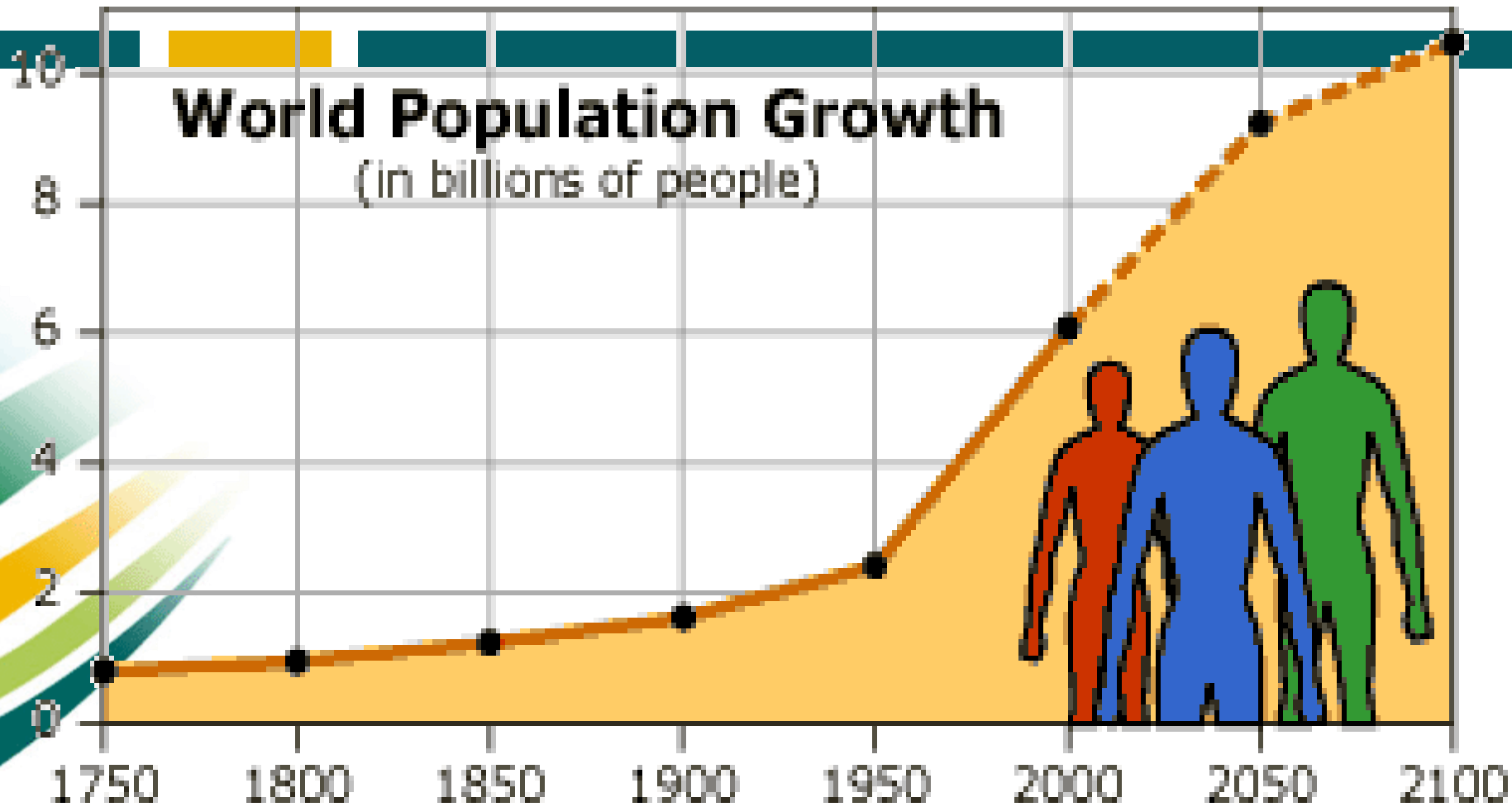# Agenda

Introduction

- **Functional traits**
- **Genomics to system biology in animal science**

OMICS for analyzing diseases in livestock species

- **Genomics**
- **Transcriptomics**
- **Proteomics**

Conclusion

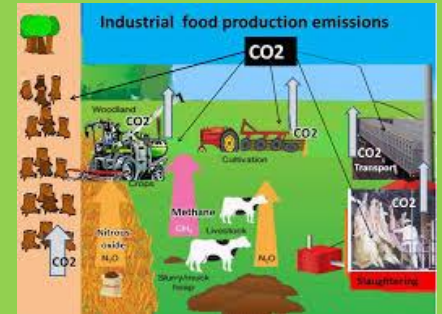**Will there be enough food to support the projected population of 9.2 billion in 2050?**

BREEDING GOALS

$$\Delta G = \frac{r \times i \times \sigma_a}{L}$$

CONSUMERS DEMANDS

ENVIROMENTAL IMPACT

Industrial food production emissions

FOOD QUALITY and SAFETY

PLAN
Continuous Improvement in...
ACT
QUALITY MANAGEMENT
SAFETY MANAGEMENT
DO
CHECK

Milk yield vs reproductive traits traits?

Is Reproductive Decline Caused by Greater Milk Production?

Milk production for United States Dairy cows has increased by approximately 20% in the last 10 yr (USDA
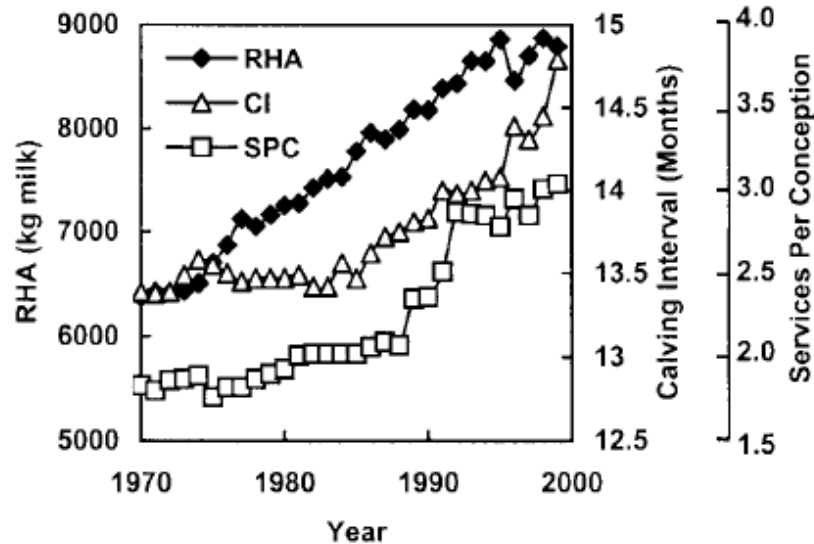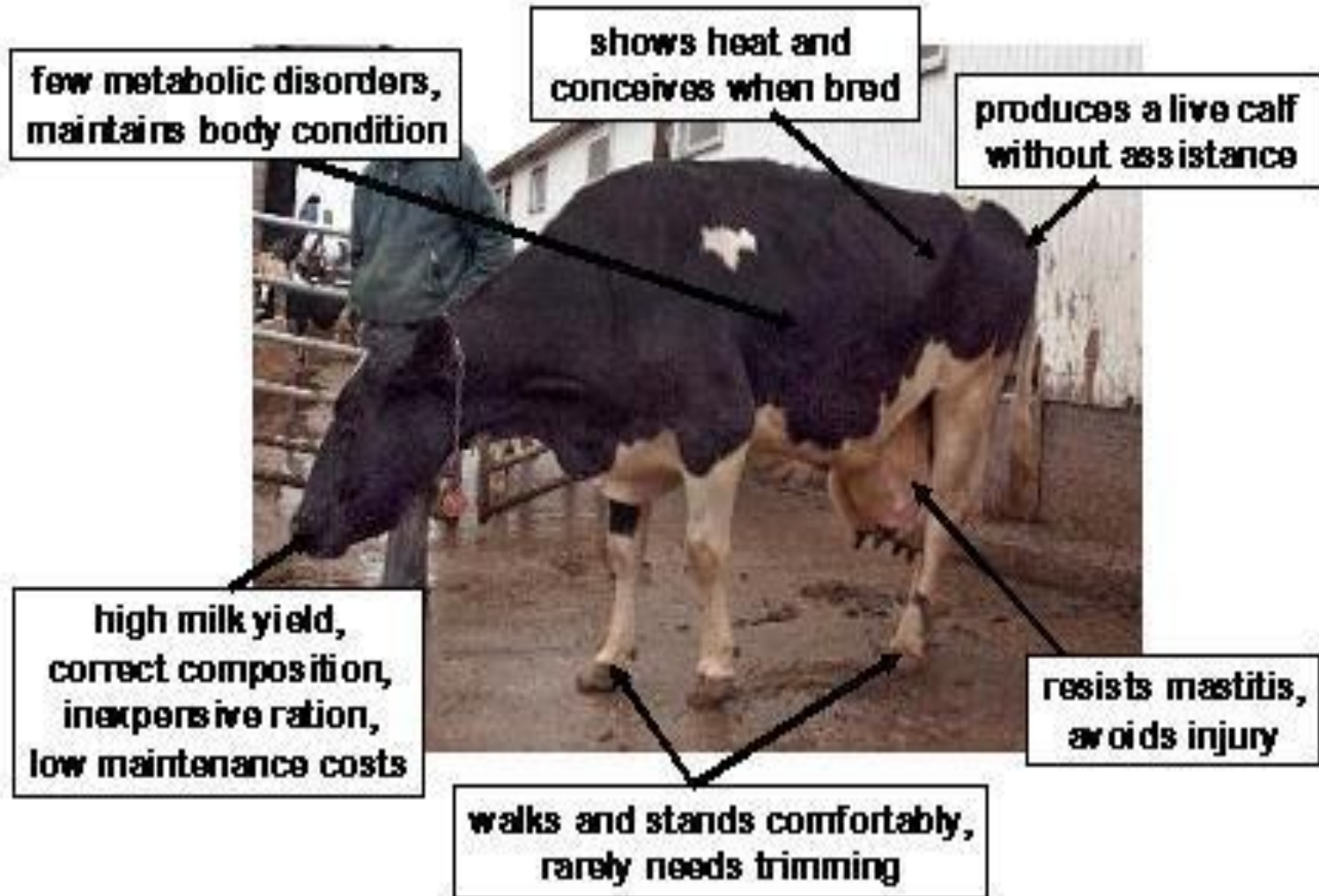
Figure 2. Rolling herd average (RHA, kg milk per lactation), calving interval (CI), and services per conception (SPC) for 143 dairy herds continuously enrolled in the Raleigh DHIA record system from 1970 to 1999 (personal communication, J. S. Clay, Dairy Records Management Systems, Raleigh, NC).

