

SABRE's Cutting Edge

CUTTING EDGE GENOMICS FOR SUSTAINABLE ANIMAL BREEDING

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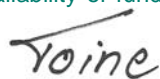
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SABRE's Second Year

SABRE started on 1 April 2006 and is due to finish on 31 March 2010. This means that we have now passed the halfway mark. After an epic few months of hard work by all SABRE participants, the 2nd SABRE Annual Report was submitted to the European Commission on 20 June 2008. We have pleasure in informing you that the scientific review has now been completed; Our reviewers concluded that the project made remarkable progress despite its complexity and very large consortium size; and the plans for the next 18 months have been approved..

Our thanks go to all of you who contributed (financially, scientifically and administratively) to the promising results achieved. We look forward to an even more successful second half of this project, building on the achievements to date.

For the near future, we'd like to draw your attention to our upcoming Conference (10-11 September 2008) and availability of funding for short-term placements with SABRE partners.



Toine Roozen
SABRE Operations Manager



Chris Warkup
SABRE Co-ordinator

SABRE Progress - an overview

In addition to the success stories presented on the following pages, progress has been made in the following Work Packages and areas:

In WP2 (Epigenetics), **work on healthy adult cloned cattle** is delivering new information on global DNA methylation - a publication that will attract much interest is in preparation, so watch this space. An imprinted region on bovine chromosome 9 was identified from a bull with an abnormally high paternal stillbirth rate. First results point to a diet-dependent regulation of the imprinted IGF2 pathway in pigs.

In WP3 about **30,000 porcine SNPs** have been identified and **15,000 validated chicken SNPs** have been made available to consortium members. **Analysis pipelines** that enable the analysis of microarray data using pathways have been developed and made available to participants within SABRE. WP3 and WP6 have jointly developed an **animal trait ontology (ATO)** for "fertility" and a web based 'wikisaurus' has been implemented to aid in the further development of ATOs for additional traits.

WP4 has generated a large number of experimental resources related to **gut health and functionality in pigs and chickens**, and **transcriptomics results** from a number of studies are now being analysed.



An **experimental E. coli mastitis trial** in WP5 has successfully been carried out using 32 Danish Holstein Friesian cows carrying either the high or low resistance QTL haplotype. Preliminary statistical analyses of the clinical data indicate an **association between the QTL haplotype and the somatic cell count, the pathogen count and the length of infection**.

Transcriptomics studies on heifers in WP6 have resulted in submission of two papers on **oestrus genes and pathways**. In the same WP, two **QTL for twinning rate and fertility** are being pursued in the Israeli Holstein population.

For the first time, a convenient quantitative method has been established to **measure cuticle deposition on eggs** (WP7).

In WP8, aggressive pigs, as assessed by individual aggression phenotyping soon after weaning, show higher **levels of aggression and skin lesions** on mixing prior to transport than do pigs with lower aggression scores.

In WP9, over **4800 samples** from pigs have been analysed for **Androstenone and Skatole**. A 7k SNP panel (over 5k useful SNPs, see page 3) has been analysed on **1000 Danish Landrace sib pair males** matched for high and low skatole. The association analysis will be completed shortly.

First results on demonstration of **genomic selection** (WP10) indicate that the progeny proofs of Norwegian Red bulls could be predicted with an **accuracy of 0.55-0.6** from genotyping with 25k SNPs (after estimating SNP effects in another part of the data). Results on 60k SNPs in a Holstein bull set will be completed shortly.



SABRE Success Stories: The first 2 Years

At the end of the second year of this four-year project, some of the larger experiments are well underway and parts of the project are beginning to deliver results. The most notable results of the SABRE project during the first two years are given on the next two pages. Where the stories indicate that you can read more on the SABRE website, you are advised to go to: www.sabre-eu.eu >> SABRE Results (<http://www.sabre-eu.eu/SABREResults/tabid/366/Default.aspx>)

MIXBLUP software (WP1)

The MIXBLUP software has been developed for gene- and marker-assisted genetic evaluation using best linear unbiased prediction, which is the common methodology for genetic evaluation. The software was initially developed for classical genetic evaluation without the use of markers or genes by MTT Agrifood Research Finland. The adaptation for gene- and marker-assisted genetic evaluation has been implemented by ASG Lelystad in collaboration with MTT. To increase the user-friendliness, ASG and MTT have developed a more user-friendly interface. With MIXBLUP, genetic evaluation can be performed in limited time on large livestock populations. Our industry partners are currently testing the software with great satisfaction and implementing it in their breeding programs. We are working on a business plan for marketing the software to other partners.

