

# Development of In Vivo Mastitis Models

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

## Genomics for Animal Health: Outlook for the Future

13- 14th October 2009, Muséum National d'Histoire Naturelle, Paris, France

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## Mastitis\* is a costly disease!

150-250€ per clinical case

1.000.000.000 € per year

\*inflammation of the mammary gland mostly due to bacterial infections

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## General Aim

...early host-pathogen interaction via transcriptome profiling in...

### Subclinical Mastitis

- more often
- hard to detect
- often „contagious“ pathogens

### Acute clinical Mastitis

- lethal in severe cases
- often self-healing
- often ubiquitous pathogens

...Experimental Mastitis Model

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## Model Animals

„600kg variability“ = 30.000 mice

use „standardized“ cows!

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## Animal Model

- Aim:**
  - Induction of an **acute clinical** mastitis with **Escherichia coli** and a **subclinical – (chronic)** mastitis with **Staphylococcus aureus**
- Animals:**
  - Holstein-Frisian heifers („naive“)
  - 3rd-5th month of 1st lactation
  - Prescreening: weekly 6 weeks prior to challenge:*
  - healthy (general health status, udder health)
  - Somatic cell count (SCC) <100.000 /ml (quarter milk)
  - milk free from mastitis pathogens
  - Estrus at day of challenge
- Challenge Dose**
  - 500 CFU **E. coli** und 10.000 CFU **S. aureus**
  - Isolates from clinical mastitis

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## Animal Model

6 h  
12 h  
24 h  
72 h

Mastitis?

