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Comparative multi-tissue gene expression profiles related to milk performance in cattle

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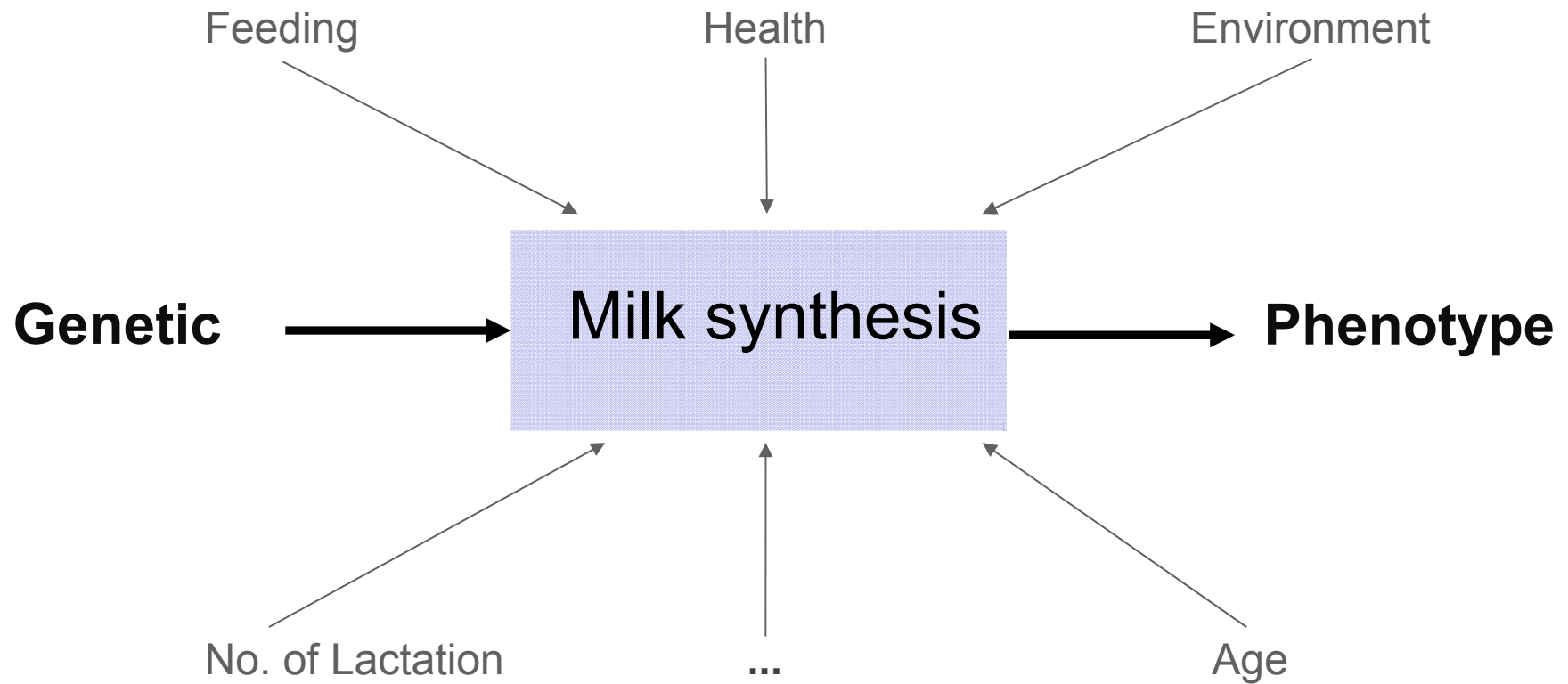
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Motivation



Motivation

Transcriptome



<http://www.affymetrix.com>

Microarray-Data

e.g., Mammary gland
Liver
Adipose Tissue



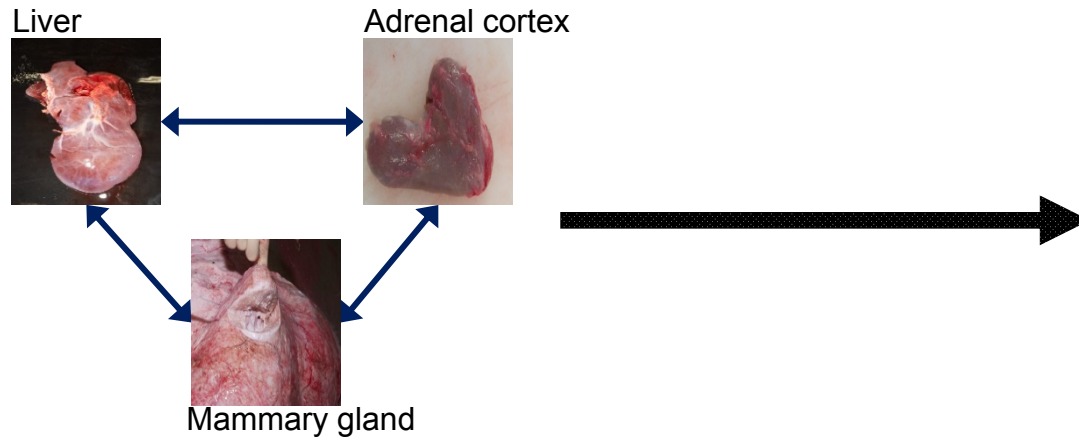
Phenotype



Milk performance

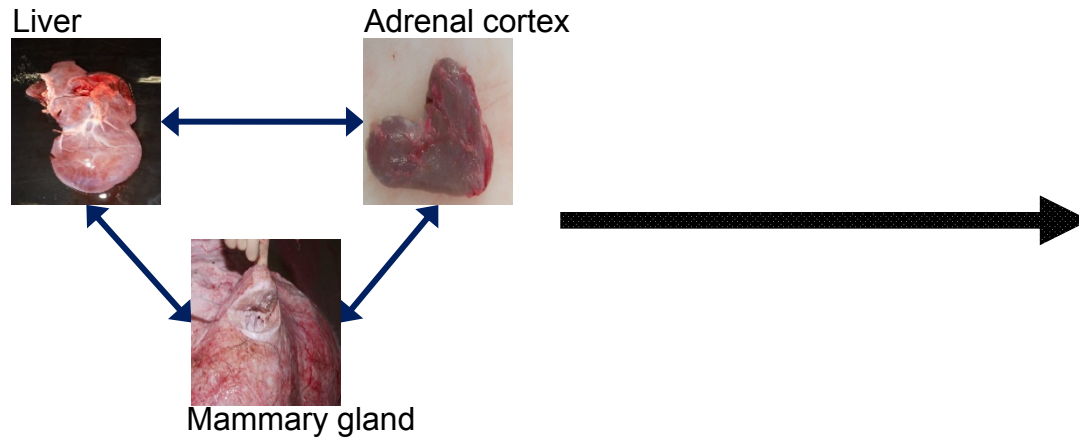
Motivation

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Motivation

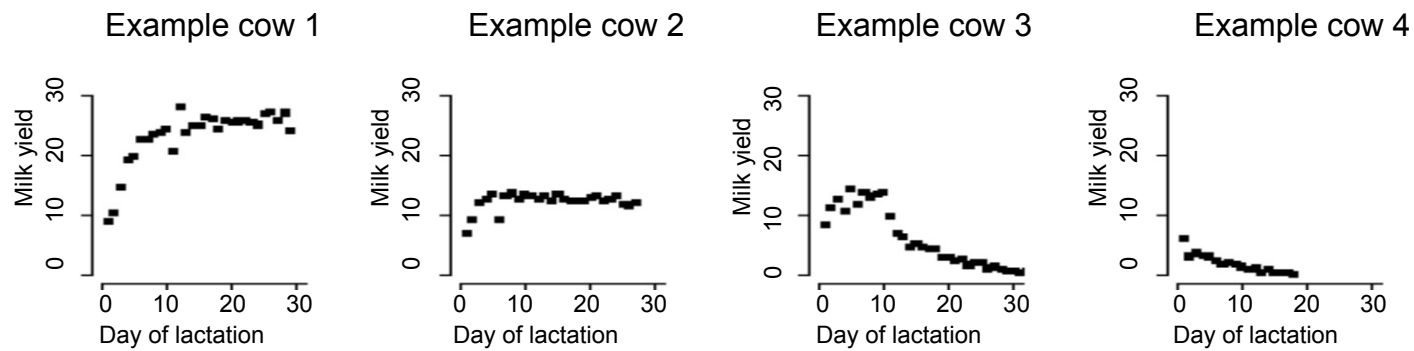
Transcriptome



Phenotype

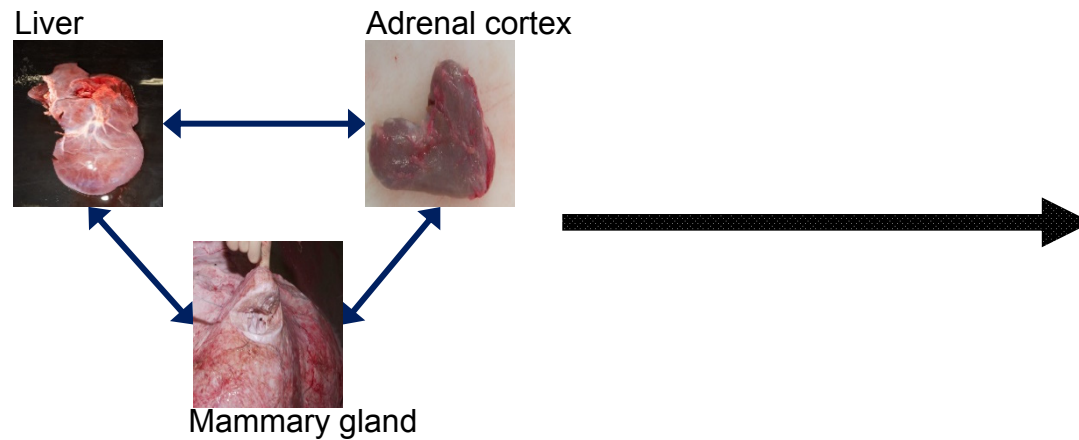


F2-population (Charolais x German Holstein; Kühn *et al.* 2002, *Arch. Tierz.*)



Motivation

Transcriptome



Aims:

- 1) Comparison of gene expression profiles in mammary gland, liver and adrenal cortex
- 2) Detection of biosignature candidates for milk performance at the transcriptome level

Experimental data



74 F₂ cows (2nd lactation) :

Gene expression data (mammary gland, liver, adrenal cortex; day 31±3 pp. 2nd lactation)

1. RNA extraction RNeasy[®] Mini Kit (Qiagen)
2. GeneChip[®]Bovine Genome Array (Affymetrix)
3. GCRMA Normalization
4. Filter: Genes expressed in > 75% of the cows (MAS5)

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→ Mammary gland: $n_{\text{genes}} = 5691$