Scientists and companies interested in the software can contact Roel Veerkamp (ASG Lelystad, The Netherlands): Roel.Veerkamp@wur.nl

eQTL analysis (WP1)

A computational framework for high-throughput statistical analyses of combined gene expression data and genotypic data (eQTL analysis), developed as part of SABRE WP1, will be of direct interest to scientists (academia and industry) who work with eQTL analysis.

To uncover the genetic architecture of complex traits such as feed efficiency, obesity and diabetes is a challenging task. Recently, the integration of gene expression data and genotypic data has been explored as a way to infer causal relationships among genes and complex traits. This approach exploits the naturally occurring DNA variations in the genome and the perturbations these variations give rise to at the molecular level, which in turn lead to complex traits. Here we present a computational framework for high-throughput statistical analyses of combined gene expression data and genotypic data.

Regulatory genomic regions for complex

traits and expression traits are identified by single trait analyses using either a regression method or a variance component method. A novel multiple trait analysis for identifying regulatory regions associated with a group of genes was developed. The multiple trait analysis is based on methodology originally developed for gene expression data testing whether a given group of genes is significantly associated with a particular phenotype. Genes can be grouped together in any meaningful way, for example based on gene function or chromosomal location. Using this methodology it is possible to identify regulatory regions affecting functionally related genes and it is complementary to analyses at the level of individual expression traits.

Contact Peter Sørensen (University of Aarhus/Faculty of Agricultural Sciences) for details: PSO@agrsci.dk

QTL Express & GridQTL (WP1)

Fast, efficient and robust methods to map QTLs for single traits have already been developed by researchers at the Institute of Evolutionary Biology (IEB) at the University of Edinburgh and at the Roslin Institute. These methods are available via "QTL Express" (<http://qtl.cap.ed.ac.uk>). Due to an increase in population size, numbers of markers, numbers of phenotypes, and complexity of the genetical models, novel methodology and much more powerful computing resources are required; GridQTL is a 5-year UK Research Council funded programme (with co-funding from SABRE) with the aim to develop a freely available Grid based platform for the analysis of multiple traits with high density markers with complex genetic models.

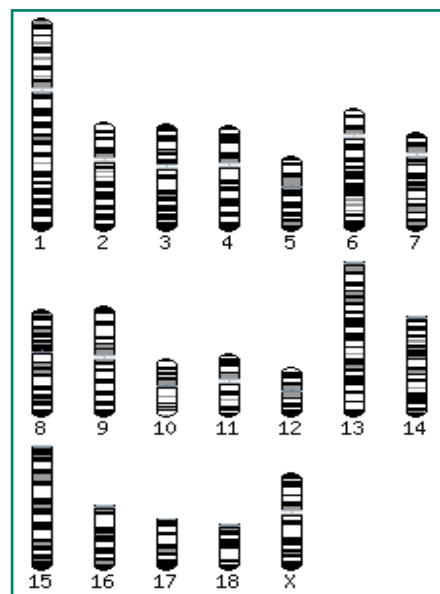
GridQTL (www.gridQTL.org.uk) will provide an essential core component of a future integrated biological system incorporating genetic, phenotypic, transcription and comparative information to allow prediction from gene sequence to consequence. You can read the full story on www.SABRE-eu.eu or contact DJ de Koning (The Roslin Institute and R(D)SVS, University of Edinburgh) for more details: dj.dekoning@roslin.ed.ac.uk

Pig Chromosomes 7 & 14 (WP3)

Within the first two years of the project an assembly and annotation have become available for porcine chromosomes 7 and 14 (SSC7 and SSC14) that cover more than 99% of these two chromosomes. A total of 1593 BAC-clones have been sequenced for the two chromosomes. The chromosomes are made available in pre-ensemble at: http://pre.ensembl.org/Sus_scrofa/index.html.



The completion of the sequence of SSC7 and SSC14 is already being used as the reference sequence for the identification of SNPs in the pig using second generation sequencing (Solexa, 454). The ultimate goal is the development of a whole genome 60K SNP chip for pigs, scheduled for the end of 2008. The availability of the finished sequences for SSC7 and SSC14 ensures the even coverage of these two chromosomes on the 60K SNP chip.





The information will be of direct interest to all partners involved in SABRE as well as all other scientists (academia and industry) that work in pigs. Furthermore, the information will also aid comparative mapping studies in other vertebrates and will therefore also be of interest to scientists working on other species.