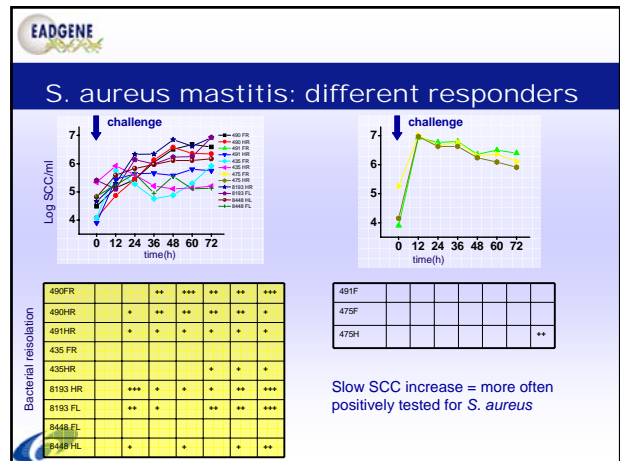
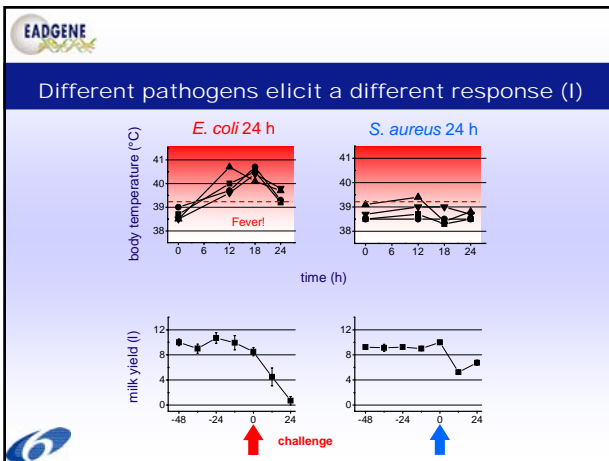
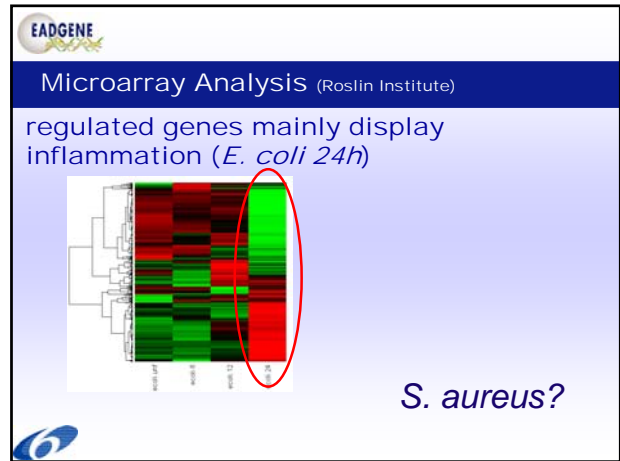
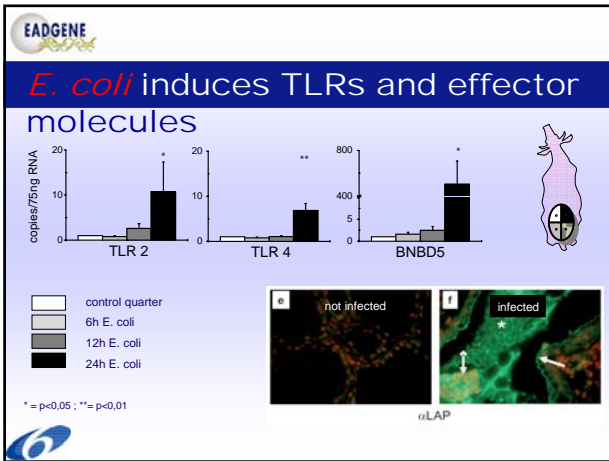
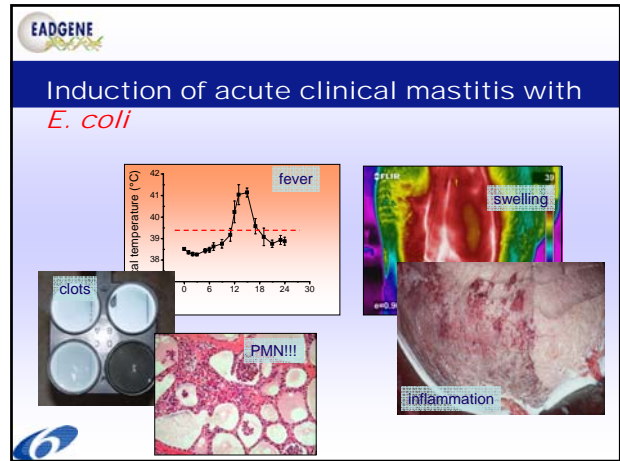
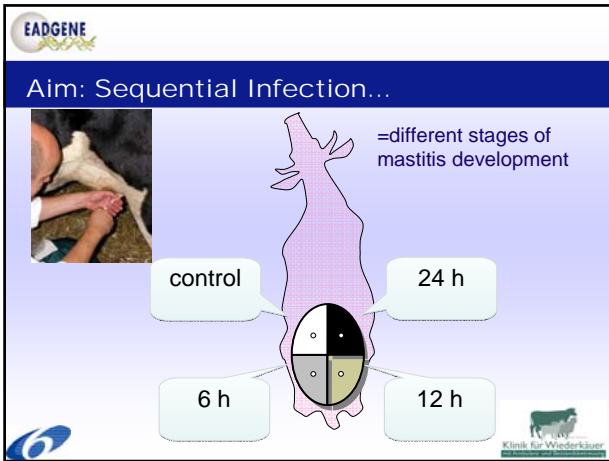
Section

- body temperature
- SCC
- diff. cell count (blood/milk)
- clinical signs (e.g. swelling)
- bacterial counts (milk)