→ Liver: $n_{\text{genes}} = 6697$

→ Adrenal cortex: $n_{\text{genes}} = 7290$

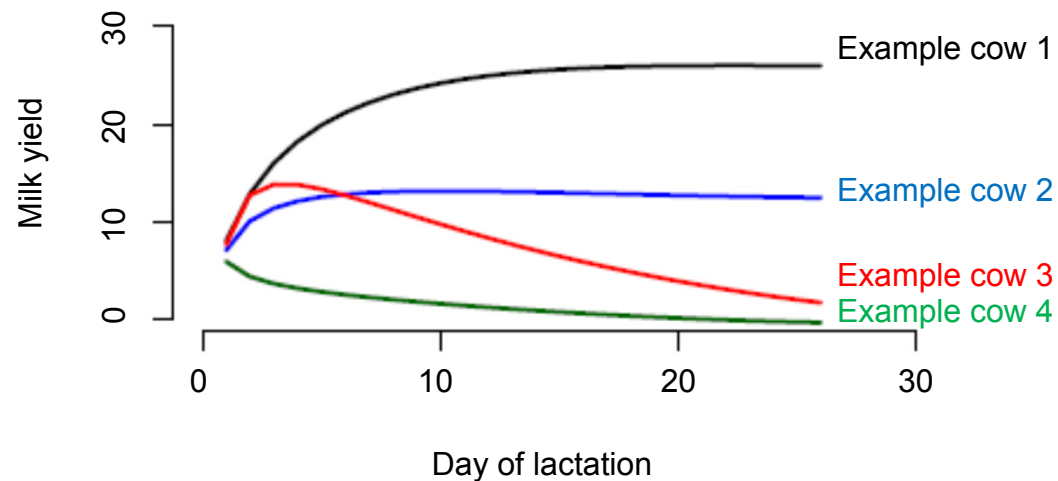
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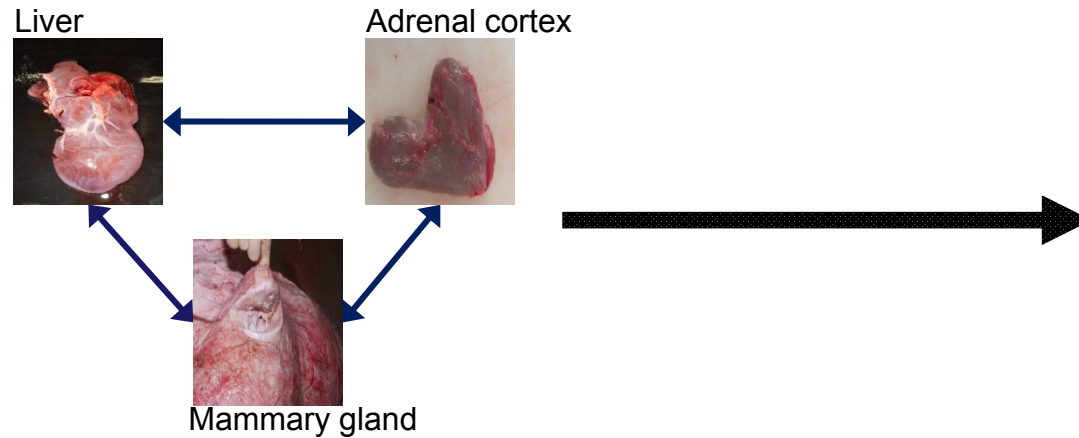
Milk data

- Milk curve estimation based on Ali and Schaeffer (1987, *Can. J. Anim.*)
- Phenotype: total milk yield until day 26 of lactation



Work packages

Transcriptome



Phenotype



1. Characterization:

Comparison of expressed genes

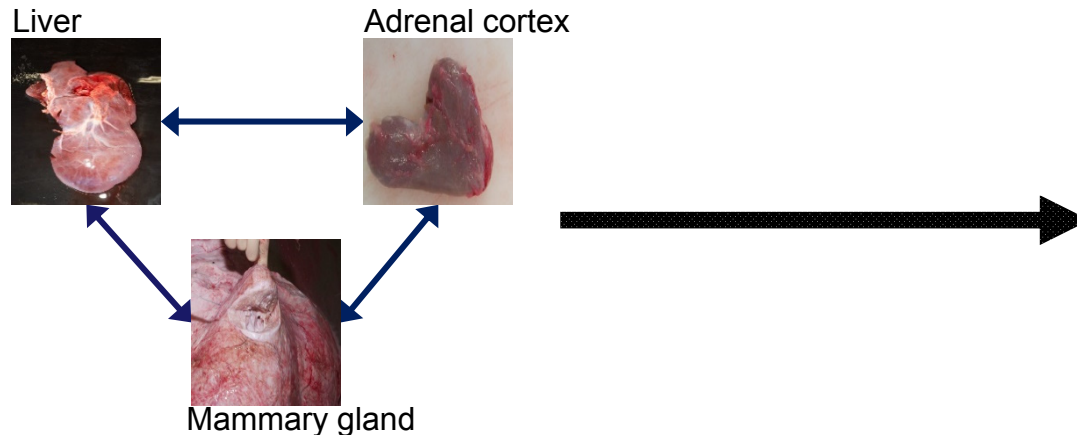
2

Material and methods



Work packages

Transcriptome



1. Characterization:

Comparison of expressed genes

Phenotype



2. Association with milk yield

Univariate: spearman rank correlation (FDR*; $\alpha = 0.05$)

Multivariate: partial least squares regression (PLS)

Goodness of prediction: $\rho(y, \hat{y})$

a) Tissue specific ($n_{\text{genes}} \in \{5691, 6697, 7290\}$)

