SABRE

CUTTING EDGE GENOMICS FOR SUSTAINABLE ANIMAL BREEDING

Nutritional effects on epigenetic modifications and their inheritance in pigs

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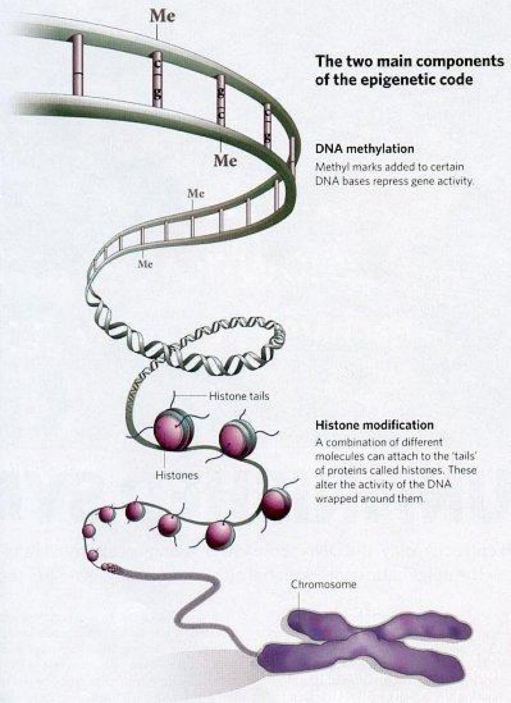
Food Quality and Safety

Background (1)

Epigenetics is the study of heritable changes of genome function that occur without changing of the DNA sequence.



The two main components of the epigenetic code

DNA methylation

Methyl marks added to certain DNA bases repress gene activity.

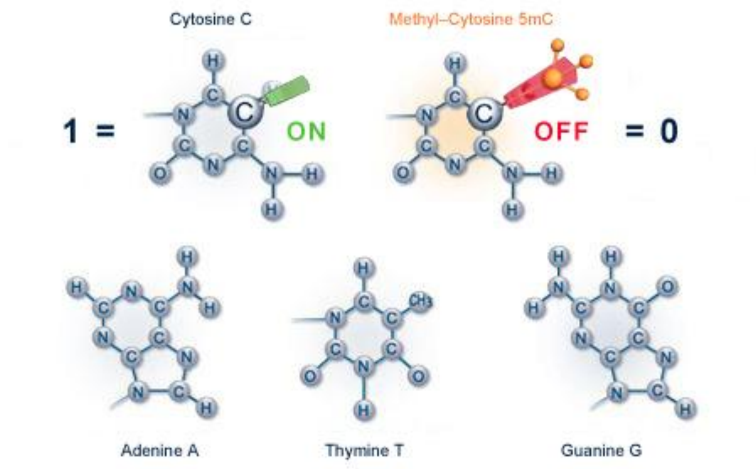
Histone modification

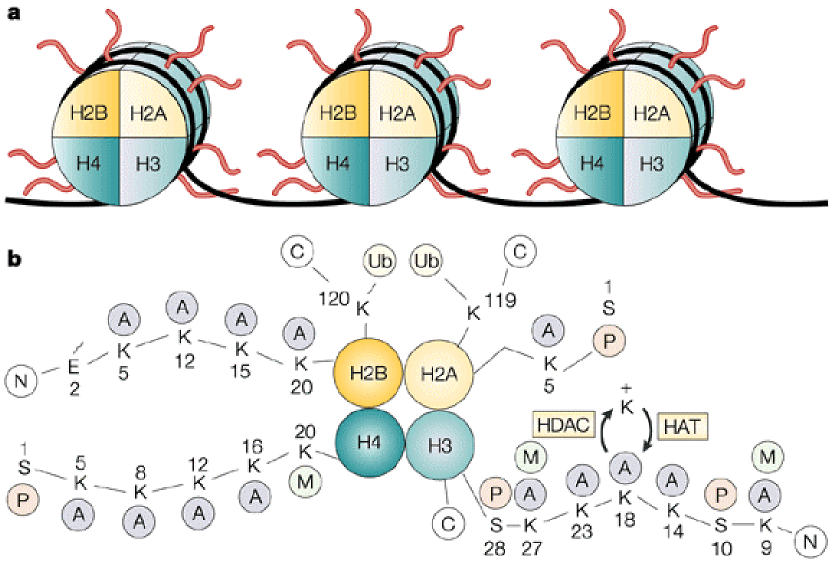
A combination of different molecules can attach to the 'tails' of proteins called histones. These alter the activity of the DNA wrapped around them.

