The interest of our team is focused on understanding the nature and the role of the epigenetic information within the peri-conception window, which encompasses gametogenesis, fertilization and early embryonic development.

Our efforts are mostly centered on DNA methylation, how it influences gametic production and integrity, and impacts on phenotypes at following generations. Our approach is mainly fundamental, using the mouse as a mammalian model. We are also extending our knowledge to human through collaborations with fertility centers.

Studying the epigenetic setting of germ cells allows investigating several crucial aspects of mammalian biology such as transposon control, genomic imprinting and early lineage commitment. Studying DNA methylation in the window of conception leads also to mechanistic insights into the spatio-temporal control of genomic methylation specificity, including components of histone modification and RNA-directed pathways (small and long).

Figure 1: Expression analysis by RNA-seq of different classes of transposons in testes of Dnmt3L-/- mice at different ages post-conception.
Our work extends over these different aspects, through the use of fine developmental and molecular dissection, combined with genetic tools (CRISPR) and genome-wide sequencing approaches.

Our work can be subdivided in three themes related to the role of epigenetics in mammalian reproduction.

1. The first focuses on the protection of the male germ line against transposons. These genetic parasites make up the majority of the mammalian genomes and can impact on genome architecture and function in a variety of ways. We are investigating the cellular and genetic damages that transposons can inflict on the male germ line, as well as the cooperation of different levels of transposon control, including specialized small interfering RNAs. This aspect is developed mostly in the mouse model, but we are also investigating transposon regulation during normal human spermatogenesis and in germ cell tumors.

2. The second aspect deals with the importance of epigenetic processes in the female germ line. Oocyte methylation is particularly involved in the control of parent-specific expression of imprinted genes. We have been developing a genome-wide methylation screening for the identification of new imprinted genes, and are investigating the mechanisms underlying imprinted regulation. We are also screening for new targets of oocyte methylation, and in particular for genes that are epigenetically programmed in the oocyte for their participation to the first lineage decision after partum.
fertilization.

3. Finally, we are investigating the mechanisms underlying the acquisition of DNA methylation patterns, in an attempt to identify the positive and negative drivers of DNA methylation. We are using biologically relevant in vivo material, such as germ cells and early embryos, but are also developing cellular models of DNA methylation switch.

Correct DNA methylation patterns are paramount for the generation of functional gametes capable of forming viable offspring, but also for the regulation of pluripotency states and the maintenance of genome architecture and expression in somatic cells. Our work, not only impacts on the field of reproduction and development, but also on stem cell biology and cancer.

Key publications

Year of publication 2019

Roberta Ragazzini, Raquel Pérez-Palacios, Irem H Baymaz, Seynabou Diop, Katia Ancelin, Dina Zielinski, Audrey Michaud, Maëlle Givelet, Mate Borsos, Setareh Aflaki, Patricia Legoix, Pascal W T C Jansen, Nicolas Servant, Maria-Elena Torres-Padilla, Deborah Bourc'his, Pierre Fouchet, Michiel Vermeulen, Raphaël Margueron (2019 Aug 28)

**EZHIP constrains Polycomb Repressive Complex 2 activity in germ cells.**

*Nature communications* : 3858 : [DOI: 10.1038/s41467-019-11800-x](https://doi.org/10.1038/s41467-019-11800-x)

Year of publication 2017

Maxim V C Greenberg, Juliane Glaser, Máté Borsos, Fatima El Marjou, Marius Walter, Aurélie Teissandier, Déborah Bourc'his (2017 Jan 2)

**Transient transcription in the early embryo sets an epigenetic state that programs postnatal growth.**

*Nature genetics* : 110-118 : [DOI: 10.1038/ng.3718](https://doi.org/10.1038/ng.3718)

Year of publication 2016

Joan Barau, Aurélie Teissandier, Natasha Zamudio, Stéphanie Roy, Valérie Nalesso, Yann Hérault, Florian Guillou, Déborah Bourc'his (2016 Nov 19)

**The DNA methyltransferase DNMT3C protects male germ cells from transposon activity.**

*Science (New York, N.Y.)* : 909-912
Marius Walter, Aurélie Teissandier, Raquel Pérez-Palacios, Déborah Bourc'his (2016 Jan 27)
An epigenetic switch ensures transposon repression upon dynamic loss of DNA methylation in embryonic stem cells.
eLife : DOI : 10.7554/eLife.11418

Year of publication 2015

Natasha Zamudio, Joan Barau, Aurélie Teissandier, Marius Walter, Maté Borsos, Nicolas Servant, Déborah Bourc'his (2015 Jun 26)
DNA methylation restrains transposons from adopting a chromatin signature permissive for meiotic recombination.
Genes & development : 1256-70 : DOI : 10.1101/gad.257840.114

Year of publication 2014

Rachel Duffié, Sophie Ajjan, Maxim V Greenberg, Natasha Zamudio, Martin Escamilla del Arenal, Julian Iranzo, Ikuhiro Okamoto, Sandrine Barbaux, Patricia Fauque, Déborah Bourc'his (2014 Mar 5)
The Gpr1/Zdbf2 locus provides new paradigms for transient and dynamic genomic imprinting in mammals.
Genes & development : 463-78 : DOI : 10.1101/gad.232058.113