DGAT1 K232a polymorphism greatly affects mammary gland activity of milk component synthesis

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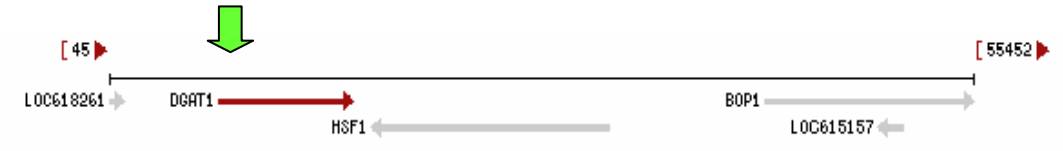
Session S15 - Number 4578

DGAT1 K232a mutation and consequences

BTA14

QTL affecting milk fat



Exon 8

Double substitution

…AGGT**AA**GAAGGCC… …Gly-Lys-Lys-Ala-Asn… ➡ **KK, High Fat Content**

…AGGT**GC**GAAGGCC… …Gly-Lys-Ala-Ala-Asn… ➡ **aa, Low Fat Content**

-11 g/kg ⇩ Fat content

+ Variation of FA composition

- Substrate specificity for C8:0>C16:0>C4:0>C18:0 acylCoA
- K232a mutation could affect enzyme maximal speed (Grisart *et al.*, 2004) and specificity (Schennink *et al.*, 2007)

DGAT1 issue

What are the molecular mechanisms underlying variation of milk fat content and fatty acid composition with the DGAT1 K232a mutation ?

Variation of milk production traits

With the aa, low fat content genotype :

significant reduction of fat content and milk fat globule size

tendency of increased milk production and lactose yield

no difference for protein content and yield and fat yield

Variation in fatty acid composition

With the aa, low fat content genotype :

more saturated middle chain and unsaturated long chain fatty acids

less unsaturated middle chain fatty acids

=> Comparable to Schennink *et al.*, 2007 and 2008 results

Gene expression profiling: microarray analysis

~ 9 973 genes

~ 13 746 genes

“Super slide”

25 % of overlapping between the 2 slides

= 14 567 genes with Ingenuity annotation

~55 % of the bovine genome

* CRB = Centre de Ressource Biologique GADIE (INRA, France)

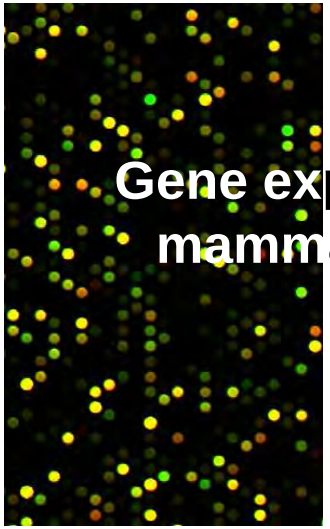
Strategy

6 pairs (full or half sibs)
Pin-au-Haras
(Holstein x Normande)

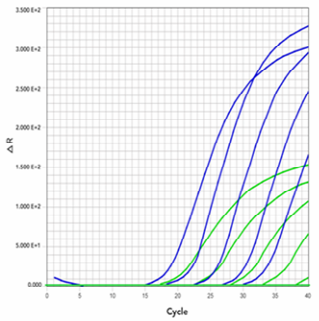
KK, high fat content

aa, low fat content

UE Theix

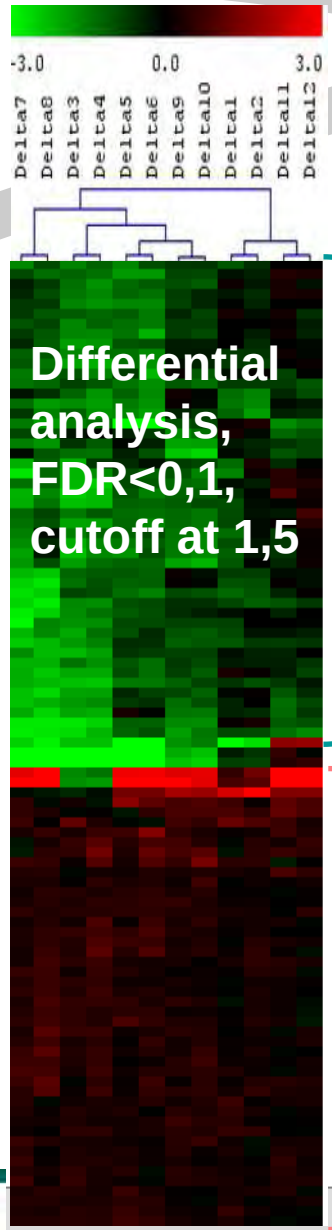


Gene expression in mammary gland



Milk production traits and fine milk composition

General microarray results



228 down-regulated genes with aa, low fat content

Cytoskeleton proteins

(actins, keratins, tropomyosin)

Post-translational modifications of the proteins

(*LBP*, *B4GALT5*)

Immune response

(complement, interleukins, interferon, chemokine, integrin)

Lipid metabolism

(LDL and chylomicron captation, catabolism)