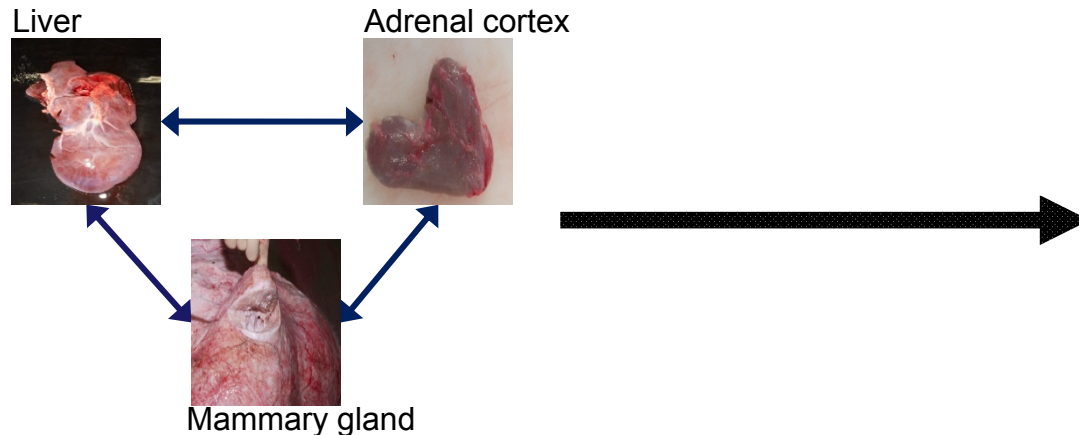
b) All tissues ($n_{\text{GE}}=19678$)

*Benjamini & Hochberg, 1995,
J. R. Stat. Soc. B.



Work packages

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Phenotype



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Biological interpretation: Ingenuity Pathway Analysis (IPA)

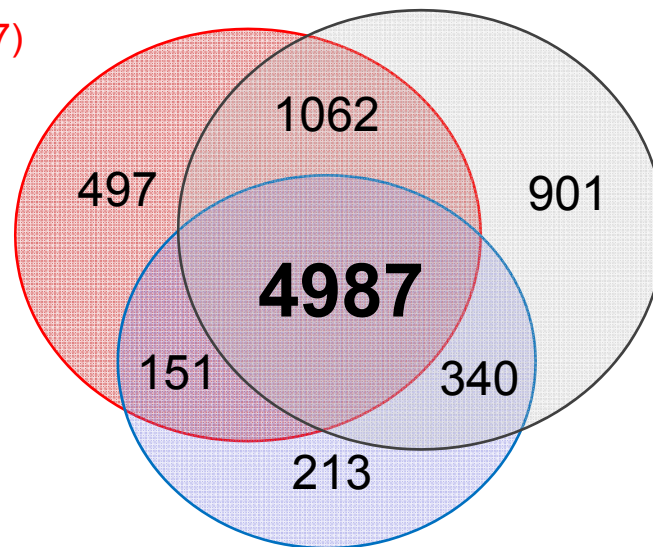
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1. Characterization

Liver ($n_{\text{genes_exclusive}}=497$)

- LXR/RXR activation
- Acute phase response signaling
- ...



Adrenal cortex ($n_{\text{genes_exclusive}}=901$)

- Catecholamine biosynthesis
- Glucocorticoid biosynthesis
- ...

Mammary gland ($n_{\text{genes_exclusive}}=213$)

- Granulocyte adhesion and diapedesis
- IL-12 signaling and production in macrophages
- ...

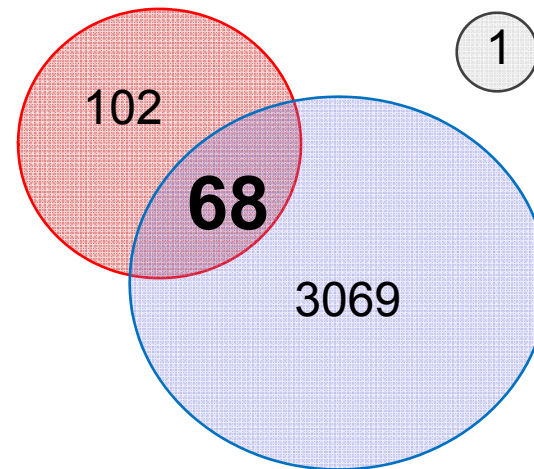
IPA: Fisher exact test

2. Association with milk performance

Univariate Analysis: Correlation between single gene and milk performance

Liver ($n_{\text{genes}}=170$)

- Fatty acid β - oxidation I
- ...



