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Sperm DNA methylation analysis in swine reveals conserved and species-specific methylation patterns and highlights an altered methylation at the GNAS locus in infertile boars

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► **To cite this version:**

Annabelle Congras, Martine Yerle-Bouissou, Alain Pinton, Florence F. Vignoles, Sylvain Foissac, et al.. Sperm DNA methylation analysis in swine reveals conserved and species-specific methylation patterns and highlights an altered methylation at the GNAS locus in infertile boars. Conference 2014 Epiconcept "Epigenetics and Periconception Environment", Oct 2014, Vilamoura, Portugal. 72 p. hal-02739006

HAL Id: hal-02739006

<https://hal.inrae.fr/hal-02739006>

Submitted on 2 Jun 2020

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Epigenetics and Peri-conception Environment

Vilamoura, Portugal

01 - 03 Octobre 2014

➤ Présentation orale

Sperm DNA methylation analysis in swine reveals conserved and species-specific methylation patterns and highlights an altered methylation at the GNAS locus in infertile boars

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In the last decade, more and more studies have reported aberrant pattern of methylation in sperm DNA of patients with an altered spermogram. It is also admitted that epigenetic reprogramming during germ cell development is a key mechanism for the production of functional gametes and the proper development of the embryo. As poor semen quality is also a key issue for farm animals' productivity, we studied the methylation profile of sperm DNA of fertile and infertile boars.

We first described and compared the methylome and hydroxymethylome in sperm DNA from two fertile boars by combining MeDIP-Seq and Reduced Representation Bisulfite Sequencing. We then focused on the methylation level of imprinted genes in poor-quality semen by MeDIP-qPCR and single base methylation analysis by bisulfite conversion and pyrosequencing.

Methylome analysis and its comparison with mouse and human data revealed the high conservation of the methylation pattern of sperm cells between mammals: sperm DNA is highly methylated with the exception of CpG islands and promoters. We nevertheless observed some discrepancies between species, like in the promoter of the developmental gene POU5F1 which was highly methylated in human sperm only, suggesting a different dynamics of activation of this gene following fertilization. We compared global level of sperm DNA methylation between fertile and infertile boars but we did not observed significant differences between these two groups. We then selected 42 loci of interest, most of them known to be imprinted in human or mice and quantified their DNA methylation levels in fertile and infertile boars. Comparison between these two groups of board revealed that one imprinted region, the GNAS locus, shows an increase in 4 out of 8 infertile boars with low semen quality. This increase in DNA methylation is associated with an altered expression of the genes belonging to the GNAS locus, suggesting a new role for this locus in the proper formation of functional gametes.