Read the full story on the SABRE website. Contact Carol Churcher (The Wellcome Trust Sanger Institute, Carol@sanger.ac.uk) for additional information.

7.5K Pig SNP Panel (WP9)

A panel of ~7000 high quality SNPs (single nucleotide polymorphisms) will facilitate genetic mapping in pigs. The panel is primarily to be used in genetic research (Pig Breeding, Animal Health and Human Medicine). Presently, the SNPs are for genotyping using the Illumina Infinium genotyping assay and the first assays are under production by Illumina Inc. The panel provides information that facilitates development of genotyping assays.

The panel is a result of scientific input from several partners including University of Aarhus, Faculty of Agricultural Sciences; Roslin Institute (Edinburgh); Norwegian University of Life Sciences and The Wellcome Trust Sanger Institute. Funding from a variety of sources including Danish Meat Association, Norwegian Research Council, EU (through the SABRE project) and others have made the development of the panel possible.

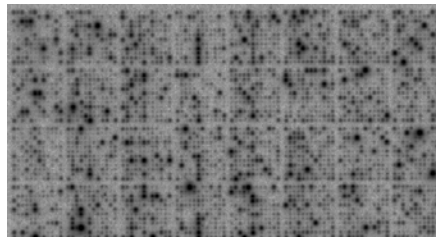
Contact Christian Bendixen at the University of Aarhus, Faculty of Agricultural Sciences for more details: Christian.Bendixen@agrsci.dk

Pig ACTH Results (WP8)

Genes differentially expressed in Meishan and Large White piglet adrenal glands in basal condition and in response to ACTH have been identified in work by Pierre Mormede (SABRE WP8).

In the adrenal glands of seven-week-old male Large White (LW) and Meishan (MS) piglets, no change was found in the expression of known key regulator proteins of the ACTH signalling pathway or of steroidogenic enzymes. However, *Mdh2*, *Sdha*, *Sucg2*, genes involved in the tricarboxylic acid (TCA) pathway, were over-expressed in MS pigs. Moreover, up-regulation of *Star* and *Ldlr* genes in MS and/or in response to

ACTH suggest that differences in the adrenal function between MS and LW may also involve mechanisms requisite for cholesterol supply to steroidogenesis.



A database on genes differentially expressed in Meishan and Large pig adrenals in basal condition and in response to ACTH has been deposited in the NCBI Gene Expression Omnibus data repository under accession number GSE8377.

These data have been published: Hazard D. *et al* (2008). Gene array and real time PCR analysis of the adrenal sensitivity to adrenocorticotrophic hormone in pig. *BMC Genomics*. 2008 Feb 27;9(1):101.

For further information you can contact Pierre Mormède (INRA): Pierre.Mormede@bordeaux.inra.fr.

Shell Gland Genes (WP7)

The use of microarrays on the shell gland has resulted in lists of genes which are differentially expressed in the shell gland. By defining the transcriptome in this way gives us two routes to exploit the information.

Firstly in combination with the results of the QTL analysis we can identify genes which are both expressed in the shell gland and which are in the region of QTLs.

Secondly we can directly identify genes which we may wish to examine for variation that can be associated with egg shell quality.

Contact Yves Nys (INRA) for further information: yves.nys@tours.inra.fr.

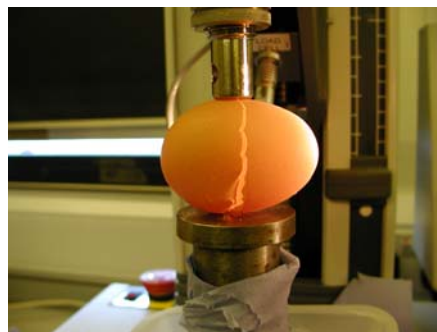


Egg Shell Quality QTL (WP7)

Previous association studies have indicated that SNPs in candidate genes known to be present in the egg shell matrix (ovalbumin, ovocalyxin 32 and ovocleidin 116) were potentially valuable for selection for shell quality.

The region round these genes has been resequenced in a pedigree line used to breed brown egg layers. The SNPs in the region have been genotyped in around 1800 animals and the results are being analysed to discover if any SNPs are better predictors of egg shell quality and if specific haplotypes may exist which are better for selection. The results will be used to optimise the markers for use in selection.

