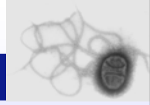
EADGENE European Animal Disease Genomics Network of Excellence for Animal Health and Food Safety

Animal Disease Genomics: Opportunities and Applications
10th - 11th June 2008. Edinburgh. UK

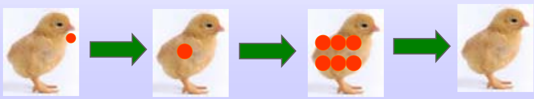
Resistance to salmonella in chicken: which genetic control corresponds to which animal model ?

Some *Salmonella* features

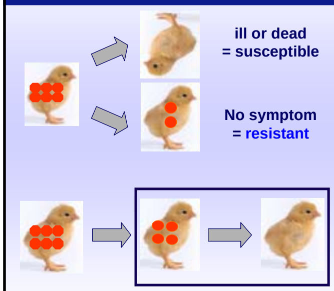


- Gram- bacteria
- Several hundreds of specific or ubiquitous serotypes
- One major species: *Salmonella enterica*
- *S. enterica* serotype Enteritidis is responsible for most human food-borne infections

Salmonella infection steps in chicken



Resistance or resistance to carrier-state ?



Disease resistance
S. Pullorum
S. Gallinarum
Studied to improve animal health
... but an asymptomatic carrier state is possible

Carrier-state resistance
S. Enteritidis
S. Typhimurium
Studied to improve food safety

Infection models

Salmonella infection: chicken models

- Infection models vary according to:
  - Age at inoculation
  - Route of inoculation
  - Serotype and dose inoculated
  - Time post inoculation
  - The trait used to assess resistance
- No universal model

Infection models

Historical perspective (1)

1. First part of 20th century: need to reduce animal losses
   - *S.* Pullorum, *S.* Gallinarum
   - High doses of inoculum
   - Mortality rate
   - Oral, intra-peritoneous or subcutaneous inoculation
   - Young to very young (day-old) chicks

Infection models

Historical perspective (2)

2. Second part of 20th century: concerns about food safety

S. Enteritidis and *S.* Typhimurium incriminated

2.1 Focus on general resistance

High inoculum doses on young chicks
Mortality rate or bacteria load assessed

2.2 Focus on carrier-state resistance

Chicks or adult hens
Lower dose of inoculum
Phenotyping several weeks later (bacteria load)

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Infection models

Different ways of assessing resistance

- **Mortality rate**
  On young chicks
- **Bacteria counting in different organs**
  Spleen/ liver/ ovary/ caeca (systemic infection)
  Caeca (excretion)
- **Antibody response to salmonella vaccination**
  No obvious link with variations in resistance or in carrier state resistance

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Impact of chicken genetic background

- Studies demonstrate between-line differences
- Genetic origin of differences

➡ **Which are the genes involved?**

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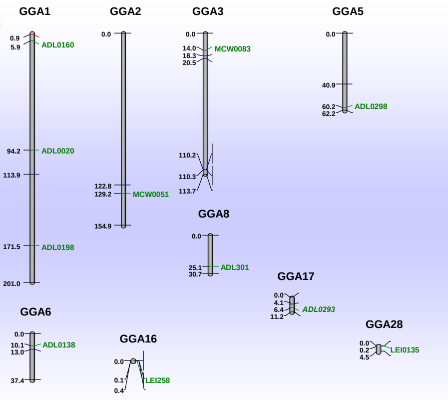
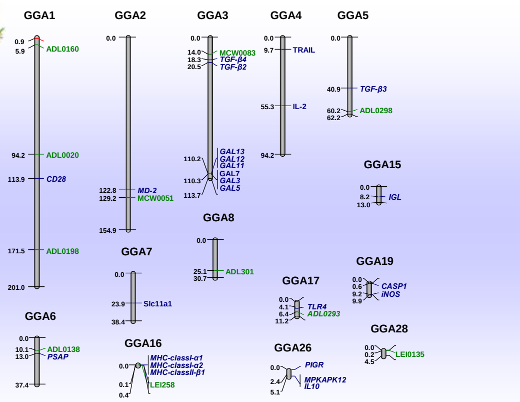
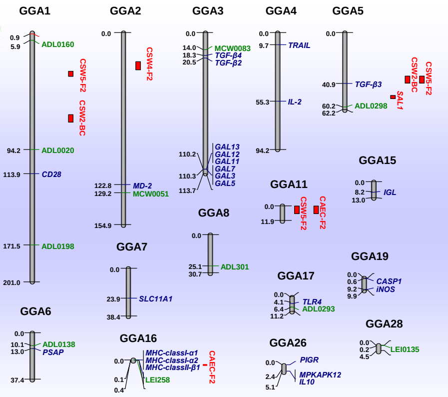


Microsatellites: antibody response



Microsatellites: antibody response
Candidate genes: antibody response or bacteria load



Microsatellites: antibody response
Candidate genes: antibody response or bacteria load
QTL: bacteria load

Salmonella resistance genes

Overview

Serotype
S. typhimurium or *S. enteritidis*
Inoculation
subcutaneous, intra-muscular, intravenous, intra-oesophageal or oral
Age at inoculation
1 day to 13 weeks, peak of laying
Interval post-inoculation
3 days to 5 weeks
Trait
Antibody response, excretion, caecal/ spleen/ liver loads

45 loci
15 infection models

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Salmonella resistance genes

Overview

- **Most loci identified in only one infection model**
  - **Not tested in other models**
  - **Tested but not significant**
- **4 exceptions: *SLC11A1*, *TLR4*, *MHC* and *SAL1***

➡ **Which parameters are responsible for the variations observed between experiments?**

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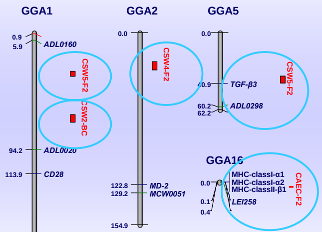
Salmonella resistance genes

Genes differ according to the chicken line

QTL analysis
Experimental inbred lines N and 61

- F2 progeny
- Chicks

Tilquin *et al* 2005



➡ **Validation in commercial lines (laying hens) underway by single locus analyses.** Calenge *et al* 2008, in prep.