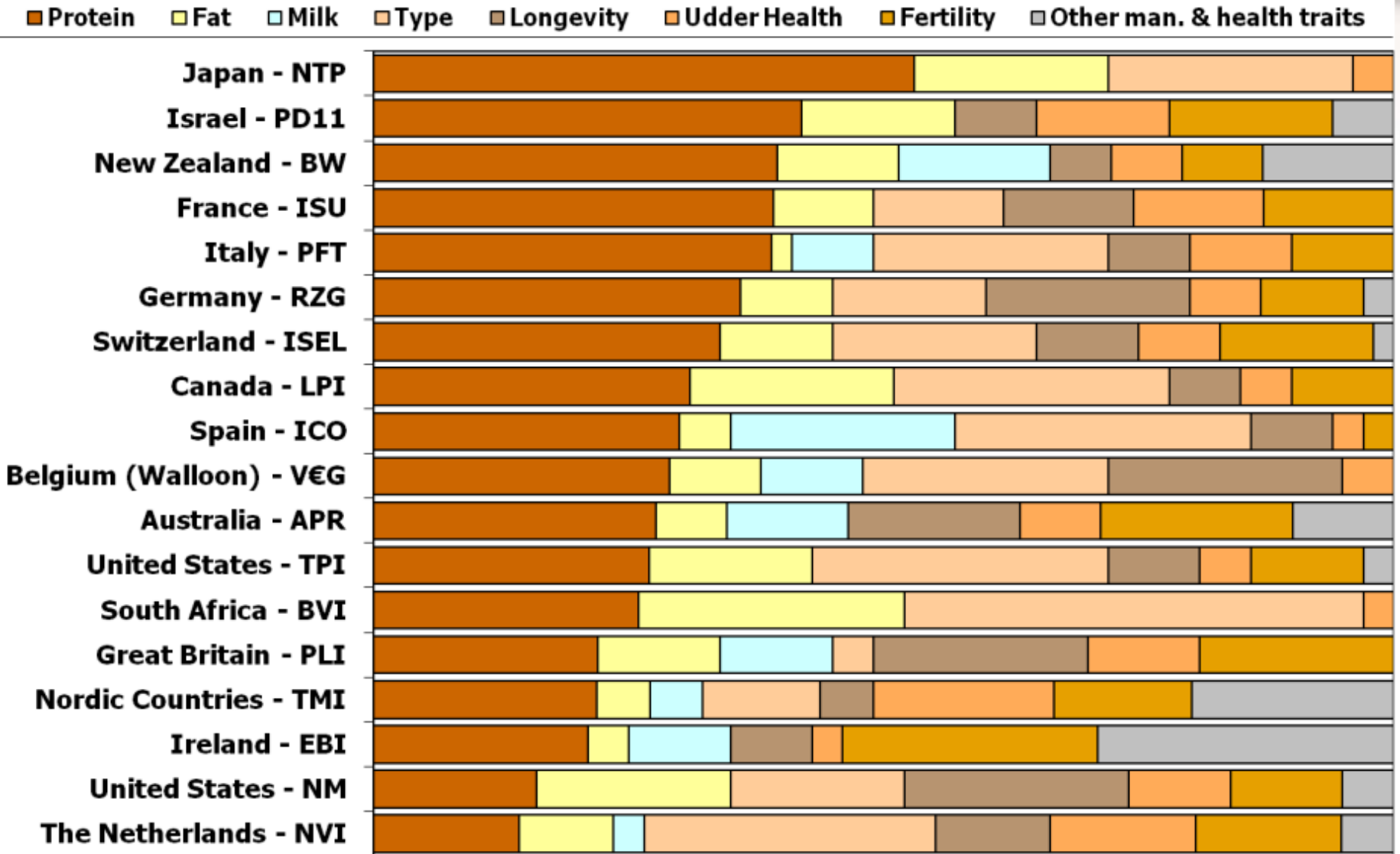Data from Lucy et al, Journal of Dairy Science, 2001, 84(6): 1277-1293

The Perfect Cow

few metabolic disorders, maintains body condition

shows heat and conceives when bred

produces a live calf without assistance

high milk yield, correct composition, inexpensive ration, low maintenance costs

resists mastitis, avoids injury

walks and stands comfortably, rarely needs trimming

What are functional traits?

❖**The ICAR* Functional Traits Working Group currently is working on:**
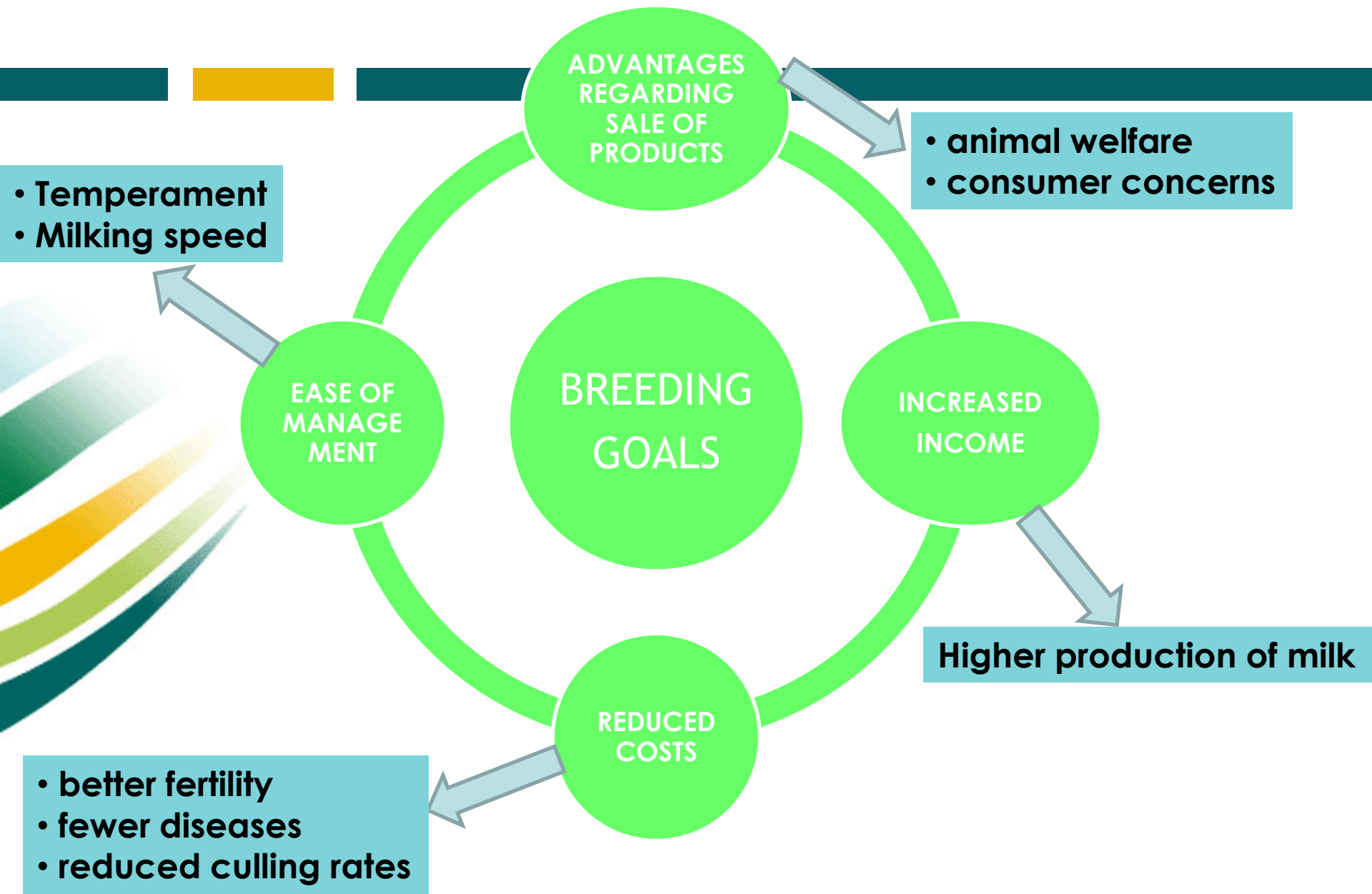
   ❖**General health traits**