Background (2)

DNA methylation

Histone modification





Nature Reviews | Cancer

non-histone proteins such as Polycomb and trithorax group proteins

Background (3)

It is hypothesized that nutrition affects DNA methylation and histone modifications and these changes are transmitted to the next-but-one generation.

The experiment was inspired by a epidemiological study from Överkalix cohorts, northern Sweden and mouse studies.

[Corpulent Grandfathers, Sick Grandchildren]

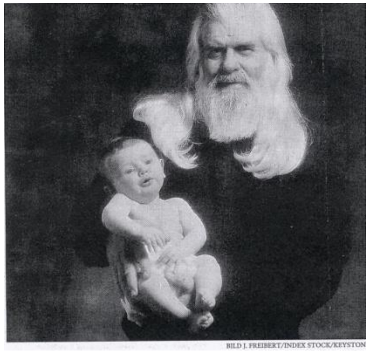
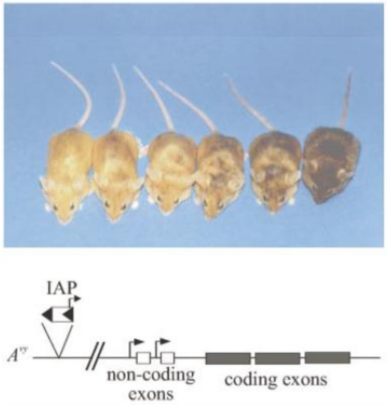
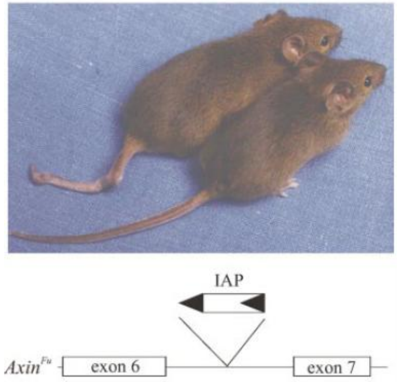


BILD J. FREIBERT/INDEX STOCK/KEYSTON

Tages-Anzeiger 10.01.2003



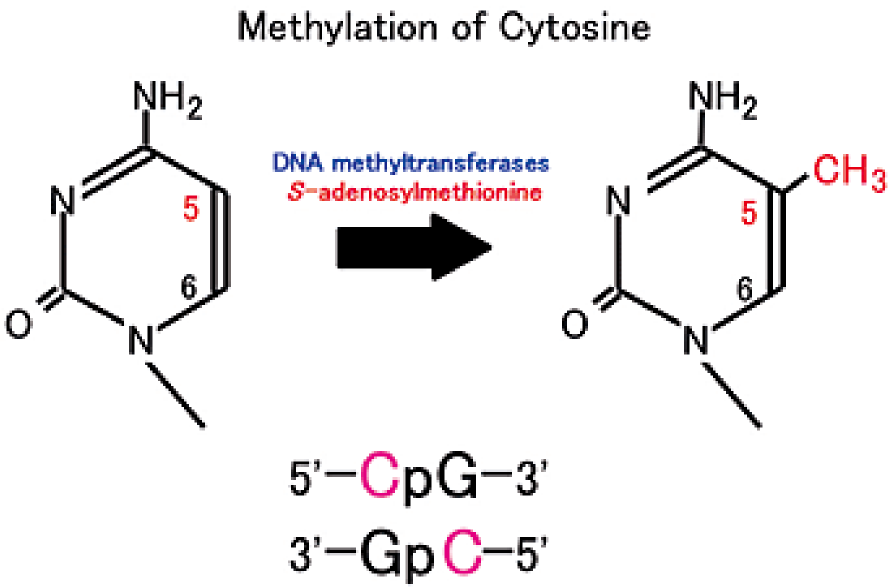
Morgen et al., 1999



Rakyan et al. 2003

Background (4)

DNA methylation



DNA is methylated by DNA methyltransferase, which catalyzes the transfer of a methyl (m) group from *S*-adenosylmethionine (SAM) to the 5-position of a cytosine nucleotide adjacent to guanine (CpG) to produce a 5-methyl-2-deoxycytidine (5-mC)

