Use of health data for research

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Health Data Conference
"Challenges and benefits of health data recording in the context of food chain quality, management and breeding"
30-31 May, 2013, Aarhus, Denmark
Use of Health Data

ANIMAL HEALTH ISSUES

- Animal Welfare
- Animal Health
- Production traits

Intensification and specialization of livestock sector
ANIMAL HEALTH ISSUES

- Animal Welfare
- Integrated Animal Health Management
- Production traits

Intensification and specialization of livestock sector
Use of Health Data

**ANIMAL HEALTH MANAGEMENT**

- Animal Welfare
- Integrated Animal Health Management
- Production traits

**Disease control strategies**
- Prevention + Cure
- Important decisions on
  - Animal (selection, culling, vaccination...)
  - Pathogen / Environment (chemotherapy, biosecurity...)

**Important step with potentially major effects**

*Needs: Critical evaluation + integrated approach*

=> quality of health data !!

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NEED OF HEALTH DATA FOR RESEARCH:
FOR AN INTEGRATED APPROACH OF DISEASE CONTROL

Prevention

Control

Eradication
NEED OF HEALTH DATA FOR RESEARCH:
FOR AN INTEGRATED APPROACH OF DISEASE CONTROL

- Breeding for disease resistance
- Novel vaccine development
- Feeding systems
- Management procedures / biosecurity

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Need of Health Data for Research:

For Breeding for Disease Resistance

- Genetic Markers
- Disease Resistance Phenotypes
- Underlying Mechanisms
Use of Health Data

NEED OF HEALTH DATA FOR RESEARCH

Lack of Disease Phenotypes

- Easy to measure & relevant phenotypes
- Finer phenotypes / mechanisms

THE PHENOTYPIC GAP!!
NEED OF HEALTH DATA FOR RESEARCH: VALIDATING DISEASE RESISTANCE PHENOTYPES

A classical approach:

- Weight Gain
- Plasma Col
- Hematocrit
- Lesion
- Rectal T°
- Oocyst count

Sensitive
Resistant

EXPERIMENTAL
NEED OF HEALTH DATA FOR RESEARCH: VALIDATING DISEASE RESISTANCE PHENOTYPES

A classical approach:

EXPERIMENTAL

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Need of Health Data for Research: Validating Disease Resistance Phenotypes

A classical approach:

- Small Set of Disease Phenotypes
- Large scale study
  - Pilot study
  - Experimental
- Commercial
NEED OF HEALTH DATA FOR RESEARCH: VALIDATING DISEASE RESISTANCE PHENOTYPES

A classical approach:

Small Set of Disease Phenotypes

COMMERCIAL Pilot-study

EXPERIMENTAL Large scale-study
Use of Health Data

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

Breeding for disease resistance

Genetic Markers

Genetic Variability for recorded health traits

Disease Resistance Phenotypes

Underlying Mechanisms

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## Use of Health Data

### CRITICAL EVALUATION PRIOR INTEREST FOR DISEASE RESISTANCE

= PRIOR MEASURING MORE HEALTH TRAITS

<table>
<thead>
<tr>
<th>Disease</th>
<th>Disease score (Industry-eco-public-welfare-zoono.)</th>
<th>Genetic Variation</th>
<th>Priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastitis</td>
<td>**</td>
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<tr>
<td>Bovine leukemia</td>
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<tr>
<td>Gastrointestinal parasites</td>
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<td>**</td>
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<tr>
<td>Paratuberculosis</td>
<td>**</td>
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<tr>
<td>Bovine TB</td>
<td>(*)</td>
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<tr>
<td>Bacterial pneumonia</td>
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<tr>
<td>E. coli</td>
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<tr>
<td>FMD</td>
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<tr>
<td>Brucellosis</td>
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<tr>
<td>IBR</td>
<td>(*)</td>
<td>*</td>
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</tr>
<tr>
<td>Salmonella spp</td>
<td>**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BVD</td>
<td>**</td>
<td></td>
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</tr>
</tbody>
</table>

