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Julie Demars, Jean-Noël Hubert, Nathalie Iannuccelli, Sophie Leroux, Céline Vandecasteele, Paul Terzian, Thomas Faraut, Christophe Klopp, Cécile Donnadiou

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Genomic imprinting in livestock species

- Challenges of long reads sequencing from ONT -

Julie Demars¹, Jean-Noël Hubert¹, Nathalie Iannuccelli¹, Sophie Leroux¹, Céline Vandecasteele², Paul Terzian³, Thomas Faraut¹, Christophe Klopp³, Cécile Donnadiou²

¹GenPhySE, Université de Toulouse, INRAE, ENVT, F-31326 Castanet-Tolosan, France
²INRAE, GeT-PlaGe, Genotoul, F-31326 Castanet-Tolosan, France (<https://doi.org/10.15454/1.5572370921303193E12>)
³Sigenae, GenPhySE, Université de Toulouse, INRAE, ENVT, F-31326 Castanet-Tolosan, France

ONT enables straightforward parental origin of methylation identification

- Comparison of methylseq capture [1] and ONT [2] to enlarge the identification of parental-specific methylation (Figure 1)
- Variants calling are concordant between methylseq capture and ONT (Figure 2a-b)
- DNA methylation, especially hemimethylation, are highly correlated between methylseq capture and ONT (Figure 2c-d)

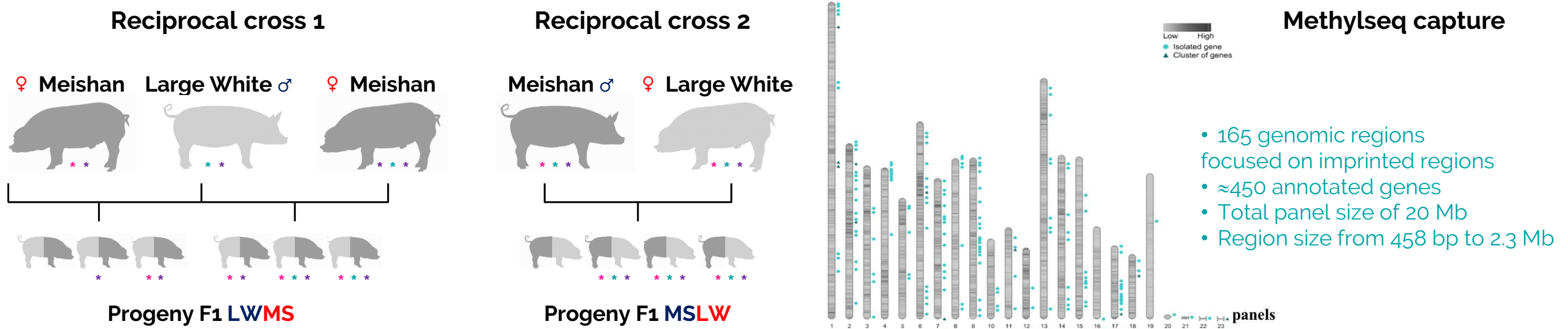


Figure 1: Schematic overview of the strategy. Reciprocal crosses between Large White and Meishan pigs have been produced (n=15) to unambiguously discriminate the parental phase of variants. Different genotyping methods have been used including the Affymetrix® Axiom Porcine Genotyping Array (Axiom_PigHDv1) and variant calling from both methylseq capture and ONT. DNA methylation status has been analysed from either methylseq capture or ONT. Methylseq capture is focused on 165 genomic regions expected to carry imprinted genes based on orthologous comparisons with human and mouse data. Coloured stars represent which technology have been used with high density SNP array (pink), methylseq capture (green) and ONT (purple), respectively.