Adrenal cortex ($n_{\text{genes}}=1$)

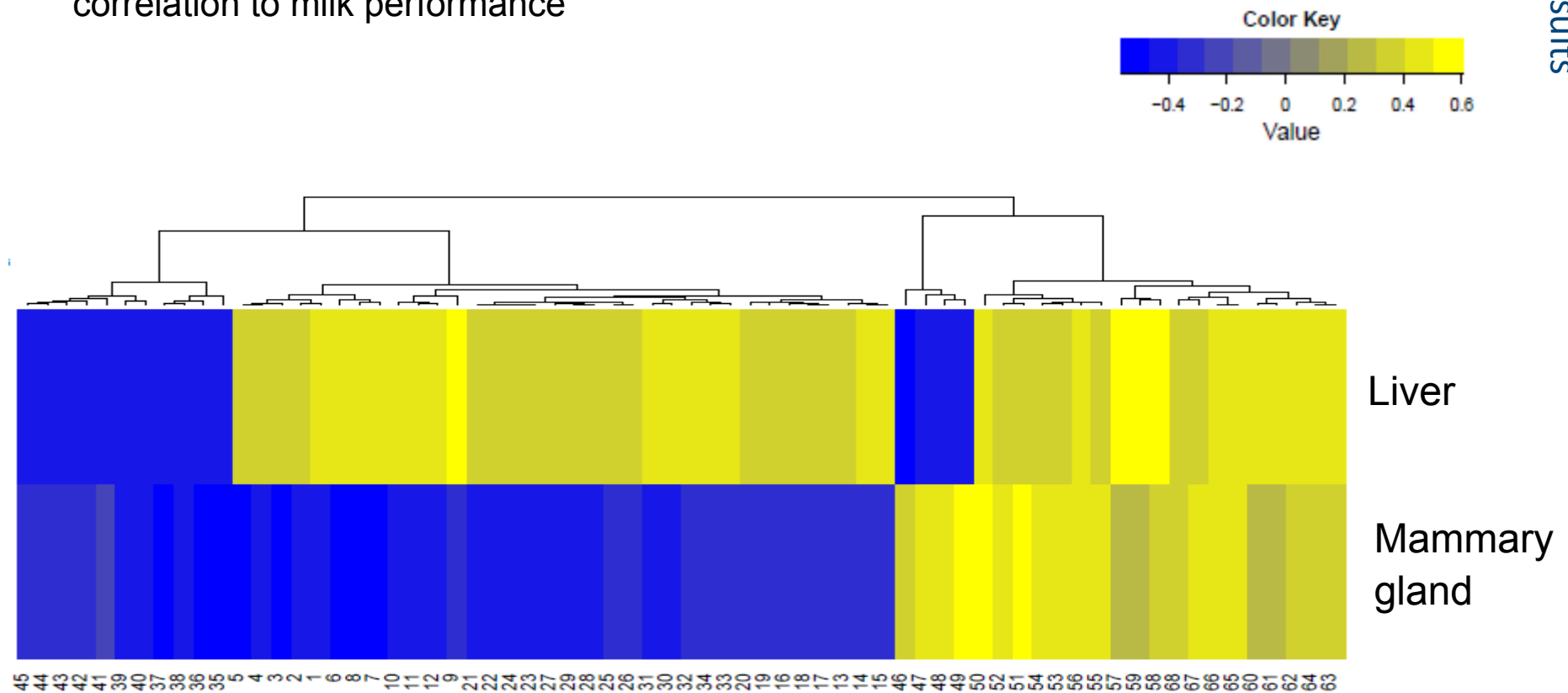
- Transmembrane protein 232

Mammary gland ($n_{\text{genes}}=3137$ genes)

- Regulation of eIF4 and P70S6K Signalling
- ...