Davies et al., 2008
Use of Health Data

IDENTIFYING GENETIC MARKERS OF HEALTH TRAITS

Mapping studies
SNPs identified

Make use of advanced genome enabled technologies!
IDENTIFYING GENETIC MARKERS OF HEALTH TRAITS

Validated Disease Phenotypes

Genetic markers for resistance traits

EXPERIMENTAL

COMMERCIAL

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NEED OF HEALTH DATA FOR RESEARCH: FOR BREEDING FOR DISEASE RESISTANCE

Breeding for disease resistance

Genetic Markers

Underlying Mechanisms

Disease Resistance Phenotypes

Understanding (Black-Box) Control Diagnostic

Genetic Variability for recorded health traits
Use of Health Data

IDENTIFYING GENETIC MARKERS & UNDERLYING MECHANISMS OF HEALTH TRAITS

- Validated Disease Phenotypes
- Transcriptomic
- Immune function

Better understand regulation of the disease process

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IDENTIFYING GENETIC MARKERS & UNDERLYING MECHANISMS OF HEALTH TRAITS

Whole-Genome association analysis of susceptibility to paratuberculosis in Holstein cattle

Transcriptomics => Identify genes being transcribed in a particular tissue at a particular time

QTL approach => Identify mutations underlying genetic variations seen between hosts
Use of Health Data

IDENTIFYING GENETIC MARKERS & UNDERLYING MECHANISMS OF HEALTH TRAITS

Whole-Genome association analysis of susceptibility to paratuberculosis in Holstein cattle

Complementary approach towards genetic / functional disease markers

Steps to give tools to dissect, understand & utilize host genetic variation
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NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE...BIOMARKERS

Breeding for disease resistance

Genetic Markers

Underlying Mechanisms

Disease Resistance Phenotypes

PHENOTYPES FOR RESEARCH
=> BIOMARKERS!

Understanding (Black-Box)
Control Diagnostic

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NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

Experimental ("controlled") challenge

Farm recorded health data

Field health data

PHENOTYPES FOR RESEARCH
=> BIOMARKERS!
Use of Health Data

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

Experimental (“controlled”) challenge

Farm recorded health data

Field health data

PHENOTYPES FOR RESEARCH => BIOMARKERS!

ROBUSTNESS
Use of Health Data

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

Experimental ("controlled") challenge

Farm recorded health data

Standardisation

Make use of differences

Field health data

PHENOTYPES FOR RESEARCH
=> BIOMARKERS!

ROBUSTNESS

Conference
ICAR
Aarhus, Denmark

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Use of Health Data

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

- Experimental ("controlled") challenge
- Farm recorded health data
- Field health data
- Epidemic surveillance => lots of prior data + confirmation
  Ex: Bovine TB

PHENOTYPES FOR RESEARCH => BIOMARKERS!

ROBUSTNESS

Epidemic surveillance => lots of prior data + confirmation
Ex: Bovine TB

INRA
SCIENCE & IMPACT

ICAR 2013
Use of Health Data

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

Experimental (“controlled”) challenge

Farm recorded health data

Cohort of animals (from breeding companies)

Field health data

Make use of outbreaks
Ex: PRRS

PHENOTYPES FOR RESEARCH
=> BIOMARKERS!

ROBUSTNESS

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE
Use of Health Data

**NEED OF HEALTH DATA FOR RESEARCH**: FOR BREEDING FOR DISEASE RESISTANCE

**Experimental (“controlled”) challenge**

- Farm recorded health data
- Field health data

**Livestock exposed to extremes environment/diseases = reservoir of health data (and genotypes)**

**PHENOTYPES FOR RESEARCH => BIOMARKERS!**

**ROBUSTNESS**
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Use of Health Data

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

• Detailed health records?
• Use of animal performance as a proxy?
• Identifying underlying immunological correlates?

PHENOTYPES
FOR RESEARCH
=> BIOMARKERS!

ROBUSTNESS

NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

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NEED OF HEALTH DATA FOR RESEARCH:
FOR BREEDING FOR DISEASE RESISTANCE

- Detailed health records?
- Use of animal performance as a proxy?
- Identifying underlying immunological correlates?