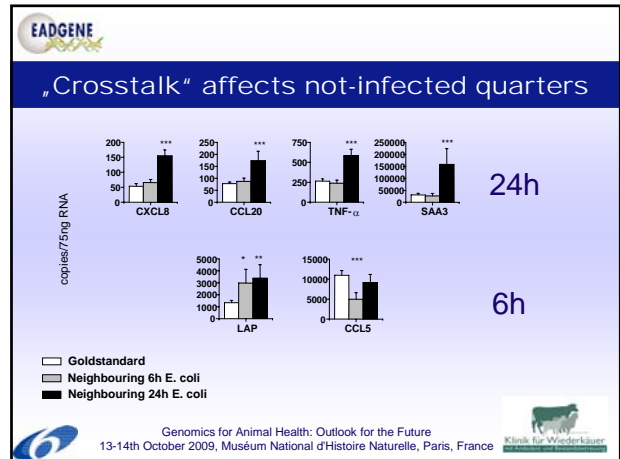
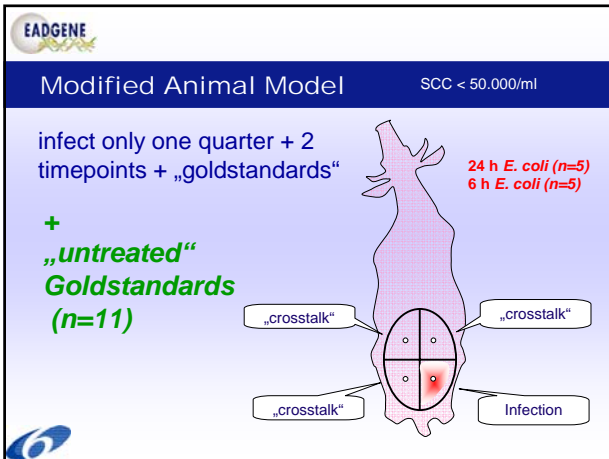
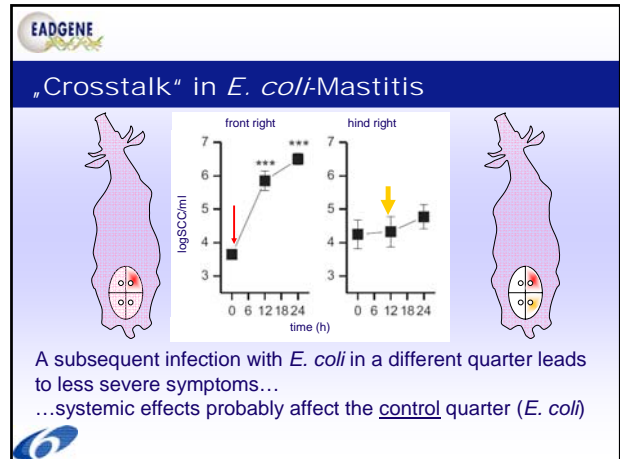
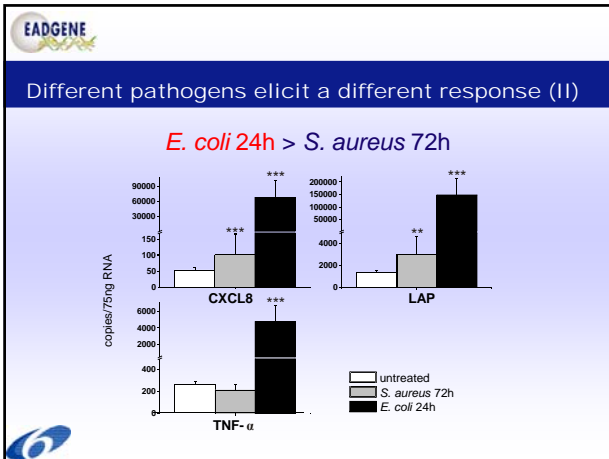
- Pathology
- Histology
- Sampling

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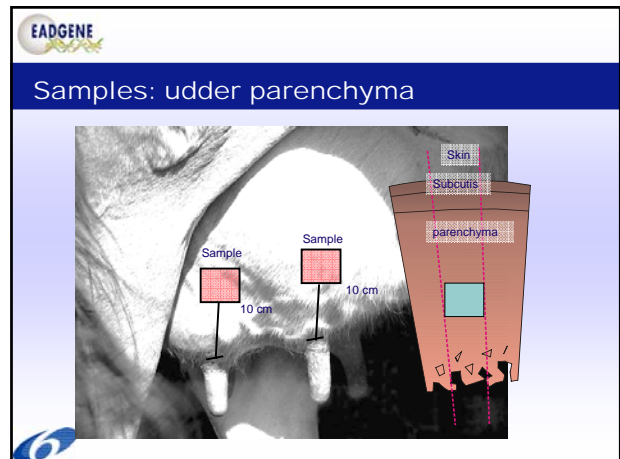


