

Milk microRNA composition depends on dairy cow breed

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MILK MICRORNA COMPOSITION DEPENDS ON DAIRY COW BREED

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CONTEXT

Mother's reflect

Direct link between microRNAs expression in the mammary gland and their level in milk

Le Guillou et al., 2012; Laubier et al., 2015; Alsaweed et al., 2016

Healthy food

Milk is a source of nutrients for neonate and adult

Milk composition influences consumer health in both short and long terms

Kongerslev Thorning et al., 2016; Mosca et al., 2017

microRNAs

Affect functions such as immunity, growth, development or cell proliferation Kosaka et al., 2010

Present in large quantities in milk Weber et al., 2010

Impact

- microRNAs are transmitted from mother to infant
- Potential action across species and influence of milk effects on consumer health Title et al., 2015; Manca et al., 2018

Mammary Gland

Offspring '

Consumer

Milk

Factors for microRNA composition variation

Nutrition Breeds



Does milk microRNA composition (miRNome) vary according to the genetic background?

Comparison of milk miRNomes in Normande vs. Holstein dairy cows

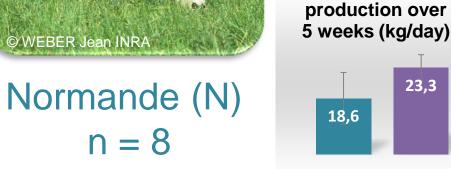
EXPERIMENTAL MATERIAL

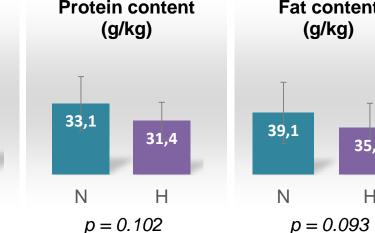
Primiparous cows raised together in the experimental farm



Mann & Whitney analysis

Two breeds with contrasted lactation performances **Dairy milk** (g/kg)





(mg/cl) p = 0.063



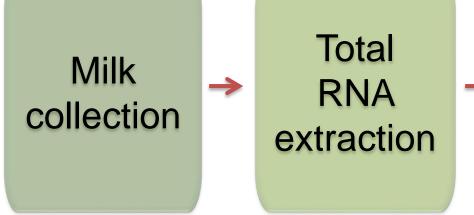
Holstein (H) n = 9

Principal component

analysis

Normande

METHODS



Small RNA libraries Illumina

Small RNA-seq Illumina

Sequences processing: adaptors removing (CutAdapt) and sizing (17-28 nt)

Bio-informatic analysis miRDeep2 : genome blasting (BosTau8), annotation (miRBase), microRNA prediction and quantification. Redundancies filter (parse_miRDeep2_output.pl) (Le Guillou et al.,2014)

p = 0.006

Statistical analysis: PCA (ade4 package), counting threshold identification (Bioconductor HTSFilter), differential analysis via Limma (voom)

RESULTS

The list of microRNAs in milk is common to both breeds



with variable abundancies, and consists of 957 annotated and 1,422 predicted microRNAs

Major milk microRNAs are the same for both breeds

microRNA abundance in Holstein (H) and Normande (N) milk microRNA % of reads bta-miR-148a-3p 19.4% 19.8% > 40 % of bta-miR-30a-5p 14.4% 16.4% milk reads bta-miR-22-3p 8.1% 7.8% bta-miR-26a-5p 4.5% 4.2% bta-miR-27b-3p 3.9% 3.3% bta-miR-186-5p 3.5% 3.1% 3.7% bta-miR-21-5p 3.2% 3.1% bta-miR-181a-5p 3.0% 4.1% bta-miR-141-3p 2.5% 2.1% bta-let-7a-5p bta-chr10_2883_mt-5p 2.3% 2.3% 1.7% bta-miR-30d-5p 1.3% bta-chr20_18762_mt-3p 2.1% 1.4% bta-miR-92a-3p 1.6% 1.4% bta-miR-191-5p 1.6% 0.6% bta-miR-375-3p 1.6% bta-let-7f-5p 1.3% 1.5%

Milk miRNome differs between breeds

182 milk microRNAs are significantly different between breeds (p<0.05)

Normande Holstein

58 microRNAs are more abundant in Holstein milk (53 known, 5 predicted), including:

miR-26a-5p, miR-27b-3p, let-7a-5p, let-7c-5p, miR-30d-5p, miR-375-3p, and miR-660-5p

124 microRNAs are more abundant in Normande milk (17 known, 107 predicted), including:

miR-10a-5p, miR-142-3p & -5p, miR-221-3p, miR-222-3p, miR-223-3p & -5p, and miR-451-5p

Genes and pathways targeted by these microRNAs are particularly related to the regulation of milk fat synthesis and metabolism, and protein processing in endoplasmic reticulum

Comparison with bovine mammary miRNomes

1.2%

0.9%



bta-miR-660-5p

12 of the major milk microRNAs (in red in the previous table), of which the 3 most significant, are also the most expressed in Holstein lactating mammary gland

4 microRNAs show a significant enrichment in milk compared to mammary gland

microARN	Milk	Mammary
	Rank	Rank
bta-miR-30d-5p	12	48
bta-miR-191-5p	15	45
bta-miR-375-3p	16	59
bta-miR-660-5p	18	100

Centre de Recherches de Jouy-en-Josas

Variations according to breed in milk are also observed in mammary gland for 5 microRNAs



Between Holstein and Montbéliarde breeds: miR-30c-5p, miR-143-3p and miR-340-3p



Between Holstein and Limousine breeds: *miR-375-3p* and *miR-2285t-3p*

CONCLUSION

This study allowed to evaluate genetic variations of the bovine milk miRNome according to the breeds, highlighting 182 microRNAs with significantly different levels between Holstein and Normande milk.

As milk is a source of nutrients and may influence health, the variation of its miRNome according to genetic variables, such as breeds, may have several impacts on consumers and thus requires particular attention.

MicroRNAs' evaluation in milk opens a field of investigation, as they can used as biomarkers, for downstream consequences on health, physiological or metabolic status, in animals and humans.















