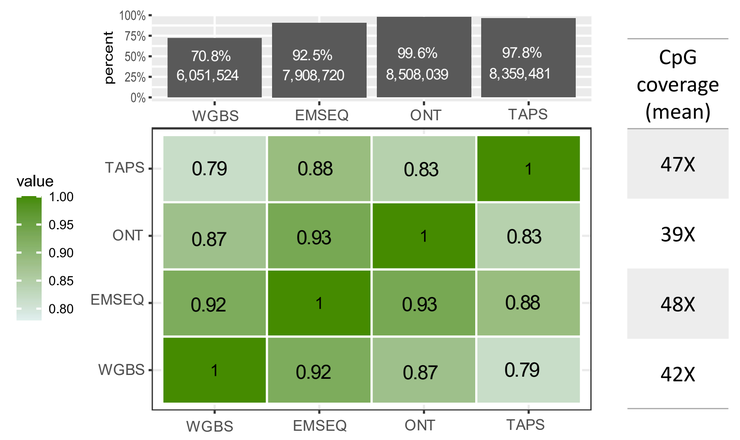
Results

Methylation analyses (Quail sample 2)

At the 10X threshold, the WGBS approach covers less than 75% of CpG sites, while EM-Seq covers around 90%, and both ONT and TAPS achieve nearly 100% coverage.



Coverage of CpG sites across technologies
The distribution of CpG site coverage and the percentage of CpG sites covered at a minimum depth of coverage



Pearson correlation matrix of CpG methylation level per-site across technologies (Filtering data: 10x < depth < 100x). Barplots above the matrix show the number of CpG sites covered by 10 or more reads and their percentage compared to the reference genome. Average CpG coverage by technology before depth filtering is shown on the right.

SNP analyses (pigs)

Filtering variants post genotyping with stringent criteria
1 - Keep only variants present on 650K for SSC1 to SSC18, n=524,117 variants
2 - Remove positions corresponding to CpG identified with rastair, n=453,192 variants
3 - Keep only bi allelic SNPs , n=350,011 variants
4 - Keep only SNPs QUAL>300 & <1300, n=155,285 variants
5 - Keep only SNPs with meanDP >15 across samples, n=129,211 variants

AB72734224

TAPS \ ONT	Homoz Ref	Hetero	Homoz Alt
Homoz Ref	**67871**	1009	232
Hetero	52	**55790**	2810
Homoz Alt	1	20	**1140**

AB72734224

TAPS \ 650K	Homoz Ref	Hetero	Homoz Alt
Homoz Ref	**68358**	714	128
Hetero	192	**55570**	2992
Homoz Alt	1	20	**1143**

AB72734233

TAPS \ ONT	Homoz Ref	Hetero	Homoz Alt
Homoz Ref	**27802**	1767	98
Hetero	81	**96344**	2217
Homoz Alt	1	78	**537**

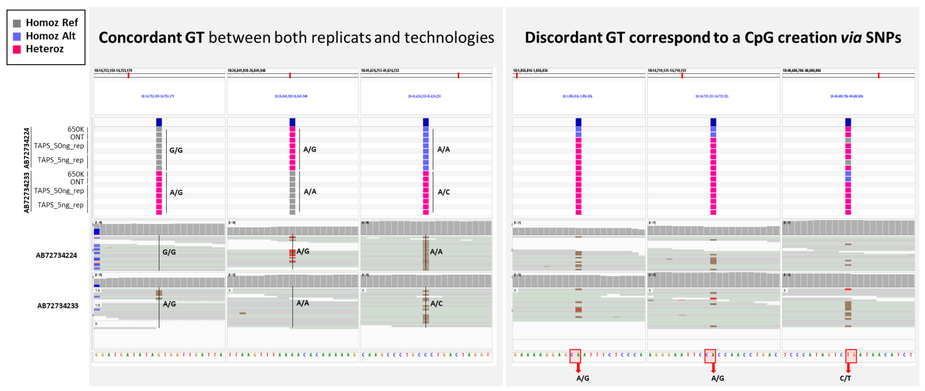
AB72734233

TAPS \ 650K	Homoz Ref	Hetero	Homoz Alt
Homoz Ref	**28173**	1480	43
Hetero	1186	**96645**	2669
Homoz Alt	3	77	**537**

Genotypes comparisons
The excess of heterozygous in TAPS libraries can be explained by *de novo* SNV-driven CpGs

	Replicates	ONT *vs.* TAPS	650K *vs.* TAPS
AB72734224_A	0.9889	0.9680	0.9686
AB72734224_B	0.9867	0.9678	0.9684
AB72734224_C	0.9870	0.9663	0.9670
AB72734233_A	0.9773	0.9671	0.9576
AB72734233_B	0.9884	0.9681	0.9585
AB72734233_C	0.9807	0.9709	0.9614

Genotypes correlations between TAPS libraries replicates and across technologies



IGV visualization of concordant and discordant genotypes

→ **A custom script was developed to resolve variant calling complexities associated with *de novo* SNV-driven CpGs.** Contact Support@watchmakergenomics.com for details.

PAG 2025, San Diego

Projet cofinancé par le Fonds Européen de Développement Régional