Three-generation pig feeding experiment

F0

Control diet

Experimental diet

X

Sows producing F1 males

F1

X

Sows producing F2 pigs

F2

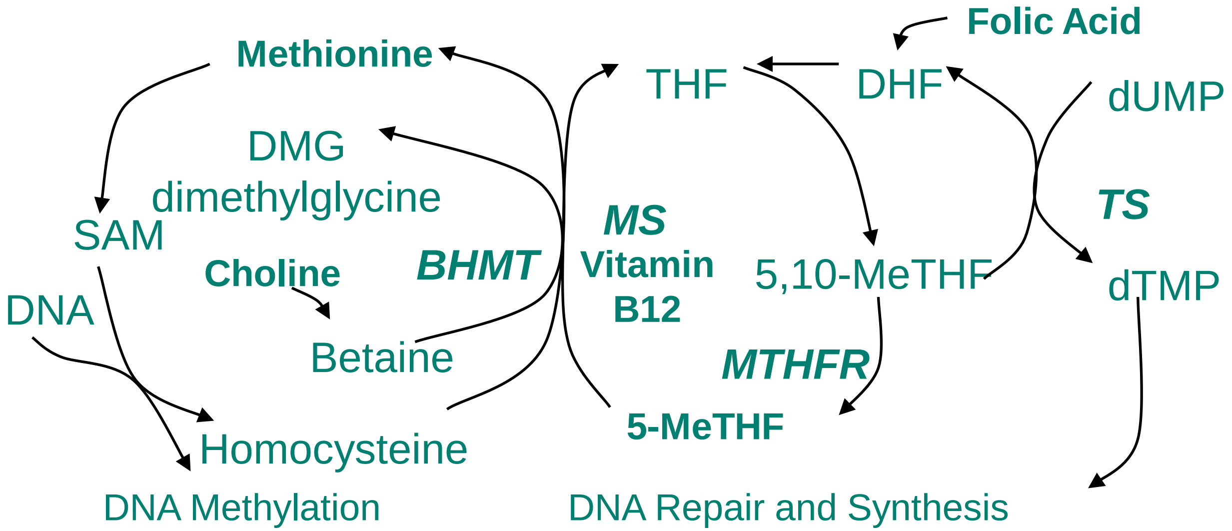
Experimental diet

Methyl donors:

Methionine, 3x
Choline, 4-7x
Betaine, 1600mg/kg

Co-factors:

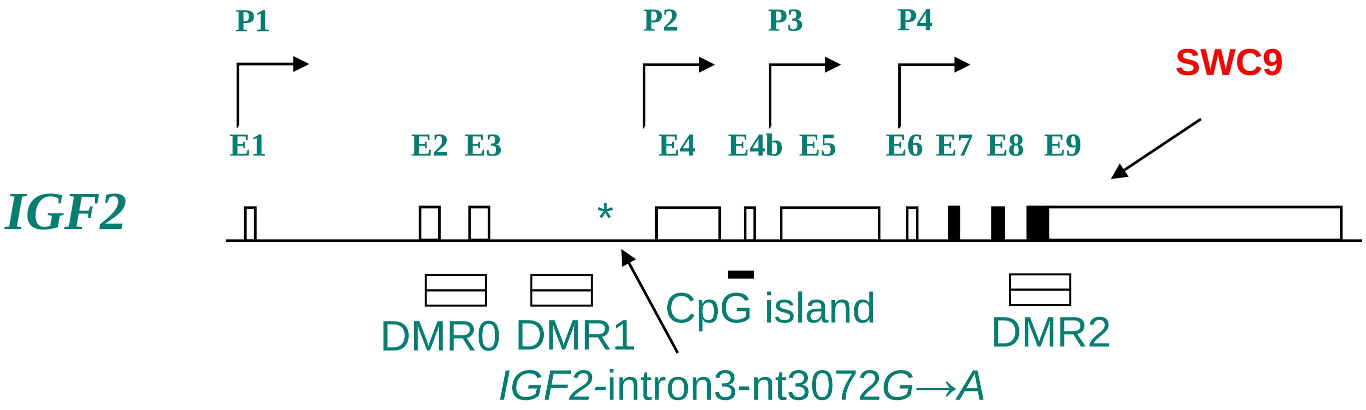
Folate, 400x
Vitamin B6, 400x
Vitamin B12, 400x