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Salmonella resistance genes

Genes differ according to the chicken's age

➡ **In commercial lines, some of the genes involved in salmonella carrier state variations in chicks are different from those identified in adult hens.**

Calenge *et al* 2008, in prep.

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Salmonella resistance genes

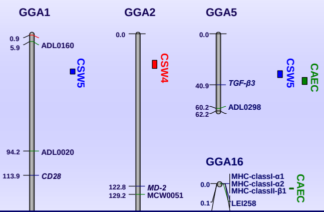
Genes differ according to the trait assessed

QTL analysis
Experimental inbred lines N and 61

- F2 progeny
- Chicks

Tilquin *et al* 2005

Excretion, 4 weeks pi (CSW4)
Excretion, 5 weeks pi (CSW5)
Caecal load (CAEC, systemic infection)



➡ **Bacteria excretion and systemic infection are most probably controlled by different sets of genes**
➡ **Importance of time post inoculation**

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Salmonella resistance genes

Genes differ according to other parameters?

- **Route of inoculation, rearing conditions, etc?**
- **To be studied…**

➡ **Are there genes common to several infection models?**

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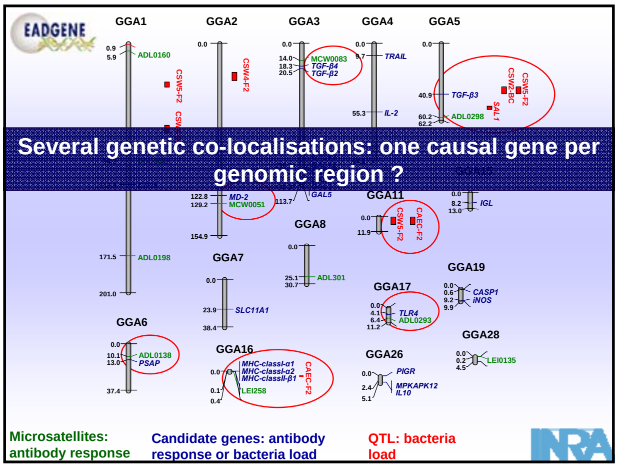
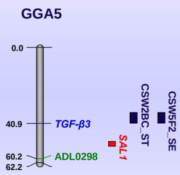
Resistance to salmonella in chicken: which genetic control corresponds to which animal model ?
Fanny Calenge, INRA, France



Genetic co-localisations

SAL1 - One genome region, several models



5 loci, 4 different models
Young chicks, different lines

Systemic infection, oral inoculation
Mariani *et al* 2001

Antibody response, intra-oesophageal inoculation
Kaiser *et al et al* 2002

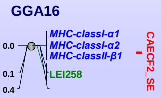
Systemic infection, intra-oesophageal inoculation
Malek and Lamont 2003

Excretion, oral inoculation
Tilquin *et al* 2005

➡ **Only one causal gene for several models?**

Genetic co-localisations

MHC - One genome region, several models



Major Histocompatibility Complex

Antibody response, chicks, subcutaneous inoculation
Zhou and Lamont 2003

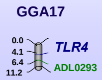
Systemic infection, adults, oral inoculation
Calenge et al 2008 (in prep)

Systemic infection, chicks, oral inoculation
Tilquin et al 2005

➡ **Which causal gene(s) for the QTL?**
➡ **Which haplotype could be used for selection?**

Genetic co-localisations

TLR4 - One gene, several models



TLR4: Toll-Like Receptor 4

Survival time, intramuscular inoculation, chicks, *S.* Typhimurium
Hu et al 1997, Leveque et al 2003

Systemic infection, oral inoculation, adults, *S.* Enteritidis, 4 weeks pi
Beaumont et al 2003

Antibody response, chicks, 10 days pi
Yunis et al 2002

➡ **Interesting candidate for both selection and theoretical studies**

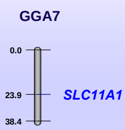
Genetic co-localisations

SLC11A1 - One gene, many different models

Solute carrier 11A1 (formerly ***NRAMP1***)

7 different models

- Adults/ chicks
- Antibody response/ systemic infection/ survival rate
- Different lines



➡ **Very interesting candidate for selection**
➡ **Same allele involved in both resistance and resistance to carrier-state?**
➡ **Same allelele in youngs and in adults?**

CONCLUSION (1)

- **Genes controlling salmonella resistance differ according to:**
  - Lines studied
  - Trait assessed
  - Chicken's age
  - Other parameters?
- **Studying different models leads to a complex sum of results but allows a precise and (more) complete description of the disease**

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CONCLUSION (2)

- Several genes or regions are good candidates for selection and more in-depth studies: ***SLC11A1***, ***TLR4***, ***MHC***, ***SAL1***?
- Several QTL interesting for selection if finely mapped or if causal genes identified
- Genes identified should be tested in different conditions before selection is considered

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SOME OUTLOOKS

- New genes will probably be identified
  - with a better coverage of the chicken genome
  - by screening new genetic materials
- Numerous candidate genes for QTL are expected from functional studies (microarrays)

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Aknowledgements

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