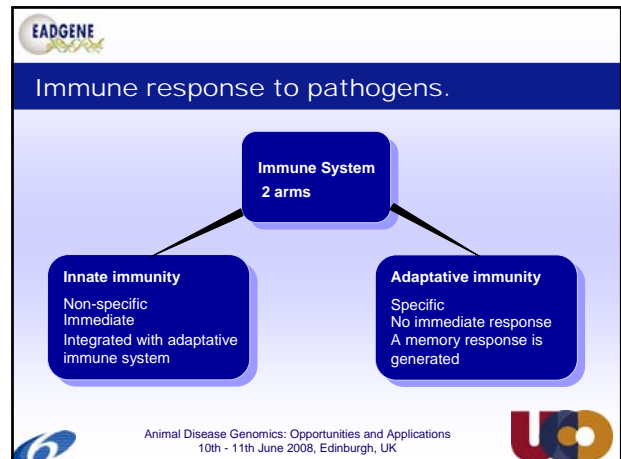


EADGENE European Animal Disease Genomics Network of Excellence for Animal Health and Food Safety

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 10th - 11th June 2008, Edinburgh, UK

Salmonella induced innate immune response in pigs
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Innate immune defense mechanisms.

- **Epithelial cell layers**, which provide a physical barrier and have bacterial killing capacity through antimicrobial substances such as defensins.
- **A diverse array of cell types**, including neutrophils, macrophages, dendritic cells and natural killer cells are important cellular components of an innate immune response.
- **Numerous soluble products**, such as cytokines, complement components and natural antibodies, are also integral parts of the innate immune system.

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Innate immune response to *Salmonella*.

- Intestinal epithelium is the host-bacteria surface where the innate response is initiated on oral ingestion of *Salmonella*.
- *Salmonella* interaction with epithelial cells results in a pro-inflammatory response characterized by the release of several cytokines and chemokines.
- Cytokines lead to the next wave of the innate immune response: cell recruitment and activation.

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Innate immune response in pigs.

- To identify host genes which control innate immune responses to *Salmonella*.
- To understand the coordinated function of the cells in innate response to infection.

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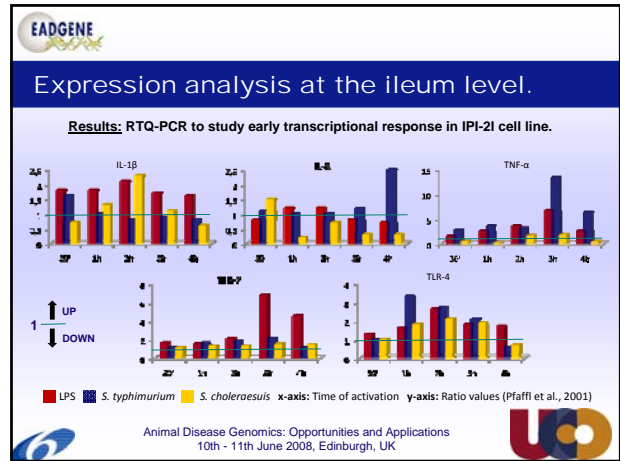
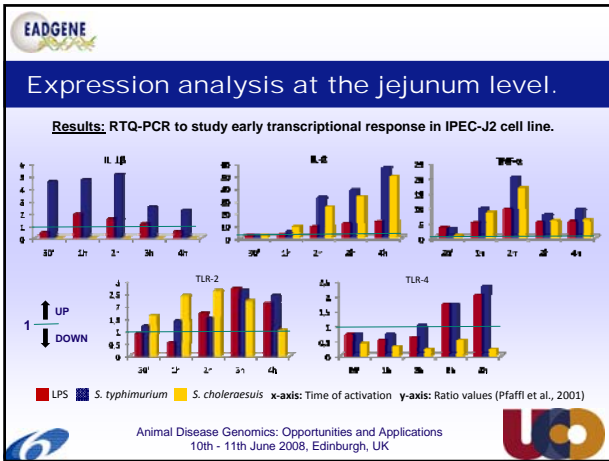
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Intestinal epithelium point of view.

Response to *Salmonella* in porcine intestinal epithelium

- > Pathogenic agent.
 - LPS.
 - *Salmonella* serovar choleraesuis.
 - *Salmonella* serovar typhimurium.
- > In vitro approach.
 - Analysis of gene expression using porcine epithelial cell lines at earlier time-points.
 - Two porcine intestinal epithelial cell lines.
 - IPEC-J2: Jejunal epithelial cell line.
 - IPI-2I: Epithelial cell line from ileum.
- > In vivo approach.
 - Global expression of proteins in healthy and natural infected (*Salmonella*) animals.