Folic Acid
Methionine
THF
DHF
dUMP
DMG
dimethylglycine
SAM
TS
MS
Vitamin B12
BHMT
Choline
5,10-MeTHF
dTMP
DNA
Betaine
MTHFR
5-MeTHF
Homocysteine
DNA Methylation
DNA Repair and Synthesis

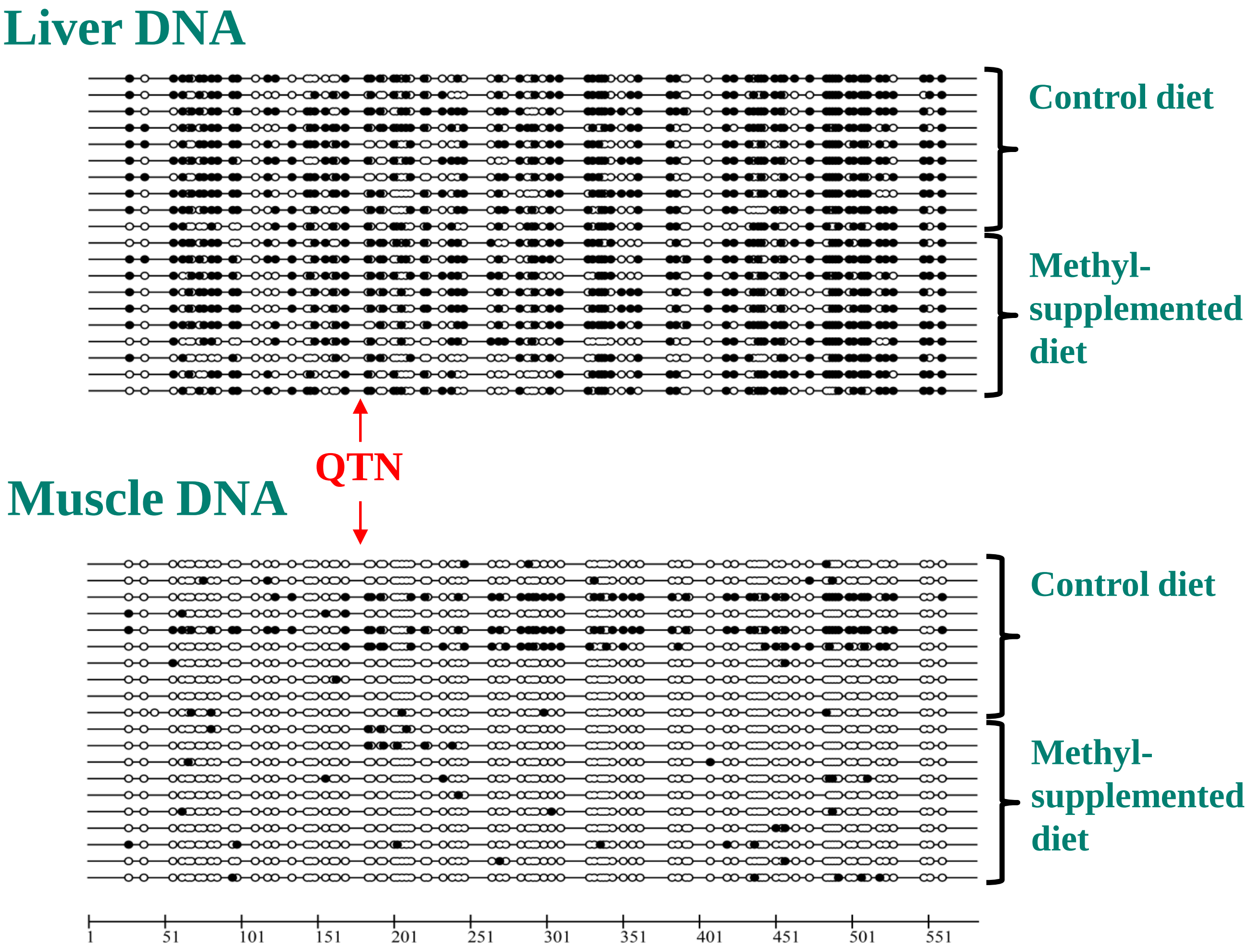
Analyses (1)

- **DNA methylation patterns (DMR0, DMR1, DMR2, CpG island, QTN region)**
- **Gene expression analysis, imprinted genes *IGF2, IGF2R***



DNA methylation analysis

IGF2 QTN region



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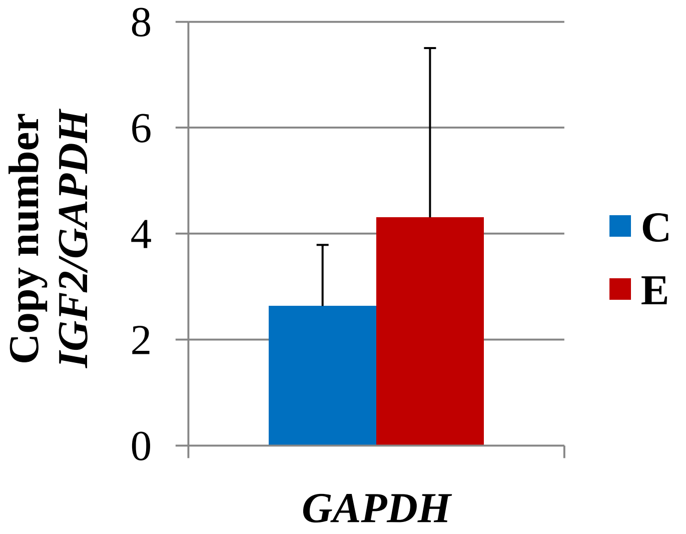
We found no significant differences in DNA methylation at the *IGF2* DMRs, at a CpG island and in the QTN region of the *IGF2* gene between the differentially fed F0 boars.

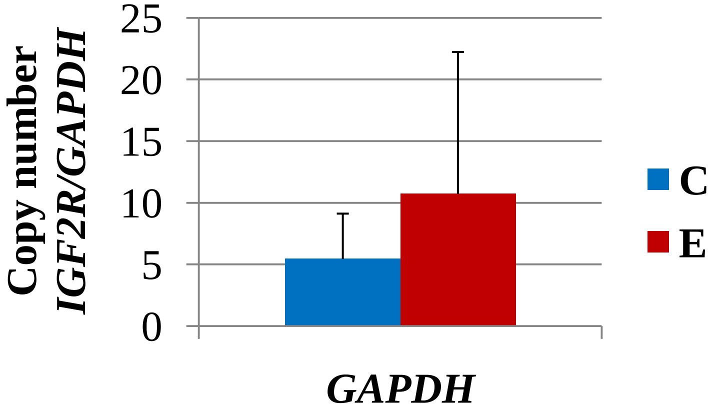
There is much variation in DNA methylation within and between individuals whereas hypermethylated regions seem to vary less.