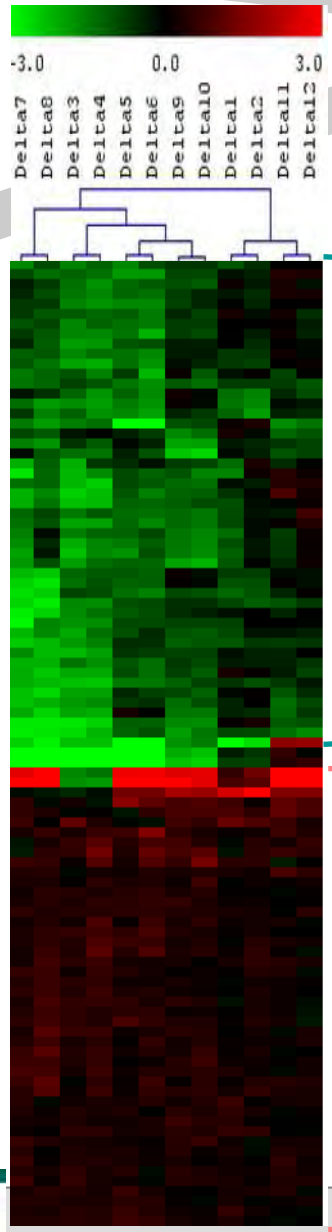
197 up-regulated genes with aa, low fat content

Milk lipid biosynthesis and secretion

- FA captation, FA, DG and PL synthesis
- Lipids secretion
- Regulation of lipid synthesis

Milk proteins (*CSN1S1*, *CSN1S2, LALBA*)

General microarray results



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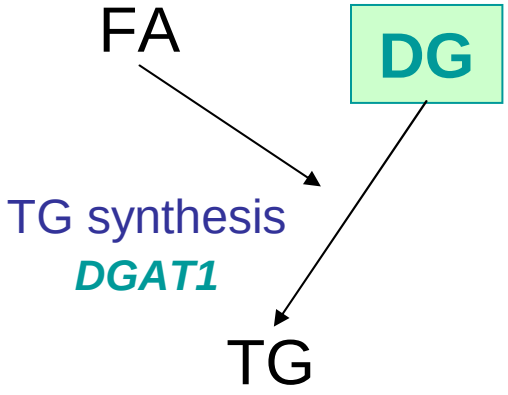
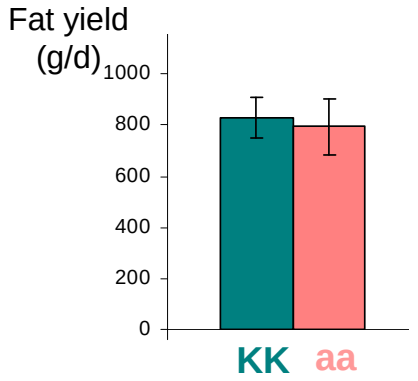
Decrease expression of DGAT1 gene but similar fat yield

aa, Low fat content
KK, High fat content





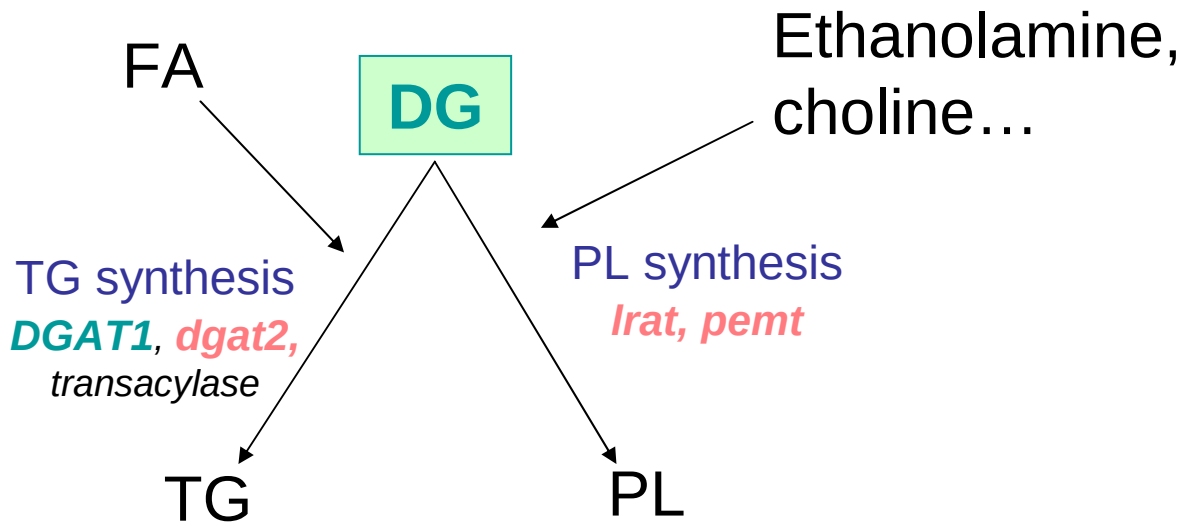
DGAT1 catalyzes the production of TG (main lipid component in milk) from DG and FA.

With aa, Low fat content genotype: less efficient **(Grisart *et al.*, 2004)** and *DGAT1* is down regulated

However, secreted fat yield is quite the same between genotypes

⇨ Alternative pathways to synthesize TG from DG ?

Differentially expressed genes



+ saturated middle chain FA
+ unsaturated long chain FA

Smaller milk fat globules

aa, Low fat content
KK, High fat content

Conclusions

❖ Variation of milk FA content with K232a mutation can be explained by:

alteration of enzyme specificity of DGAT1 (Schennink *et al.*, 2007)

alternative milk lipid biosynthesis pathways (TG, PL)

❖ Each milk component synthesis pathway seem affected by K232a mutation ! Is this representative of an increased insulin sensitivity of the mammary tissue ?

➢ Validation: genes redundancy between the 2 slides and qRT-PCR (in progress)

➢ functional annotation of some genes involved in the decrease of milk fat content.

Thanks for your attention !