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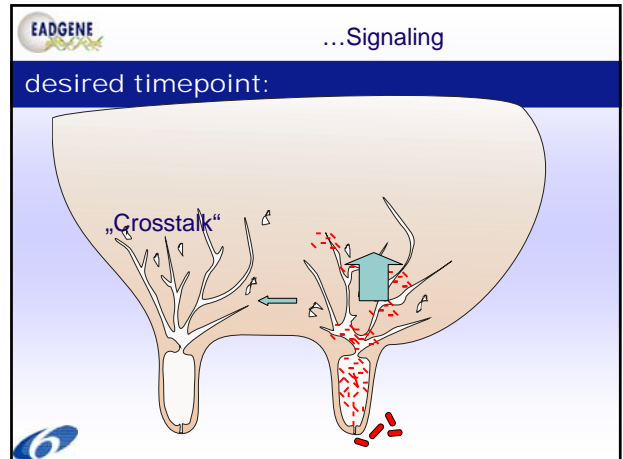
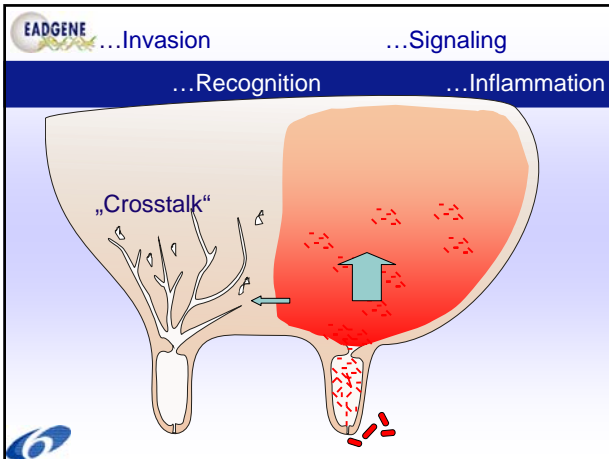
Milestone: Where are the watchtowers?

- Observed differentially expressed (inflammatory) genes are more likely to be the consequence of early host pathogen interaction (elsewhere?).

?

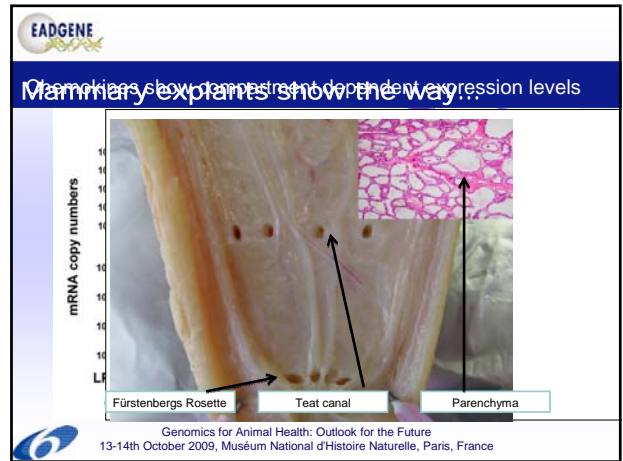


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What happens  
 between recognition and inflammation?  
 Let's develop a novel model...



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Increased sample numbers and localisations

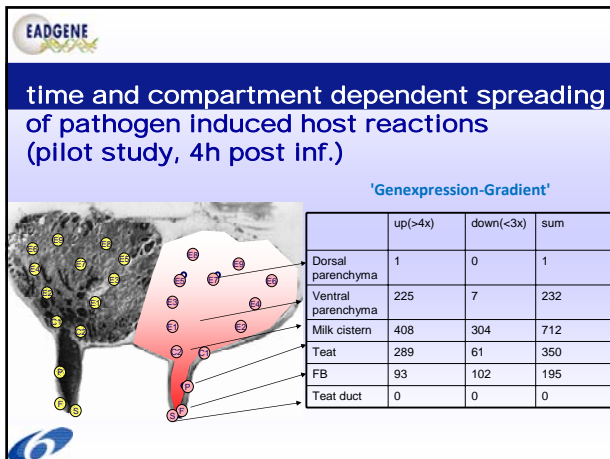
Which compartment is the key mediator?  
 Where and when are signals being generated?

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Pilot study

- increase challenge dose (5 Mio vs. 500 CFU)
- shorter period...maximum 6h
- challenge two quarters
- monitor one frequently (SCC)
- first SCC increase... **SAMPLE!!!**

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- Conclusion
- 4h / 5 Mio CFU *E. coli* is still too late for the earliest regulated gene... (3h...2h...)
  - Consider differences of the host...
  - Consider differences of the pathogen (e.g. *E. coli* vs. *S. aureus*)
  - Differential gene expression follows a gradient...
  - **Important:** Sample every compartment of the mammary gland!!!

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networking is the key---

Thanks to...

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