   ❖**Female fertility**

   ❖**Feet and legs problems**

   ❖**Udder health**

   ❖**Workability**

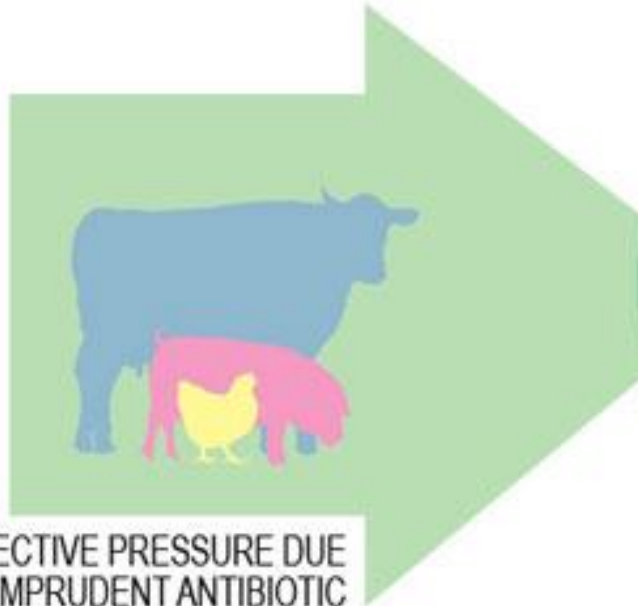*International Commitee for Animal Recording

Functional traits are being used

Legend: Protein, Fat, Milk, Type, Longevity, Udder Health, Fertility, Other man. & health traits

Countries: Japan - NTP, Israel - PD11, New Zealand - BW, France - ISU, Italy - PFT, Germany - RZG, Switzerland - ISEL, Canada - LPI, Spain - ICO, Belgium (Walloon) - V€G, Australia - APR, United States - TPI, South Africa - BVI, Great Britain - PLI, Nordic Countries - TMI, Ireland - EBI, United States - NM, The Netherlands - NVI

Source: Miglior et al., 2012

- Temperament
- Milking speed

ADVANTAGES REGARDING SALE OF PRODUCTS

- animal welfare
- consumer concerns

EASE OF MANAGEMENT

BREEDING GOALS

INCREASED INCOME

Higher production of milk

REDUCED COSTS

- better fertility
- fewer diseases
- reduced culling rates

SELECTIVE PRESSURE DUE TO IMPRUDENT ANTIBIOTIC USAGE IN ANIMALS

HUMAN HEALTH

INCREASED HUMAN MORBIDITY

INCREASED HUMAN MORTALITY

REDUCED EFFICACY OF RELATED ANTIBIOTICS USED IN HUMANS

INCREASED HUMAN HEALTHCARE COSTS
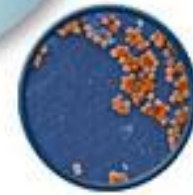
INCREASED POTENTIAL FOR CARRIAGE AND DISSEMINATION

FACILITATED EMERGENCE OF RESISTANCE IN HUMAN PATHOGENS

1. Genomics to system biology in animal science

1990 QTL MAPPING PROJECTS

2004

2009

2010

2012

2. Genomics to system biology in animal science

Genome-wide association study

Genomic selection-GEBV

Genomic prediction of progeny test

Reduce generation interval from 5 to 2 years
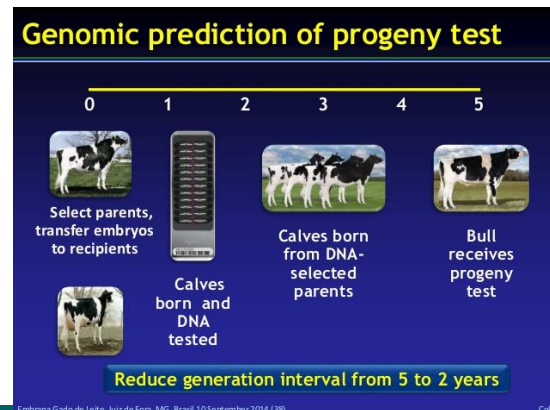
3. Genomics to system biology in animal science

MICROARRAY GENE EXPRESSION PROFILING

scanner

Affymetrix GeneChip
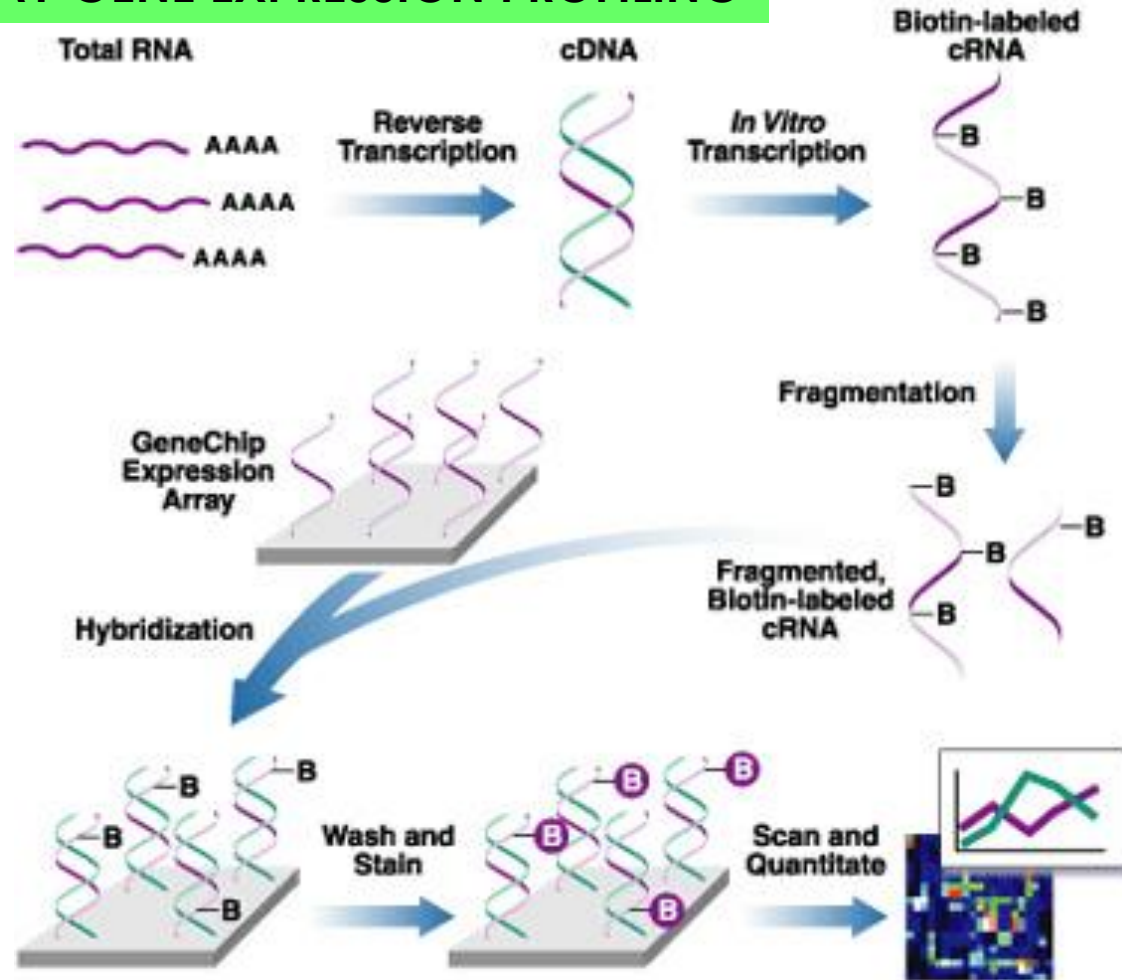
4. Genomics to system biology in animal science

