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Macrophages and dendritic cells have distinct transcriptome profiles during early infection with *Salmonella enterica* serovar Typhimurium





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SALMONELLOSIS

- zoonotic pathogen
- bovine and human disease similar
- DT104 – antibiotic resistant strain
- vaccine not that efficient
- most of studies done in mice – relevance?

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HYPOTHESIS


Salmonella may use different internalisation and survival strategies in DC and M Φ

AIMS OF THE PROJECT


- innate immunity – cattle
 - macrophages and dendritic cells
- functional genomics approach

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EXPERIMENT DESIGN



6 biological replicates




DC




M Φ

Infection with *S. