

## Effect of inflammation on epigenetic markers in the lactating mammary gland



FVB/N mouse, The Jackson Laboratory

Ivanova E.<sup>1</sup>, Hue-Beauvais C.<sup>1</sup>, Chaulot-Talmon A.<sup>2,3</sup>, Castille J.<sup>1</sup>, Aubert-Frambourg A.<sup>2,3</sup>, Kiefer H.<sup>2,3</sup>, Germon P.<sup>4</sup>, Jammes H.<sup>2,3</sup>, Le Provost F.<sup>1</sup>

<sup>1</sup> GABI, INRAE, AgroParisTech, Université Paris-Saclay, 78350 Jouy-en-Josas, France

<sup>2</sup> Université Paris-Saclay, UVSQ, INRAE, BREED, 78350, Jouy-en-Josas, France

<sup>3</sup> Ecole Nationale Vétérinaire d'Alfort, BREED, 94700, Maisons-Alfort, France

<sup>4</sup> INRAE, Université de Tours, ISP, F-37380, Nouzilly, France

### Introduction

Current strategies in animal husbandry and their consequences on animal health and welfare, and on the environment, are important societal concerns in terms of both ethics and sustainability. Ruminant **longevity** depends on phenotype expression related to health and production characteristics. Phenotype expression variability depends on genetic factors, but also **epigenetic factors** that reflect environmental influences. The goal of this project is to study **epigenetic marks** involved in **mammary inflammation** during **lactation** in the hopes of discovering **biomarkers of early inflammation** that aid in achieving a compromise between animal health and milk productivity.

### Methods

Proof of concept: mouse model of **early mammary inflammation** via intramammary LPS injections (tissue sampled **4 hours** post-injection).

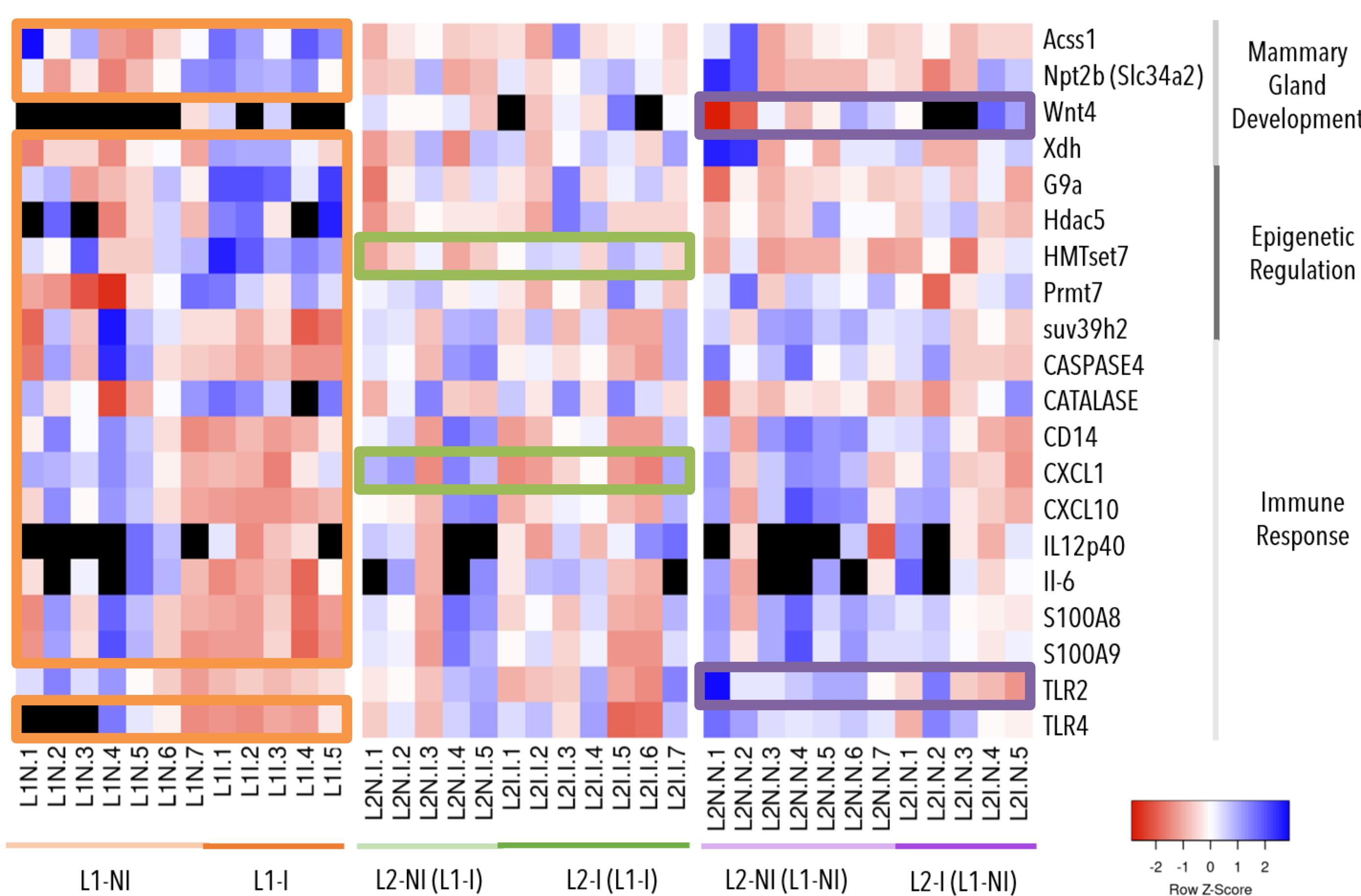
**Mammary gland samples** from 1<sup>st</sup> or 2<sup>nd</sup> lactation, with or without inflammation (5 or 7 mice).