Across a variety of environments and infection challenge conditions!
=> Large scale! Multidiscipline! Maximized use of animals!

PHENOTYPES FOR RESEARCH
=> BIOMARKERS!

Robustness

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EX 1: Joint research programme on Early responses in Salmonella

- **Different animal species.**
  - Cattle
  - Pigs
  - Chickens

- **Different Salmonella strains**
  - S. enteritidis
  - S. typhimurium

- **Different challenge models**
  - Route of infection
  - Dose of infection
  - Age before primary infection
EX 1: Joint research programme on Early responses in Salmonella

Partner 1
Experimental model 1
Host gene Expression Data

Partner 2
Experimental model 2
Host gene Expression Data

Partner 3
Experimental model 3
Host gene Expression Data

How to make the best out of health data?
Collaborative Research!
## EX 1: Joint research programme on Early responses in Salmonella

<table>
<thead>
<tr>
<th>Salmonella</th>
<th>Host species</th>
<th>Organ</th>
<th>Time post infection</th>
<th>In vitro infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE</td>
<td></td>
<td>Caeca</td>
<td>3w – 6w</td>
<td>Monocytes, Epithelial</td>
</tr>
<tr>
<td>STM</td>
<td></td>
<td>Entero,</td>
<td>1d – 1w</td>
<td>Macrophage PMN</td>
</tr>
<tr>
<td>STM</td>
<td></td>
<td>MLN</td>
<td>2 – 8 hours</td>
<td>NO SISP</td>
</tr>
<tr>
<td>SE</td>
<td></td>
<td>Intestine</td>
<td>1d – 3w</td>
<td>NO</td>
</tr>
<tr>
<td>STM</td>
<td></td>
<td>Jejunum</td>
<td>-</td>
<td>Enterocyte</td>
</tr>
<tr>
<td>STM/SE</td>
<td></td>
<td>-</td>
<td>-</td>
<td>Monocytes, PMN, DC</td>
</tr>
</tbody>
</table>
Use of Health Data

HOW TO MAKE THE BEST OUT OF HEALTH DATA?
Collaborative Research!

EX 1: Joint research programme on Early responses in Salmonella

Host responses differ significantly after Salmonella infection

Dependent on species, Salmonella strain, challenge model, cell-type

There are some similarities in gene regulation between hosts

Independent of species, challenge model

Role of TLR4
Use of Health Data

HOW TO MAKE THE BEST OUT OF HEALTH DATA?
Collaborative Research!

EX 2: Joint research programme on transcriptomic studies on mastitis

Partner 1
Experimental model 1
Host gene Expression Data

Partner 2
Experimental model 2
Host gene Expression Data

Partner 3
Experimental model 3
Host gene Expression Data

Sharing of mRNA, data, qPCR primers, protocols

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EX 2: Joint research programme on transcriptomic studies on mastitis

Use of Health Data
How to make the best out of health data?
Collaborative research!

Bovine

Clinical, Pathological, Functional Data

Microarray Data
Candidate Genes

Validation

Microarray Analyses
Bioinformatics

qPCR
TLRs
Défensines

Common Data

Common
Microarray

RNA

Exp. Inf.
S. Aureus
E. coli

Exp. Inf.
bMEC
S. uberis

In vitro
bMEC
S. aureus

Sheep
S. Aureus

Goat

EX 2: Joint research programme on transcriptomic studies on mastitis

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Use of Health Data

HOW TO MAKE THE BEST OUT OF HEALTH DATA?
Collaborative Research!