For further information contact Ian Dunn of The Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh: Ian.Dunn@Roslin.ed.ac.uk



Egg Shell Quality SNPs (WP7)

Analysis of a cross generated from two pedigree lines used in the production of brown egg laying hens has identified QTL for shell quality traits on Chromosomes 2, 3, 6 and 14. Since these are the lines are those currently used in the production of commercial products, the brown egg laying bird, these QTL are potentially useful to select hens for improved egg shell quality.

Further fine mapping of the QTL will be carried out to exploit the results within the project and segregating SNPs will be tested in independent generations of pure bred hens. If the results from these studies remain positive then the markers will be suitable for use in a selection programme for improved egg shell quality.

For further information, contact Johanna Vilkki (MTT Agrifood Research Finland): Johanna.Vilkki@mtt.fi

3rd Consortium Meeting

The 3rd SABRE Consortium Meeting was held on Tuesday 29th and Wednesday 30th January 2008. The meeting was hosted by Jean-Michel Elsen at INRA in Toulouse.



The main theme for this meeting was **"Biology"**. The two day meeting started with Work Package workshops, during which the SABRE participants were asked to prepare their contributions to the 2nd Year-end Report; Periodic Activity Report (Months 13-24) and the Implementation Plan (Months 25-42). The 71 participants then attended presentations from each of the Work Package Leaders, summarising the progress made over the previous year. A special session was dedicated to improving the data analysis capabilities of the SABRE Consortium, with presentations from WP1 and WP3 members. SABRE Participants can access PDF's of all presentations and a more detailed report of this meeting through the SABRE intranet.

Staff Changes

Dr Peter Sørensen, Senior Research Scientist at the University of Aarhus (DK), replaced his University colleagues Mogens Sandø Lund (as WP Leader of WP5 – Mammary Function) and Christian Bendixen (as SABRE board member) on 31 January 2008. Peter's main areas of expertise are implementing statistical/mathematical methods for genomic and transcriptomic data analysis.



Dr Barbara Harlizius, Research Scientist at the Institute for Pig Genetics (NL), replaced Christian Bendixen as the WP Leader of WP9 – Product Quality (Boar taint) on 15 February 2008. Barbara's research at IPG focuses on the implementation of genomics to improve product quality and health in pig breeding.

Professor Alan Archibald (The Roslin Institute and the Royal (Dick) School of Veterinary Studies, University of Edinburgh, UK) has replaced Chris Haley as SABRE Board member, following Chris' move to the Medical Research Council Human Genetics Unit.



Many thanks to Mogens, Christian and Chris for their great contributions to SABRE, and welcome to Peter, Barbara and Alan in their new roles.

SABRE Funding

Funding is available for short-term placements for scientists from New EU Member States, 'Associated Countries', 'INCO countries' and SABRE participants to visit organisations involved in SABRE.

Placements can be up to 12 weeks and are funded up to the value of €5000.

Check the "Get Involved >> Training" section of the SABRE website for full details and/or contact Carol Didcock (training@sabre-eu.eu) with any further questions you may have.

Career Opportunities

The SABRE website ("Get Involved >> Career Opportunities") contains the latest career opportunities within SABRE Partners.

SABRE Conference: 10-11 September 2008 Genomics

The 3rd SABRE conference on 10 and 11 September 2008 is taking the theme of **"Welfare and Quality Genomics"**, and will address SABRE subjects as "Fertility and Reproduction", "Product Quality", "Product Safety" and "Animal Well-being".



Our hosts will be the University of Aarhus, Faculty of Agricultural Sciences (AU-DJF, previously known as DIAS) at their Research Centre Foulum (central Jutland) in Denmark.

9 September 2008 (Satellite Meetings):

SABREtrain: 13:00-16:30

WP1: 17:00-19:00; WP6: 16:00-19:00; WP8: 16:00-18:00; WP9: 16:00-18:00

10 September 2008 (Conference Day 1):

09:00-12:00 Session 1: Welfare, Quality and Technological Advances

13:30-17:30 Session 2: Behaviour and Robustness

17:30-19:00 Session 3: Poster session

20:00: Conference Dinner

11 September 2008 (Conference Day 2):

09:00-12:30 Session 4: Welfare, Quality, Productivity; are they compatible?

14:00-17:00 OMG meeting (OMG only); 17:00-17:30 Board meeting (Board only)

Registration and further information

Registration for this event is free, but places are limited, so we urge anyone who wishes to attend to register as soon as possible to avoid possible disappointment. Further information, the **online registration form**, programme, travel and hotel information are available in the "News and Events" section of the SABRE website.

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Your comments and contributions are welcome

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Food Quality and Safety