NEXT GENERATION SEQUENCING

	Genomics	Transcriptomics	Epigenetics
Assay	Whole Genome Sequencing	mRNA Sequencing	Bisulfite Sequencing
	Exome & Targeted Sequencing	miRNA Sequencing	ChIP-Sequencing
Analysis	SNVs & Somatic Mutations	Transcript Expression	DNA Methylation
	Copy Number Variations	Alternative Splicing	Histone Modifications
	Structural Re-arrangements	miRNA Expression	Regulation Events

5. Genomics to system biology in animal science

WHAT IS THE SYSTEM BIOLOGY??????
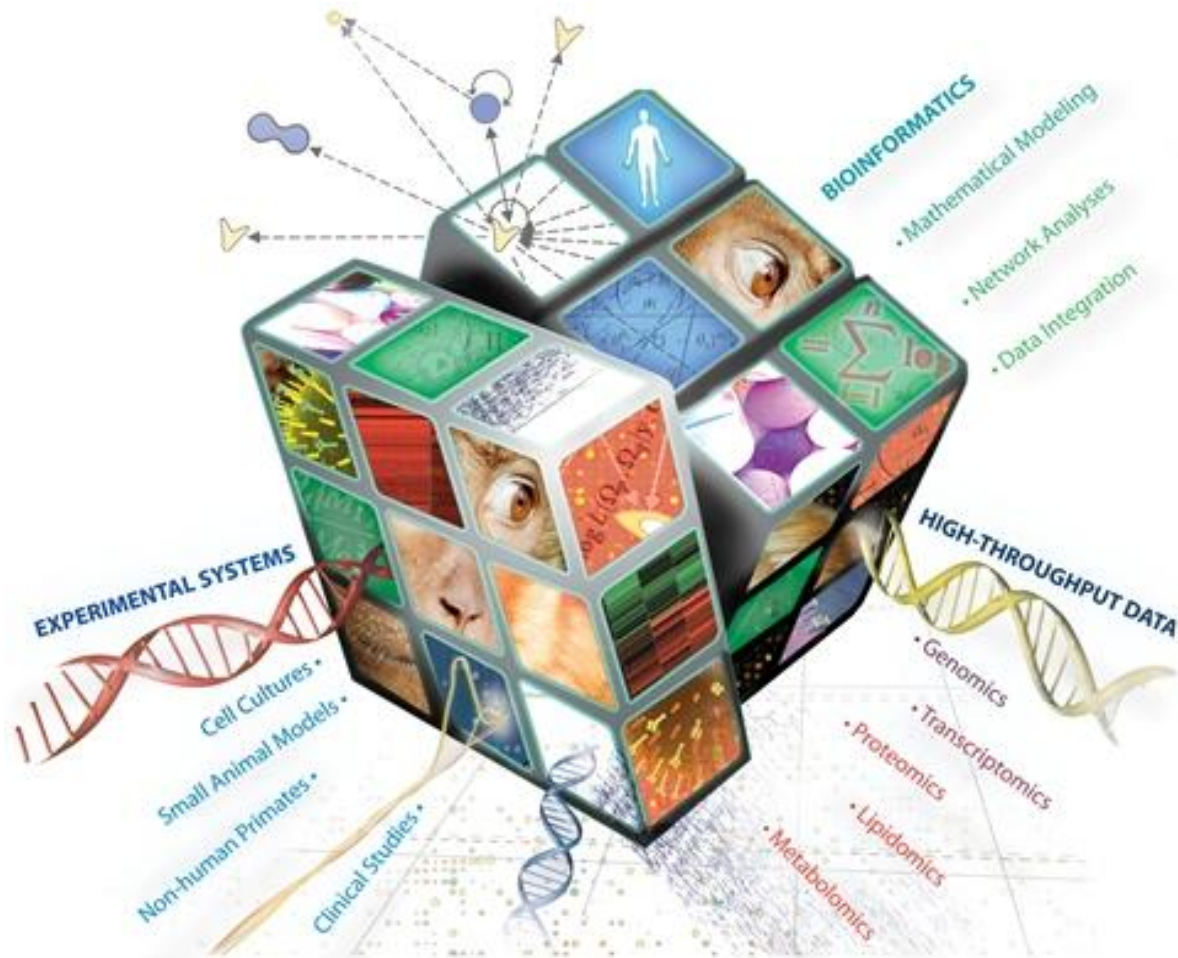
How does it integrate OMICs data and phenotypes?
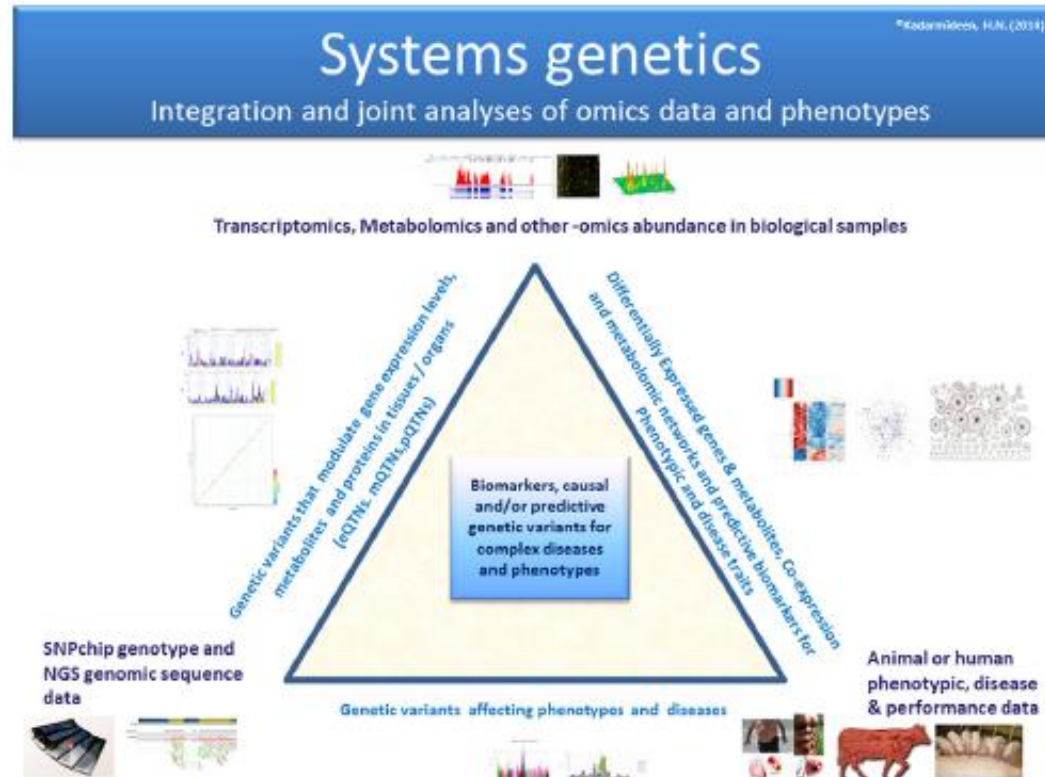
Fig. 5. Illustration of integrative systems genetics approaches that integrate genomic data and other -omics data types with diseases and phenotypic traits to detect highly predictive biomarkers, causal variants and master regulatory genes and variants in complex traits and diseases. Modified from (Kadarmideen, 2008).