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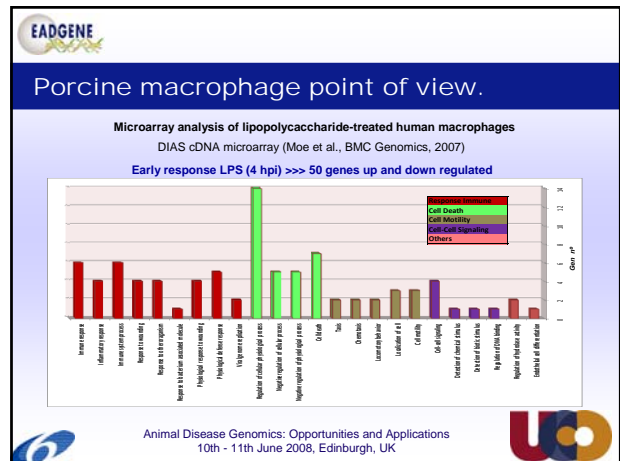
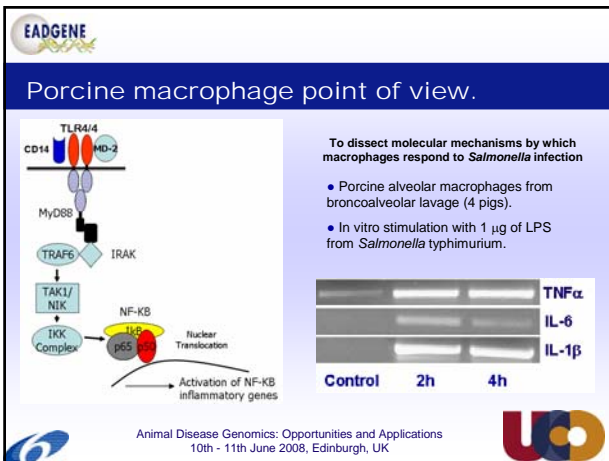
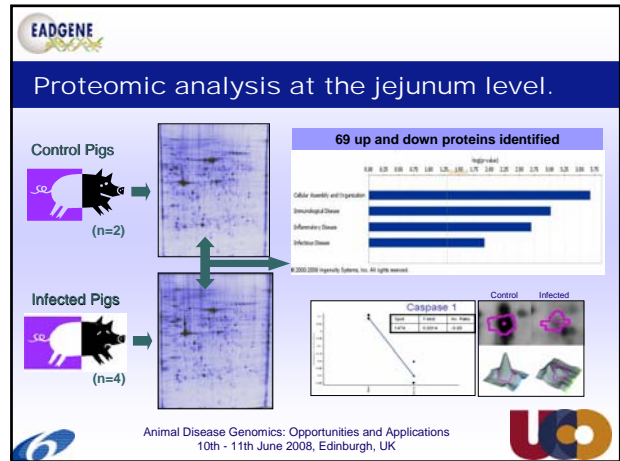


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Intestinal epithelial cell lines. Conclusions

- The porcine intestinal epithelium has the necessary immune repertoires required to achieve a robust defense against *Salmonella*.
- Different serovars of *Salmonella* elicited differing patterns of activation in vitro.
- In comparison to *S. typhimurium*, the response to *S. choleraesuis*, a pig-adapted bacteria, was less intense.

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Porcine macrophage point of view.


Microarray analysis of lipopolysaccharide-treated human macrophages
 DIAS cDNA microarray (Moe et al., BMC Genomics, 2007)

Early response LPS (4 hpi) >>> 50 genes up and down regulated

GO Systems (p-value<0.01)	Gene /Function
INNATE IMMUNITY	↑ <i>MIP1β</i> / inflammatory mediator
	↑ <i>TNFα/PS</i> / inflammatory mediator
	↑ <i>MCP1</i> / recruitment of immune cells (monocytes)
	↑ <i>IL1β</i> / recruitment of immune cells (neutrophils/M ϕ)
CELL DEATH	↑ <i>AP5</i> / apoptosis inhibitor
	↓ <i>HSP70</i> / apoptosis enhancer
	↓ <i>TGFβ2</i> / proapoptotic activity protein

Data are consistent with LPS activating a survival pathway in macrophages

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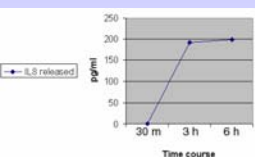



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Porcine neutrophil point of view.

To dissect molecular mechanisms by which neutrophils respond to *Salmonella* infection

- Porcine neutrophils from peripheral blood (4 pigs).
- In vitro stimulation with 1 μ g of LPS from *Salmonella typhimurium*.

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Summary.

- In response to *Salmonella*, intestinal epithelial and fagocitic cells actively modify several classes of genes and proteins involved in innate immunity. Microarray and proteomic are useful tools to characterize the response of these cells to stimuli.
- In addition to the well-known regulation of cytokine and chemokine expression, the exposure to infectious agents may regulate a number of genes and proteins involved in the inhibition of the apoptosis and the maintaining of the cell viability at the infection site.

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