Gene expression in F0 pig tissues

Liver

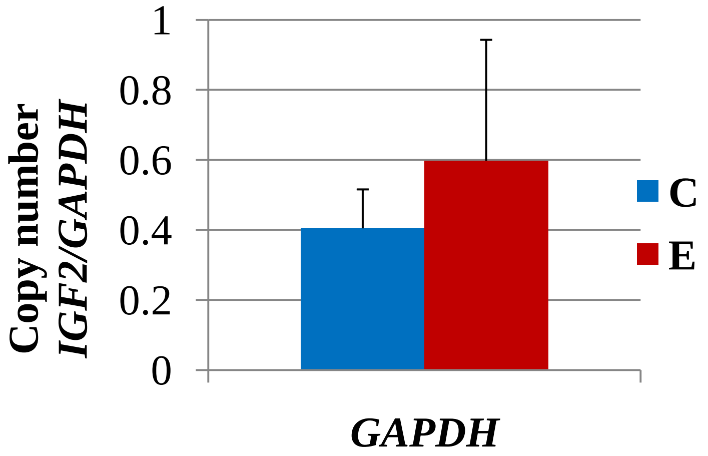


Liver

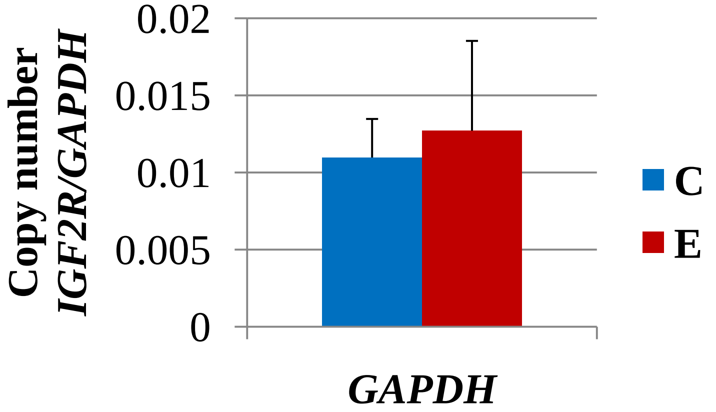


N=16

Muscle

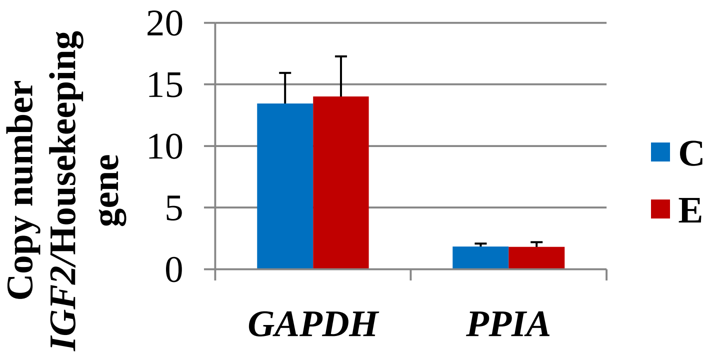


Muscle

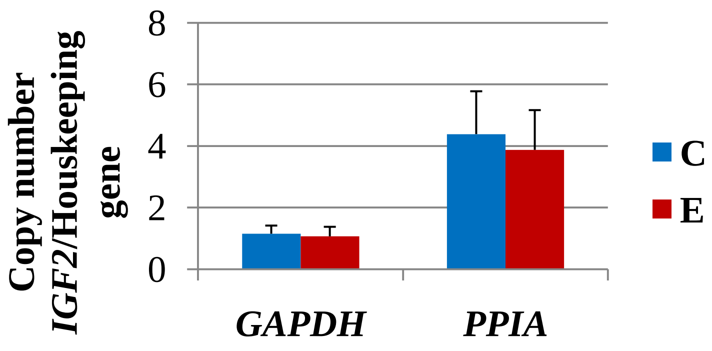


Gene expression in F2 pig tissues

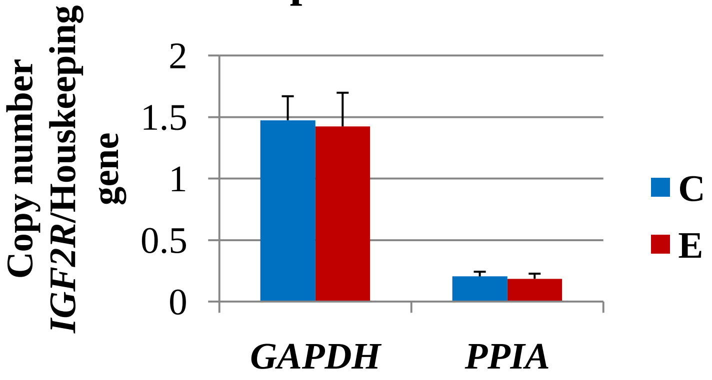
***IGF2* expression in F2 Liver**



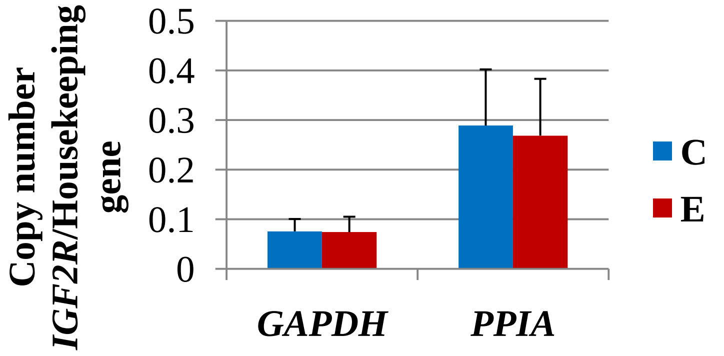