Application of OMICs tech for analyzing diseases in livestock species

Genomics

Transcriptomics

Diseases

Proteomics

Metabolomics
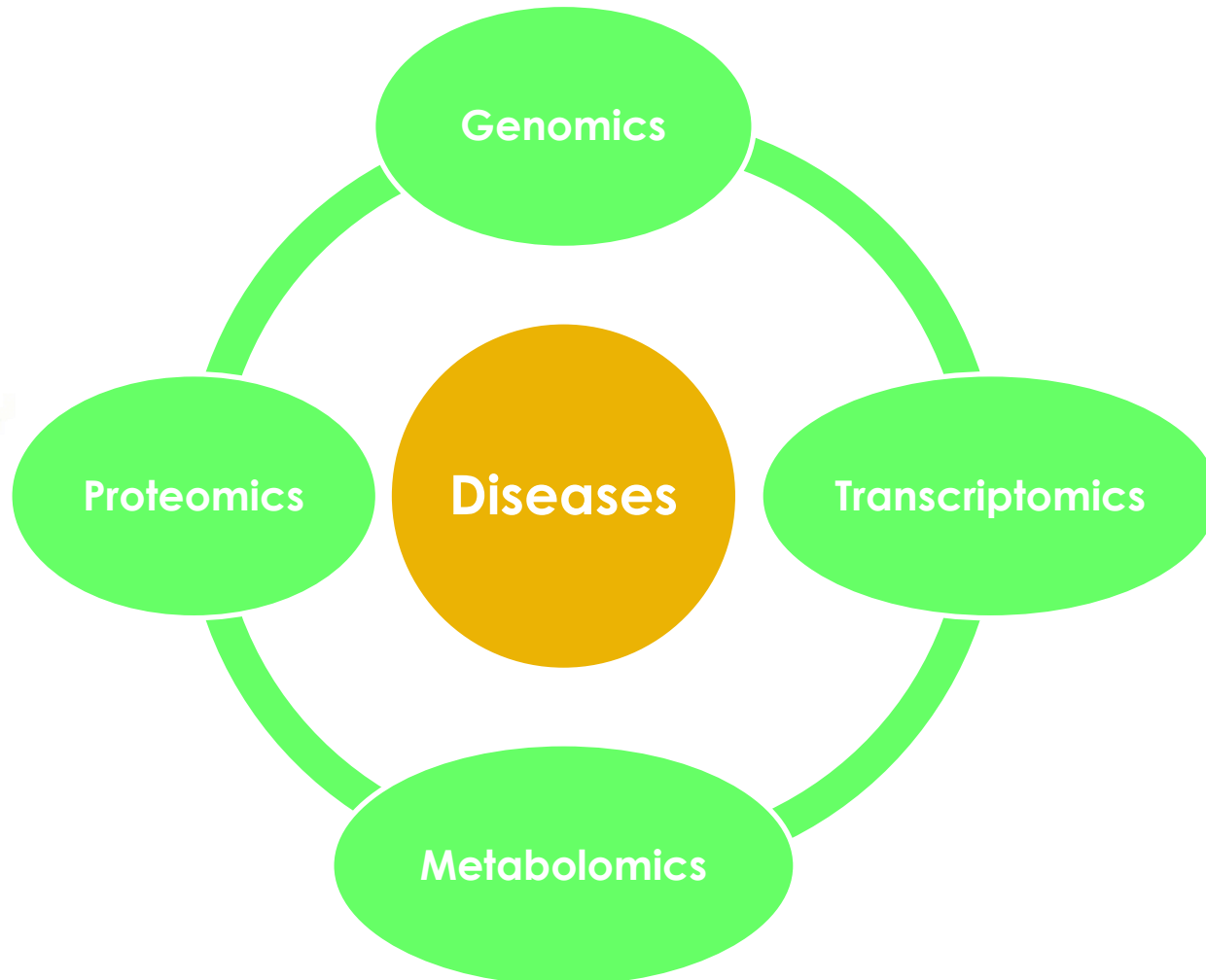
Diseases in cattle

Kind	Name
Viral	Bovine viral diarrhoea (BVD) Infectious bovine rhinotracheitis (IBR) Bovine viral syncytial virus (BRSV)
Bacterial	**Mastitis** **Lameness** **Johne's disease** Salmonellosis
Metabolic	Ketosis Milk fever (hypocalcemia) Grass tetany (hypomagnesaemia) Displaced abomasum
Fertility related condition	**Retained foetal membranes (RFM)** **Cystic ovaries** **Metritis**

GWAS for health
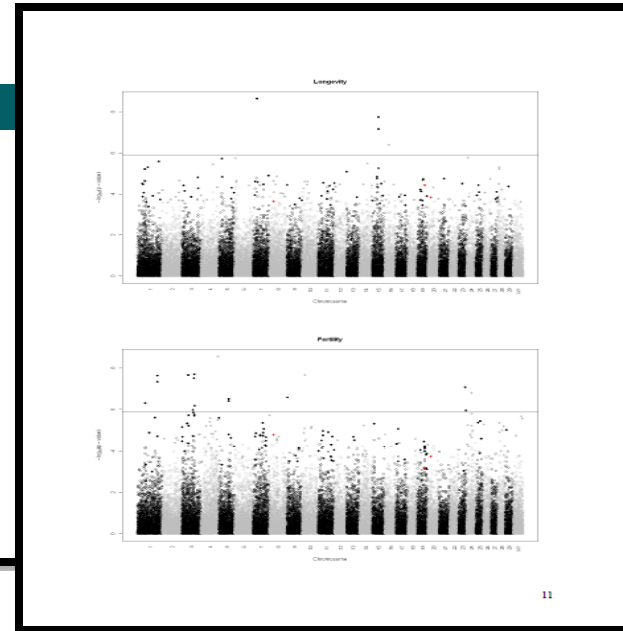
Trait	Single-SNP analysis			Multiple-SNP analysis
	Original p-values (p-value ≤ 0.05)*	Bonferroni correction (p-value $\leq 1.22 \times 10^{-6}$)*	False discovery rate (FDR) (q-value ≤ 0.05)*	Elastic net ($\alpha = 0.05$)
Longevity	5467	4	270	143
Fertility	6304	19	726	183
Cystic Ovaries	2149	-	-	-

* Threshold of significant associations

GWAS for mastitis

BMC Genetics

RESEARCH ARTICLE   **Open Access**

Genome-wide association study for somatic cell score in Valdostana Red Pied cattle breed using pooled DNA

Maria G Strillacci[1†], Erika Frigo[1†], Fausta Schiavini[1], Antonia B Samoré[2], Fabiola Canavesi[1], Mario Vevey[4], Maria C Cozzi[1], Morris Soller[3], Ehud Lipkin[3] and Alessandro Bagnato[1²*]

Figure 2 Manhattan plot of genome-wide associations for SCS trait. The red line represents the Bonferroni correc...

171 SIGNIFICANT SNP FOR SCS

52 WERE ANNOTATED WITHIN GENES

SOME INVOLVED IN THE IMMUNE RESPONSE TO MASTITIS

Table 2 Significant intragenic SNPs above the Bonferroni genome-wide threshold of 0.05

Illumina SNP name	Genbank SNP code	P-Value	BTA	SNP location	Gene symbol
BovineHD0100007623	rs137585939	4.43E-08	1	26254309	ROBO1
BovineHD0100040084	rs43273786	5.41E-08	1	141228619	NEK11
BovineHD0200004154	rs110997154	3.76E-08	2	15142189	SSFA2
BovineHD0300000560	rs110459674	inf	3	2612333	TADA1
BovineHD0300002104	rs110093914	1.87E-08	3	7276675	DDR2
BovineHD0300018913	rs42371455	1.87E-09	3	66866123	LPHN2
BovineHD0300023699	rs135870054	8.96E-10	3	87296944	ALG6
BovineHD0400026934	rs109307332	4.69E-08	4	98543003	PLXNA4
BovineHD0500003126	rs134685896	3.26E-10	5	12834395	ACSS3
BovineHD0700010213	rs133885406	4.73E-08	7	33526558	HSD17B4
BovineHD0900019961	rs136413030	3.70E-08	9	73355572	VNN1
BovineHD1000004333	rs43612234	5.32E-10	10	12722576	MEGF11
BovineHD1000009424	rs43623003	6.65E-08	10	28079552	MIR2284Z-1
BovineHD1000009428	rs110034517	5.56E-09	10	28102288	MIR2284Z-1
BovineHD1000017503	rs42486408	1.16E-09	10	60793897	TRPM7
BovineHD1100003814	rs109489659	5.53E-12	11	11771322	CCT7
BovineHD1300006368	rs109943824	1.12E-08	13	20845530	PLXDC2
BovineHD1300022672	rs41710487	4.53E-10	13	78416778	KCNB1
BovineHD1500008135	rs134980659	6.49E-08	15	28399876	THY1
Hapmap40064-BTA-36665	rs41631137	4.65E-12	15	33953859	PIK3C2A

GWAS for John's disease in sheep

Moioli, B., S. D'Andrea, L. De Grossi, E. Sezzi, B. De Sanctis, *et al., 2015 Genomic scan for* identifying candidate genes for Paratuberculosis resistance in sheep. Anim. Prod. Sci. in press.