Methods and Dataset

- * 650k genotyping n=11/15 Blood
- * Methylseq capture n=9/15 Blood and semen Short reads sequencing
- * ONT whole genome n=13/15 Blood Long reads sequencing

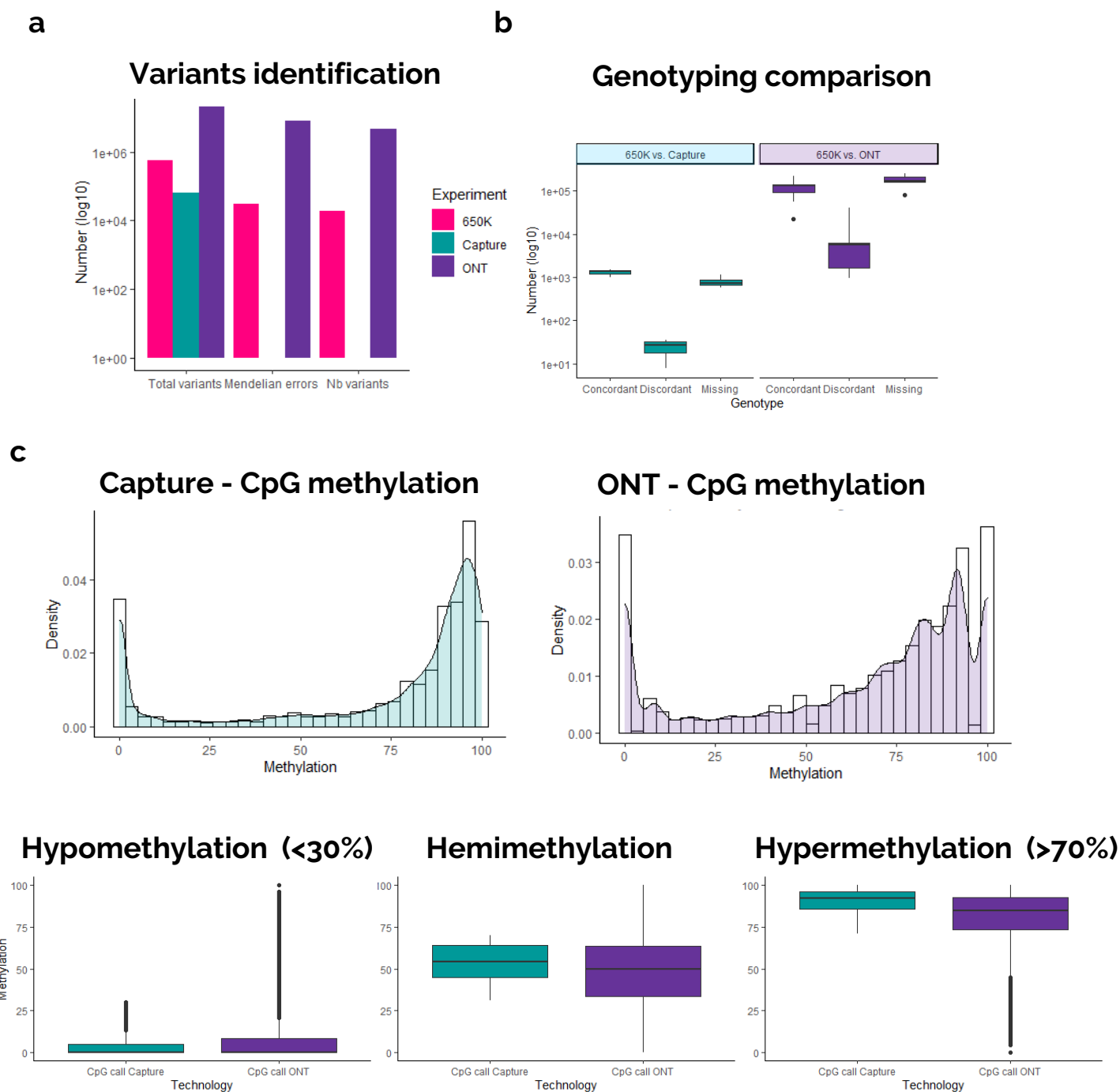
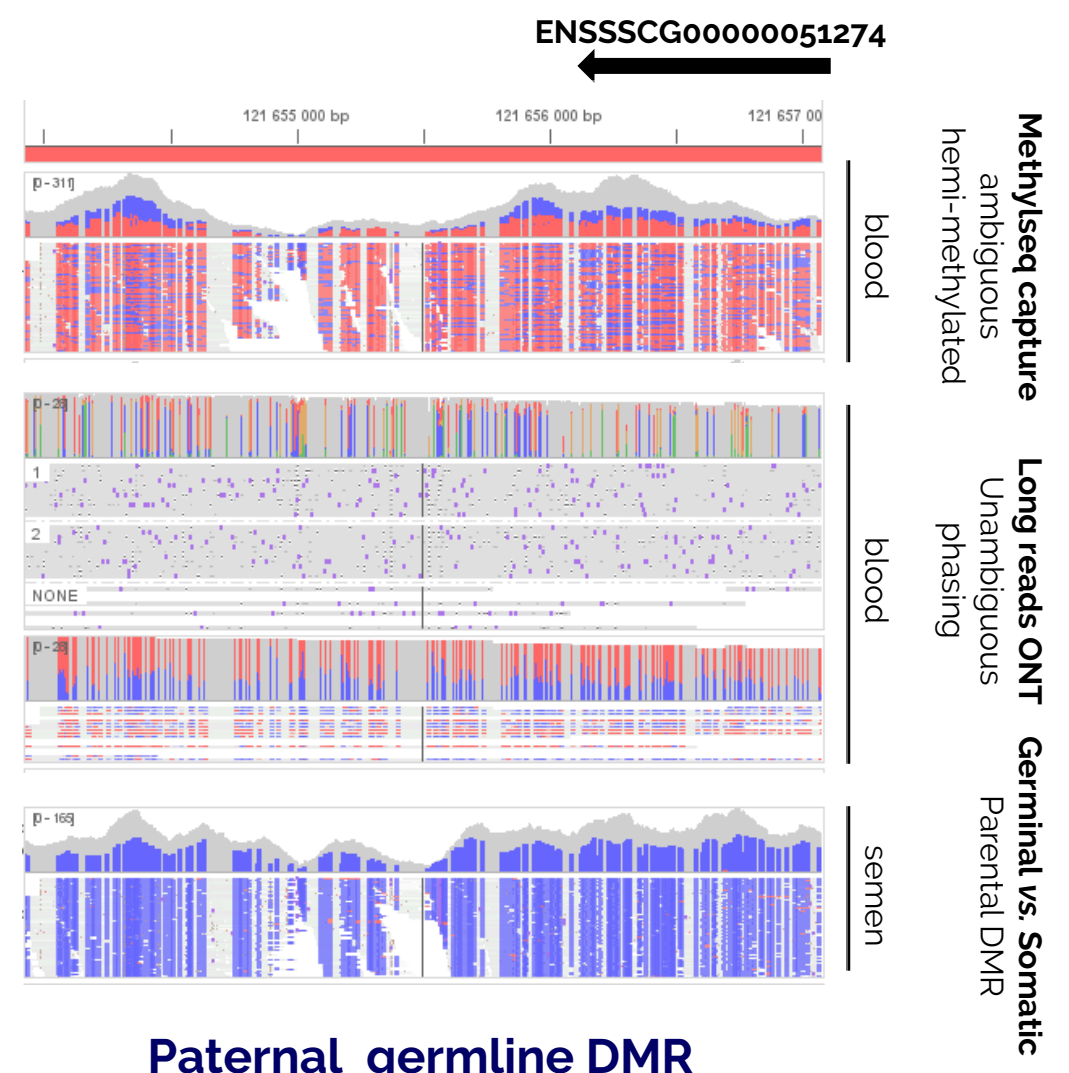


Figure 2: Evaluation of variant and hemimethylation callings from ONT. a, b. Comparisons of common genotypes between the high density SNP array, methylseq capture and ONT whole genome have been performed. c, d. Comparisons of methylation status between common CpG between methylseq capture and ONT whole genome have been analysed. The mean coverage of ONT whole genome sequencing was 40X suggesting that this coverage seemed sufficient to identify both relevant genotypes and hemimethylation pattern to tag parental differentially methylated regions such as Imprinting control Regions (ICR).

Molecular signature of genomic imprinting

- ONT identifies simultaneously both haplotypes and methylation tagging parental Differentially Methylated Regions (DMR)
- Parental-specific methylation identification from ONT requires high depth sequencing for variant calling and hemimethylation targeting



Paternal germline DMR