***IGF2* expression in F2 Muscle**



***IGF2R* expression in F2 Liver**



***IGF2R* expression in F2 Muscle**

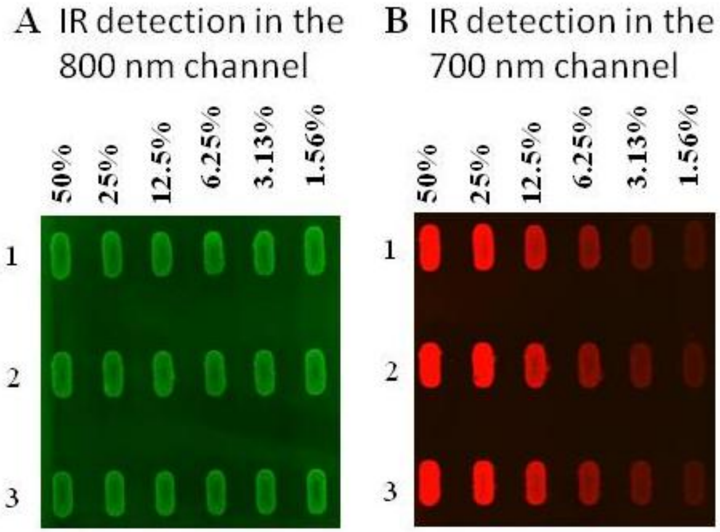


N=60

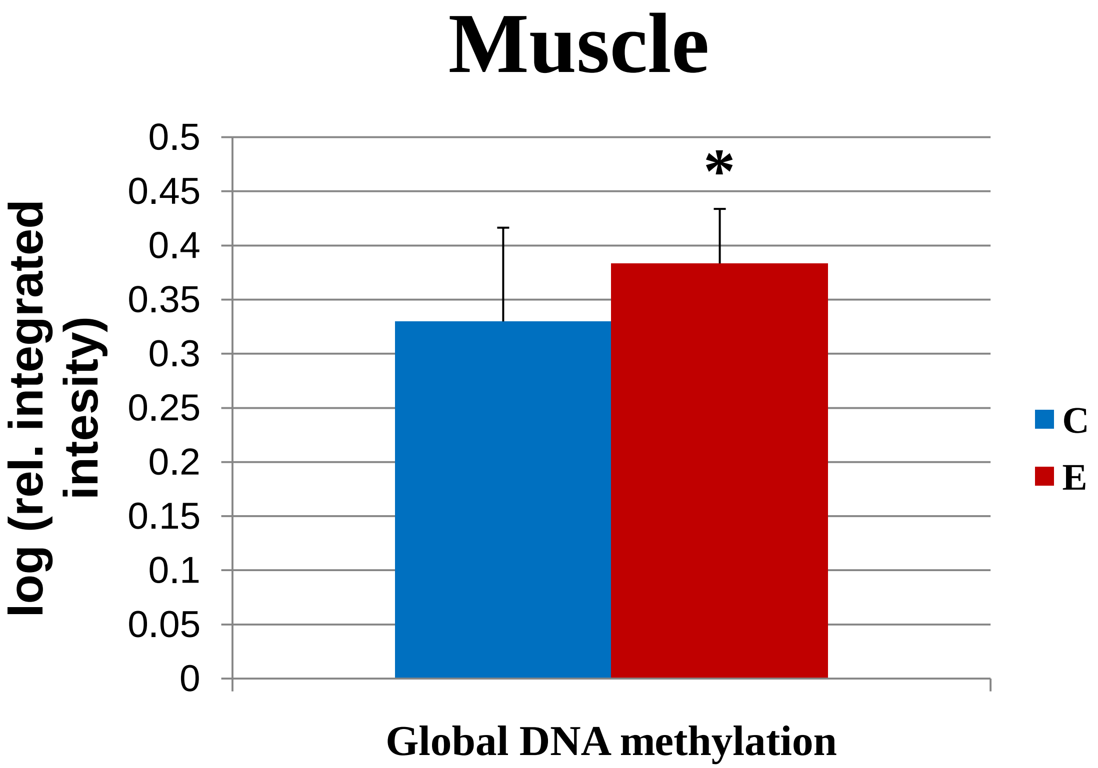
Analyses (2)

- **Global DNA methylation analysis**

- **Effect of differentially fed F0 boars on growth and carcass traits of F2 pigs**



Global DNA methylation in F2 barrows



Global DNA methylation in muscles of F2 barrows descended from methyl supplemented fed F0 boars was higher than in controls (*P*<0.05).