EX 2: Joint research programme on transcriptomic studies on mastitis

<table>
<thead>
<tr>
<th>Infected for</th>
<th>&lt;0h</th>
<th>0h</th>
<th>2h</th>
<th>6h</th>
<th>12h</th>
<th>24h</th>
<th>36h</th>
<th>48h</th>
<th>72h</th>
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<tr>
<td>EXP 1 a</td>
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<td></td>
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<td>E. coli in vivo in cattle</td>
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<tr>
<td>EXP 1 b</td>
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<tr>
<td>S. aureus 24h in vivo in cattle</td>
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<tr>
<td>EXP 1 c</td>
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<tr>
<td>S. aureus 72h in vivo in cattle</td>
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<tr>
<td>EXP 2</td>
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<td>S. uberis in vivo in cattle</td>
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<tr>
<td>EXP 3</td>
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<tr>
<td>S. aureus in macrophages in vitro in cattle</td>
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<td></td>
<td></td>
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<tr>
<td>EXP 4</td>
<td></td>
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<tr>
<td>S. aureus in vivo in goat</td>
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<tr>
<td>EXP 5</td>
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<tr>
<td>S. aureus in dendritic cells in vitro in sheep</td>
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</tbody>
</table>

2nd run

- Early time response (no signs of mastitis)
- Late time response (clear signs of mastitis)

Commonalities identified
- Early inflammatory response
- Cytokines and cell signaling

Meta-analysis
- experimental designs & sizes
- host species & tissues & pathogens,
- arrays & time points

11 gene lists analyzed
- Bovine specific response
- Goat specific response
- Sheep specific response
- General, overall response
  - Early time response
  - Late time response
  - Early time specific
  - Late time specific
- General, overall in vitro response (bovine MO & sheep DC)
- Late time in vitro response (bovine MO & sheep DC)
- Early time in vitro response (bovine MO & sheep DC)
NEED OF HEALTH DATA FOR RESEARCH

WHAT ARE THE BEST HEALTH DATA?

For general health issues:
need = best means to describe host genetic effects

Phenotypes defined narrowly ↑

Power of detection ↑

Data health collection challenging ↑

Optimizing data collection!
(need prior research)
NEED OF HEALTH DATA FOR RESEARCH

WHAT ARE THE BEST HEALTH DATA (for R&D) ?

For general health issues:
need = best means to describe host genetic effects = optimizing!
NEED OF HEALTH DATA FOR RESEARCH

WHAT ARE THE BEST HEALTH DATA (for R&D)?

For general health issues:
need = best means to **describe** host genetic effects = optimizing!

Identification of animals coping with immunosuppressive effects of stress

Ex: clinical cases of mastitis: underlying issues of immunosuppression (early lactations)
NEED OF HEALTH DATA FOR RESEARCH:
FOR AN INTEGRATED APPROACH OF DISEASE CONTROL

- Breeding for disease resistance
- Novel vaccine development
- Efficient response to Vaccination
- Improved response to the disease

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NEED OF HEALTH DATA FOR RESEARCH:
FOR AN INTEGRATED APPROACH OF DISEASE CONTROL

- Breeding for disease resistance
- Novel vaccine development

Individual assessment of
- Efficient response to Vaccination
- Improved response to the disease
Use of Health Data

**NEED OF HEALTH DATA FOR RESEARCH:**
FOR AN INTEGRATED APPROACH OF DISEASE CONTROL

**Novel vaccine development**

⇒ **Study vaccine requirements**
⇒ **Measure vaccine effectiveness**

*Ex: PRSV, BRSV, FMDV...*

**Field health data**

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ICAR 2013 Conference
INRA Science & Impact
A NEW DIMENSION FOR INTEGRATION OF HEALTH DATA

Use of Health Data

Interactions

HOST

PATHOGEN

MICROBIOTA

ENVIRONMENT

Gut health, Respiratory health....

Research: Understand the interactions
=> to use them
=> Integrate in monitoring of health status

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HEALTH DATA : AS KEY COMPONENTS OF TRADE-OFFS

- Environment
- Economic
- Health
- Welfare

Equilibrium

Really New selection traits

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Integrate health related traits in existing multi-trait selection programmes

Use (most) the same health traits for breeding & management

Development of cost effective tools to analyse field disease outbreaks and develop predictive diagnostics

Initiatives integrating genomic approaches to vaccine development

Research including collaborations between animal health research institutions, commercial breeding & pharmaceutical companies
  - Joint acquisition of health data
  - Generating new knowledge & innovation
THANK YOU FOR YOUR ATTENTION

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