PARATUBERCOLOSIS ELISA TEST

NEGATIVE   VS   POSITIVE

30 PUTATIVE CANDITATE GENE FOR DISEASE SUSCEPTIBILITY

CD109

PCP4

GWAS for calving ease in cattle

Identification of a Short Region on Chromosome 6 Affecting Direct Calving Ease in Piedmontese Cattle Breed

LAP3 SHOWS THE MOST INVOLVEMENT WITH THE TRAIT
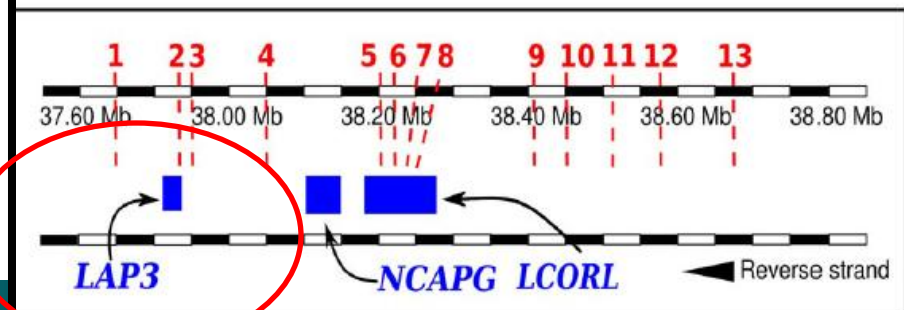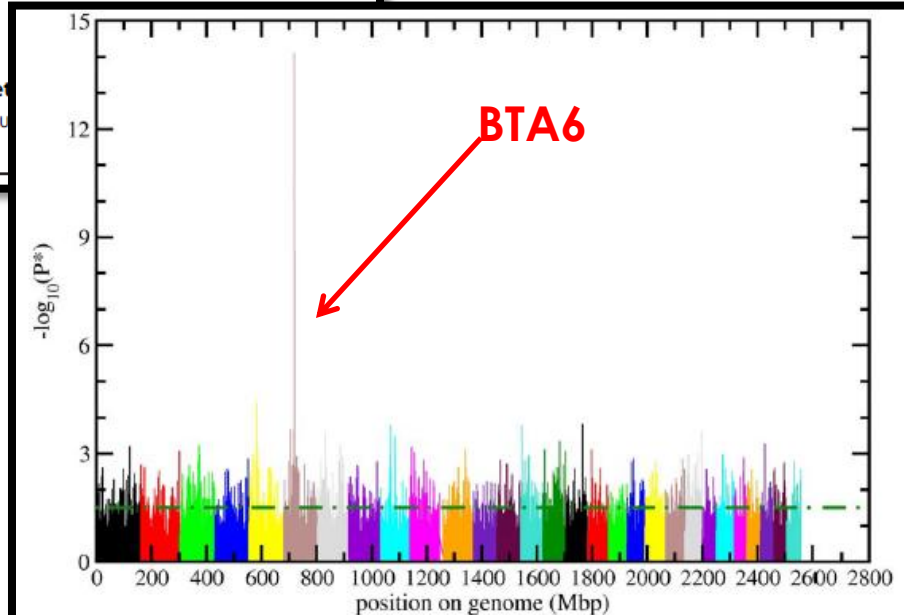
TRANSCRIPOTIMCS for paratubercolosis in cattle

MICROARRAY

Gene expression profiling of peripheral blood mononuclear cells (PBMC) from *Mycobacterium bovis* i... after *in vitro* antigenic stimulation with pu... derivative of tuberculin (PPD...

Kieran G. Meade [a], Eamonn Gormley [b], Stephen D.E. Park... Guilherme J.M. Rosa [c], Eamon Costello [d], Josep... Paul M. Coussens [c], David E. MacHugh

RESEARCH ARTICLE   **Open Access**

Genome-wide transcriptional profiling of peripheral blood leukocytes from cattle infected with *Mycobacterium bovis* reveals suppression of host immune genes

Kate E Killick[1], John A Browne[1], Stephen DE Park[1], David A Magee[1], Irene Martin[1], Kieran G Meade[2], Stephen V Gordon[1,3], Eamonn Gormley[4], Cliona O'Farrelly[5], Karsten Hokamp[6] and David E MacHugh[1,3*]

**Global Gene Expression and Systems...
Bovine Monocyte-Derived Macropha...
In Vitro Challenge with *Mycobacterium bovis***

David A. Magee[1,9], Maria Taraktsoglou[1,9], Kate E. Killick[1], Nicolas C. Nalpas[1], John A. Browne[1], Stephen D. E. Park[1], Kevin M. Conlon[2], David J. Lynn[3], Karsten Hokamp[4], Stephen V. Gordon[1,5], Eamonn Gormley[6], David E. MacHugh[1,5*]

TRANSCRIPOTIMCS for paratubercolosis in cattle

RNAseq

Nalpas et al. BMC Genomics 2013, 14:230
http://www.biomedcentral.com/1471-2164/14/230

BMC Genomics

RESEARCH ARTICLE   **Open Access**

Whole-transcriptome, high-throughput RN
sequence analysis of the bovine macropha
response to *Mycobacterium bovis* infection

Nicolas C Nalpas[1], Stephen DE Park[1], David A Magee[1], Maria Taraktsoglou[1], John A Browne[1], Kevi
Kévin Rue-Albrecht[1], Kate E Killick[1], Karsten Hokamp[3], Amanda J Lohan[4], Brendan J Loftus[4], Eamo
Step

frontiers in
IMMUNOLOGY   **ORIGINAL RESEARCH ARTICLE**
                                                        published: 04 February 2015
                                                        doi: 10.3389/fimmu.2015.00023

Analysis of the bovine monocyte-derived macrophage
response to *Mycobacterium avium* subspecies
paratuberculosis infection using RNA-seq

Maura E. Casey[1,2], Kieran G. Meade[2], Nicolas C. Nalpas[1], Maria Taraktsoglou[3], John A. Browne[1],
Kate E. Killick[1,4], Stephen D. E. Park[1,3], Eamonn Gormley[5], Karsten Hokamp[6], David A. Magee[1,3] and
David E. MacHugh[1,7] *

[1] Animal Genomics Laboratory, UCD School of Agriculture and Food Science, University College Dublin, Dublin, Ireland
[2] Animal and Bioscience Research Department, Animal and Grassland Research and Innovation Centre, Teagasc, Dunsany, Ireland

PLOS | ONE

RESEARCH ARTICLE

The Identification of Circulating MiRNA in
Bovine Serum and Their Potential as Novel
Biomarkers of Early *Mycobacterium avium*
subsp *paratuberculosis* Infection

Damien Farrell[1], Ronan G. Shaughnessy[1], Louise Britton[1], David E. MacHugh[2,5],
Bryan Markey[1], Stephen V. Gordon[1,3,4,5] *