F2 growth traits

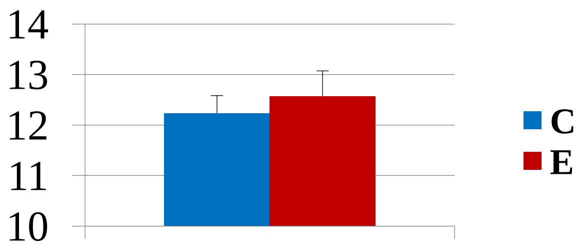
25 growth traits were measured for 60 F2 pigs.

F2 pigs descended from methyl supplemented fed F0 boars showed no significant differences in growth performance compared to the control pigs.

F2 carcass traits

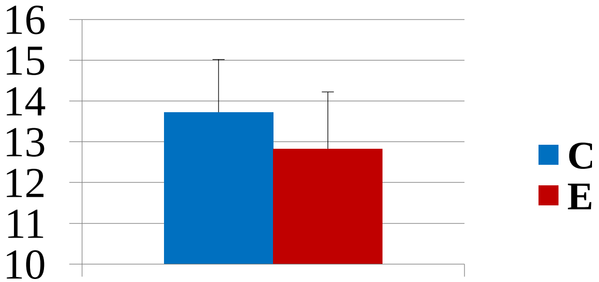
26 carcass traits were measured for 60 F2 pigs.

P=0.07



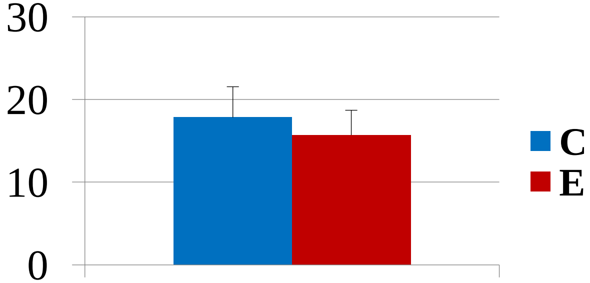
Shoulder %

P=0.09



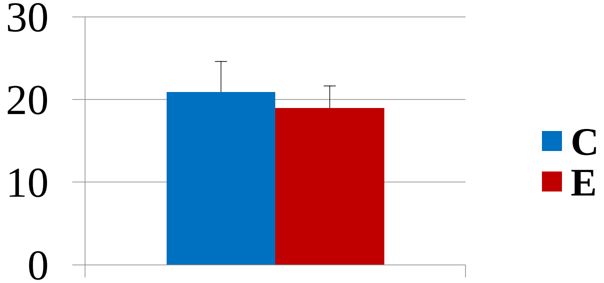
Adipose tissue %

P=0.08



Fat thickness at 10 rib, mm

P=0.09



Fat thickness at the croup, mm

Conclusions

There are indications that the methyl supplemented diet affects DNA methylation and carcass traits in the next-but-one generation.

The challenge is to separate the genetic from the epigenetic effects.

The proof of principle that diet induced epigenetic modifications are transgenerational transmitted in pigs may be established in this pedigree. This needs the finding of at least one epiallele that segregates in the experimental but not in the control line.

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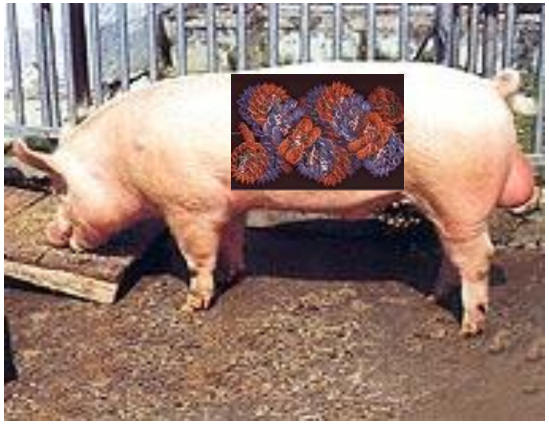

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