2. Association with milk performance

Heatmap of the 68 common genes; which show a significant correlation to milk performance



2. Association with milk performance

Multivariate Analysis: predicting milk performance using all genes

Tissue	$\rho(y, \hat{y})$
Mammary gland	0.53
Liver	0.45
Adrenal cortex	0.32

2. Association with milk performance

Multivariate Analysis: predicting milk performance using all genes

Tissue	$\rho(y, \hat{y})$
Mammary gland	0.53
Liver	0.45
Adrenal cortex	0.32
All tissue ($n_{GE}=19678$)	0.47

Investigations of top 2000 genes using all tissues for prediction:

→ Mammary gland:	1850 of 2000	(1.) 1.	(2.) 2.	(3.) 3.
→ Liver:	139 of 2000	(1.) 4.	(2.) 80.	(3.) 106
→ Adrenal cortex:	11 of 2000	(1.) 635.	(2.) 877.	(3.) 885.



Conclusions

- Tissue-specific gene expression profiles are related to specific function of mammary gland, liver and adrenal cortex
 - Associations of expressed genes to milk performance:
 - Mammary gland: high relevance
 - Liver: moderate relevance
 - Adrenal cortex: low relevance
 - Univariate and multivariate analyses basically confirmed each other
- Multi-tissue analyses enabled deeper insights into molecular mechanisms affecting milk performance

Thank you for your attention



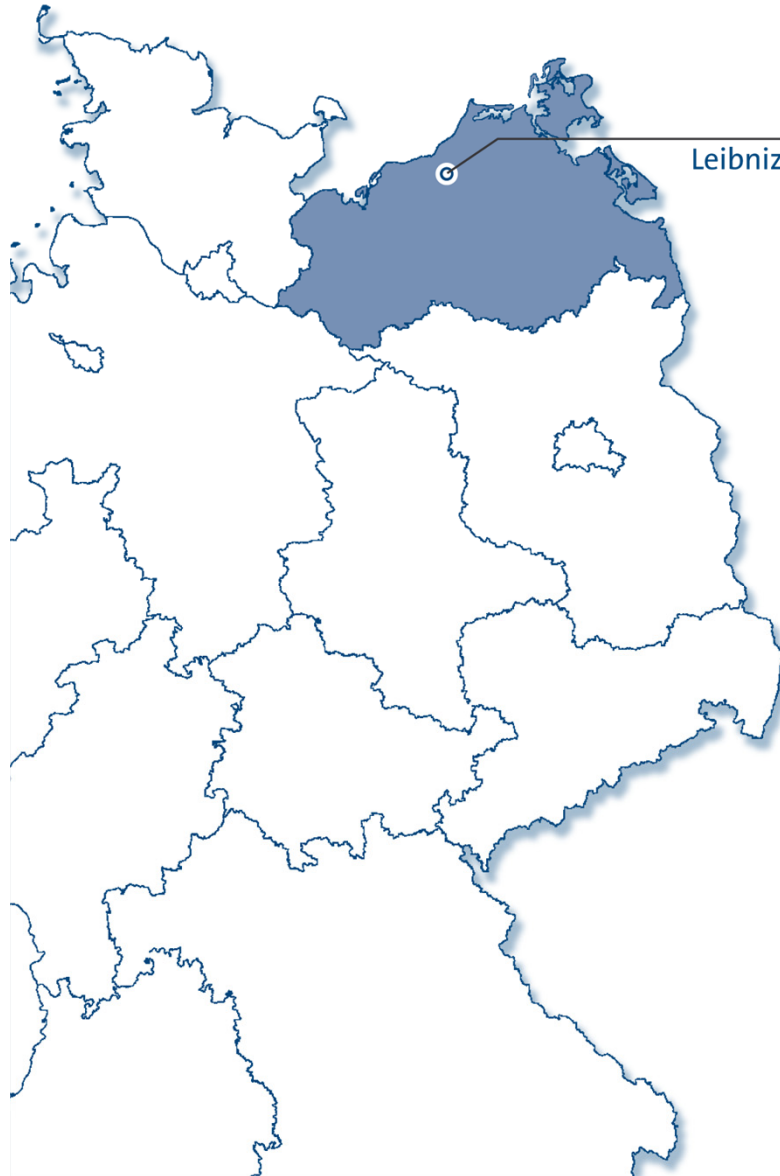
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