TRANSCRIPOTIMCS for paratubercolosis in cattle

	MICROARRAY	RNASEQ
	N° DE	
2 hpi	315	245
6hpi	466	574
TOTALE	781	819

2hpi

6hpi
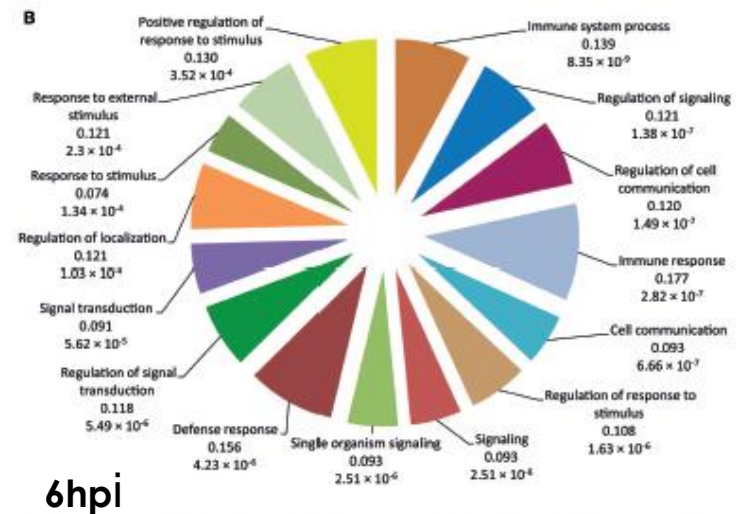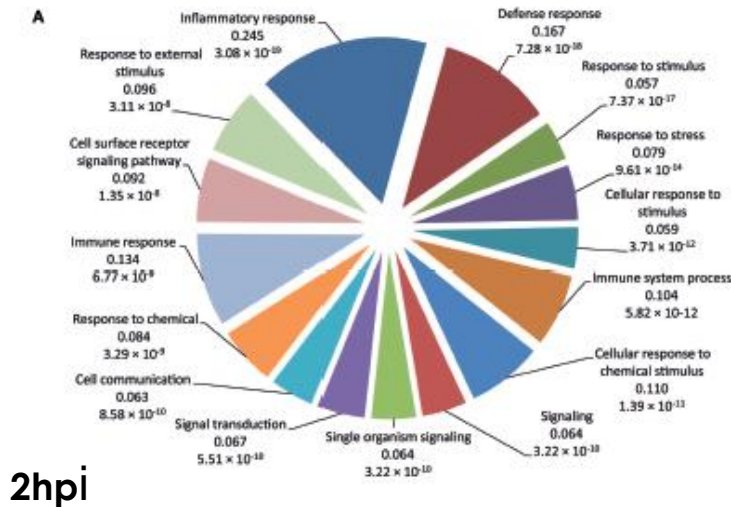
TRANSCRIPOTIMCS for mastitis

Buitenhuis et al. BMC Genomics 2011, **12**:130
http://www.biomedcentral.com/1471-2164/12/130

BMC Genomics

RESEARCH ARTICLE — Open Access

In depth analysis of genes and pathways of the mammary gland involved in the pathogenesis of bovine *Escherichia coli*-mastitis

Bart Buitenhuis[1*], Christine M Røntved[2], Stefan M Edwards[1], Klaus L Ingvartsen[2], Peter Sørensen[1]

Brand et al. Genetics Selection Evolution 2011, **43**:24
http://www.gsejournal.org/content/43/1/24

GSE Genetics Selection Evolution

RESEARCH — Open Access

Comparative expression profiling of *E. coli* and *S. aureus* inoculated primary mammary gland cells sampled from cows with different genetic predispositions for somatic cell score

Bodo Brand[1], Anja Hartmann[1], Dirk Repsilber[2], Bettina Griesbeck-Zilch[4], Olga Wellnitz[5], Christa Kühn[3], Siriluck Ponsuksili[1], Heinrich HD Meyer[4] and Manfred Schwerin[1,6*]

Lewandowska-Sabat et al. BMC Genomics 2013, **14**:891
http://www.biomedcentral.com/1471-2164/14/891

BMC Genomics

RESEARCH ARTICLE — Open Access

The early phase transcriptome of bovine monocyte-derived macrophages infected with *Staphylococcus aureus in vitro*

Anna Monika Lewandowska-Sabat[1†], Guro Margrethe Boman[1†], Alison Downing[2], Richard Talbot[2], Anne Kristine Storset[3] and Ingrid Olsaker[1*]

Bonnefont et al. BMC Genomics 2011, **12**:208
http://www.biomedcentral.com/1471-2164/12/208

BMC Genomics

RESEARCH ARTICLE — Open Access

Transcriptomic analysis of milk somatic cells in mastitis resistant and susceptible sheep upon challenge with *Staphylococcus epidermidis* and *Staphylococcus aureus*

Cécile MD Bonnefont[1,2,3], Mehdi Toufeer[2,3], Cécile Caubet[2,3], Eliane Foulon[2,3], Christian Tasca[2,3], Marie-Rose Aurel[4], Dominique Bergonier[2,3], Séverine Boullier[2,3], Christèle Robert-Granié[1], Gilles Foucras[2,3*†] and Rachel Rupp[1†]

Cremonesi et al. BMC Genomics 2012, **13**:540
http://www.biomedcentral.com/1471-2164/13/540

BMC Genomics

RESEARCH ARTICLE — Open Access

Response of the goat mammary gland to infection with *Staphylococcus aureus* revealed by gene expression profiling in milk somatic and white blood cells

Paola Cremonesi[1†], Rossana Capoferri[2*†], Giuliano Pisoni[3], Marcello Del Corvo[4], Francesco Strozzi[4], Rachel Rupp[5], Hugues Caillat[5], Paola Modesto[3,6], Paolo Moroni[3,7], John L Williams[4], Bianca Castiglioni[1] and Alessandra Stella[1,4]

OPEN ACCESS Freely available online

PLoS one

Gene Expression Profiling of Dendritic Cells Reveals Important Mechanisms Associated with Predisposition to *Staphylococcus* Infections

Mehdi Toufeer[1,2], Cécile M. D. Bonnefont[1,2,3], Eliane Foulon[1,2], Cécile Caubet[1,2], Christian Tasca[1,2], Marie-Rose Aurel[4], Christèle Robert-Granié[3], Rachel Rupp[3], Gilles Foucras[1,2*]

1 Université de Toulouse, INP, ENVT; UMR 1225, IHAP, Toulouse, France, 2 INRA, UMR1225, IHAP, Toulouse, France, 3 INRA, UR631, SAGA, Castanet-Tolosan, France, 4 INRA, UE321, Roquefort, France

TRANSCRIPOTIMCS for mastitis

Jin et al. BMC Genomics 2014, 15:181
http://www.biomedcentral.com/1471-2164/15/181

BMC Genomics

RESEARCH ARTICLE — Open Access

Transcriptome microRNA profiling of bovine mammary epithelial cells challenged with *Escherichia coli* or *Staphylococcus aureus* bacteria reveals pathogen directed microRNA expression profiles

Weiwu Jin, Eveline M Ibeagha-Awemu, Guanxiang Liang, Frederic Beaudoin, Xin Zhao and Le Luo Guan

MicroRNA Regulation of Bovine Monocyte Inflammatory and Metabolic Networks in an *In Vivo* Infection Model

Nathan Lawless,*,† Timothy A. Reinhardt,‡ Kenneth Bryan,* Mike Baker,§ Bruce Pesch,‡ Duane Zimmerman,‡ Kurt Zuelke,** Tad Sonstegard,†† Cliona O'Farrelly,† John D. Lippolis,‡,1

International Journal of Animal and Veterinary Advances 5(4): 130-142, 2013
ISSN: 2041-2894; e-ISSN: 2041-2908
© Maxwell Scientific Organization, 2013
Submitted: December 31, 2012   Accepted: February 08, 2013   Published: August 20, 2013

Sequence, Expression and Phylogenetic Analysis of Immune Response Gene
Mastitis in Buffaloes

²Priyanka Banerjee, ²Suresh K Gahlawat ¹,²Jyoti Joshi, ¹Upasna Sharma and ¹R.E
¹National Bureau of Animal Genetic Resources, Karnal, Haryana, India
²Department of Biotechnology, Chaudhary Devi Lal University, Sirsa, Harya

Richards et al. BMC Genomics 2013, 14:920
http://www.biomedcentral.com/1471-2164/14/920

BMC Genomics

RESEARCH ARTICLE — Open Access

Transcriptomic and genomic evidence for *Streptococcus agalactiae* adaptation to the bovine environment

Vincent P Richards¹, Sang Chul Choi²,³, Paulina D Pavinski Bitar¹, Abhijit A Gurjar¹,⁴ and Michael J Stanhope¹*

TRANSCRIPOTIMCS for mastitis

	Mammary gland tissue	Escherichia coli	Buitenhuis et al. [81]
Chemokine signaling pathway			
Toll-like receptor signaling pathway			
Leukocyte transendothelial migration			
Cytokine–cytokine receptor interaction			
Natural killer cell mediated cytotoxicity			
Cell adhesion molecules (CAMs)			
RIG-I-like receptor signaling pathway			
Fc gamma R-mediated phagocytosis			
B cell receptor signaling pathway			
Antigen processing and presentation			
Adipocytokine signaling pathway			
Apoptosis			
Complement and coagulation cascades			
Proteasome			
Jak-STAT signaling pathway			
Primary immunodeficiency			
Glycerophospholipid metabolism			
Pathways in cancer			
Retinol metabolism			
Fatty acid metabolism			
Fatty acid biosynthesis			
Metabolism of xenobiotics by cytochrome P450			
Glycerolipid metabolism			
Drug metabolism — cytochrome P450			