- **Gene expression** via RT-qPCR Fluidigm
- **DNA methylation** via RRBS

	Lactation 1 (L1)	Lactation 2 (L2)
Lot 1	NI	NI
Lot 2	I	NI
Lot 3	I	I
Lot 4	NI	I

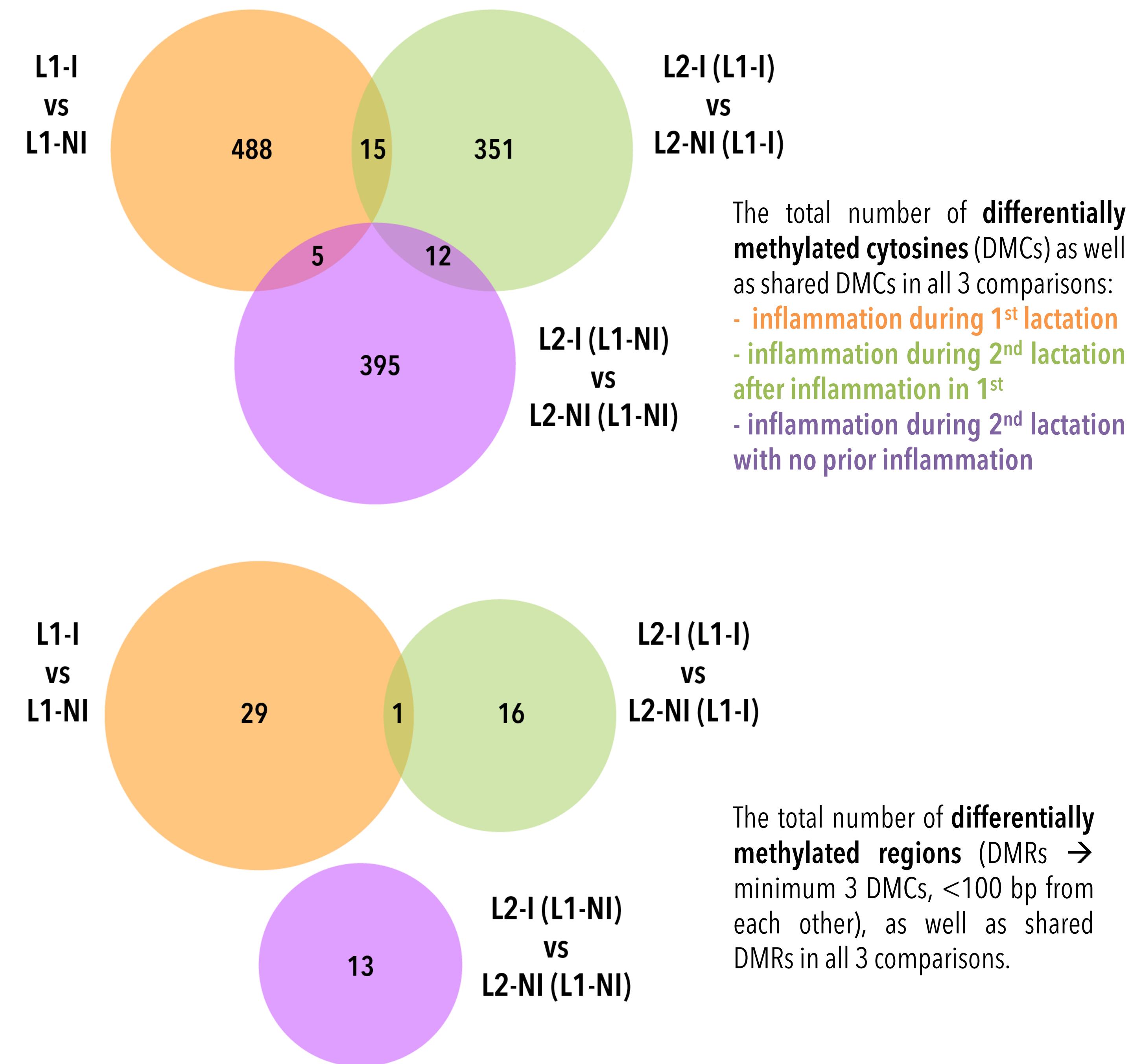
NI: non-inflamed  
I: inflamed

### Mammary inflammation affects gene expression



Inflammation provokes **different gene expression changes** depending on lactation rank, with the **most** changes observed during **1<sup>st</sup> lactation**.

### DNA methylation changes caused by mammary inflammation



### Discussion

Our results show that **differentially expressed genes** were **not differentially methylated**, suggesting other pathways for transcription regulation are involved. We found that **lactation rank** and **inflammation history** are important variables for determining markers of early mammary inflammation. Next, we will study whether differentially methylated genes in different conditions intervene in **similar signaling pathways**. Results were acquired in a mouse model with the objective of **transferring this knowledge to farmed species**. From this work, new leads will emanate which could lead to proposals for **new strategies** to be used **in breeding**.

Inflammation provokes **different DNA methylation changes** depending on lactation rank and inflammation history.