PROTEOMICS
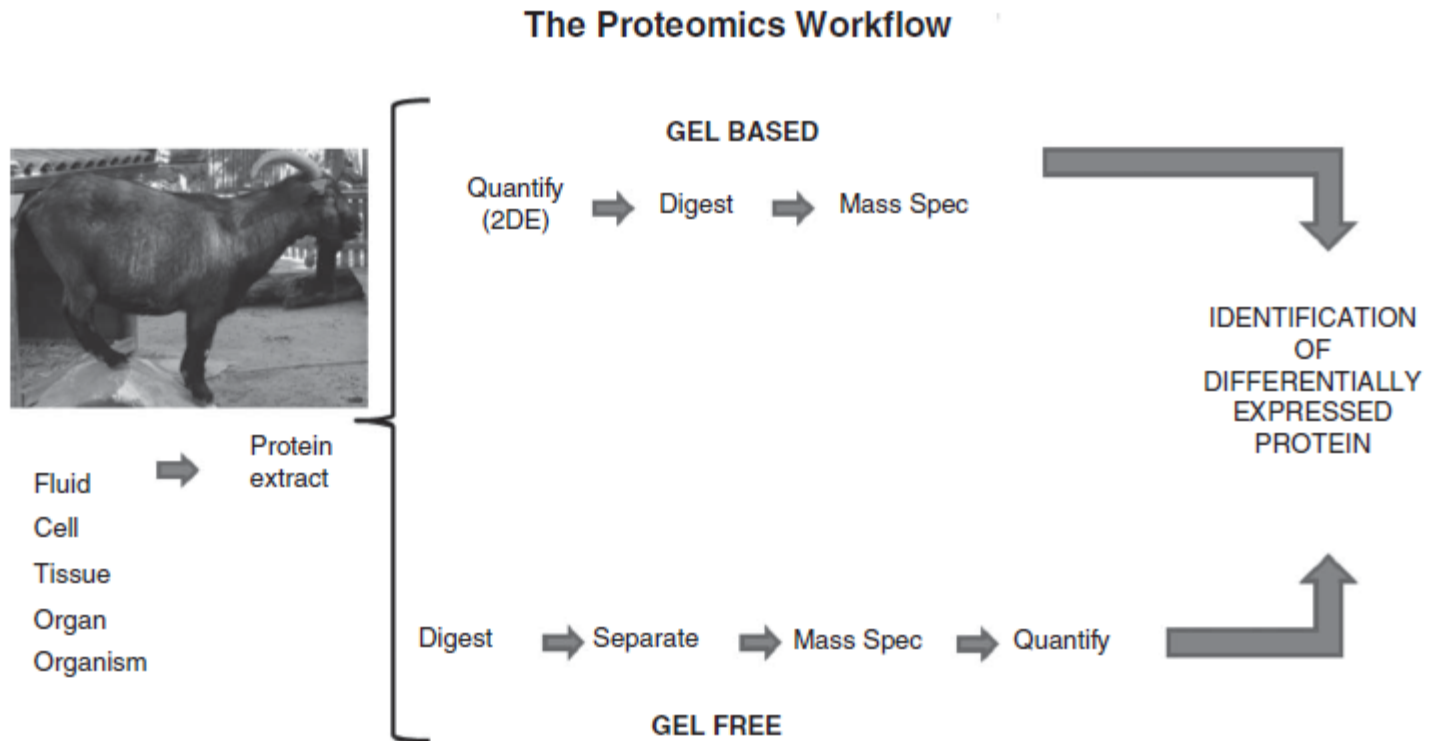
Figure 1 A schematic representation of the proteomics workflow. In proteomics, one of the two approaches are followed: gel based first, individual protein expression is quantified using two-dimensional electrophoresis and individual proteins are digested with an trypsin, and identified using MS. In the gel-free approach, the whole protein extracts are digested with trypsin, separated using ch proteins of interest identified and quantified using high-throughput MS instruments. The latter approach is particularly suitable for spec coverage levels in databases (cattle, pig, sheep, chicken and salmon).

PROTEOMICS

Available online at www.sciencedirect.com

SciVerse ScienceDirect

www.elsevier.com/locate/jprot

ELSEVIER

A peptidomic approach to biomarker discovery for bovine mastitis☆

Rozaihan Mansor[a,1], William Mullen[b], Amaya Albalat[b], Panagiotis Zere[...]
Harald Mischak[b,d], David C. Barrett[e,2], Andrew Biggs[f], P. David Eckersa[...]

Veterinary Biomarker Discovery: Proteomic Analysis of Acute Phase Proteins

Jamie L. Boehmer and Zohra Olumee-Shabon
U.S. Food and Drug Administration Center for
Veterinary Medicine Office of Research
United States of America

Review

Farm Animal Serum Proteomics and Impact on Human Health

Francesco Di Girolamo [1], Alfonsina D'Amato [2], Isabella Lante [3], Fabrizio Signore [4],
Marta Muraca [1] and Lorenza Putignani [5,6,*]

PROTEOMICS and mastitis

The Veterinary Journal
Volume 200, Issue 3, June 2014, Pages 420–425

Proteomics and pathway analysis of N-glycosylated mammary gland proteins in response to *Escherichia coli* mastitis in cattle

Yongxin Yang[a, 1], Weijun Shen[b, 1], Xiaowei Zhao[a], Huiling Zhao[a], Dongwei Huang[a], Guanglong Cheng[a]

J Vet Sci. 2014 Dec 24. [Epub ahead of print]

Comparative proteomic analysis of changes in proteins in the mammary tissue of cows infected with Escherichia coli mastitis.

Zhao XW, Yang YX, Huang DW, Cheng GL, Zhao HL.

Huang et al. BMC Genomics 2014, 15:839
http://www.biomedcentral.com/1471-2164/15/839

BMC Genomics

RESEARCH ARTICLE — Open Access

iTRAQ-proteomics and bioinformatics analyses of mammary tissue from cows with clinical mastitis due to natural infection with *Staphylococci aureus*

Jinming Huang[1*], Guojing Luo[1,2], Zijing Zhang[1,2], Xiuge Wang[1], Zhihua Ju[1], Chao Qi[1], Yan Zhang[1], Changfa Wang[1], Rongling Li[1], Jianbin Li[1], Weijun Yin[1], Yinxue Xu[2], Sonia J Moisá[3,5], Juan J Loor[3,4,5] and Jifeng Zhong[1*]

mammary tissue — **healthy vs mastitic cow**

551 N-glycosylation sites

H → **294 proteins** M → **283 proteins**

98 different glycosilated sites

mammary tissue — **healthy vs mastitic cow**

95 DE proteins

mammary tissue — **healthy vs mastitic cow**

36 UPregulated — **19 DOWNregulated**

PROTEOMICS and Salmonella in pig

Journal of Proteomics
Volume 75, Issue 14, 19 July 2012, Pages 4457–4470
Special Issue: Farm Animal Proteomics

Proteomic analysis of porcine mesenteric lymph-nodes after *Salmonella typhimurium* infection ☆

Rodrigo Prado Martins[a], Melania Collado-Romero[a], Montserrat Martínez-Gomáriz[b], ...ela Moreno[a], Juan J.

Full Text
Proteomes of Host Cell Membranes Modified by Intracellular Activities of *Salmonella enterica*

Mol Cell Proteomics 2015 14: 81–92.
First Published on October 27, 2014,

Journal of Proteomics
Volume 118, 6 April 2015, Pages 112–129
Protein dynamics in health and disease

Development of a computational framework for the analysis of protein correlation profiling and spatial proteomics experiments ☆

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RESEARCH ARTICLE

A Multi-Omic View of Host-Pathogen-Commensal Interplay in *Salmonella*-Mediated Intestinal Infection

Brooke L. Deatherage Kaiser, Jie Li, James A. Sanford, Young-Mo Kim, Scott R. Kronewitter, Marcus B. Jones, Christine T. Peterson, Scott N. Peterson, Bryan C. Frank, Samuel O. Purvine, Joseph N. Brown, Thomas O. Metz, Richard D. Smith, Fred Heffron, Joshua N. Adkins ✉

CONCLUSIONS

- **Traditional traits**
  - **...nctional traits**

...eder needs
...nsumers den...
...irements impact

...omics
...scriptomics
...eomics

healthy, happy herds...

FOOD SAFETY AND QUALITY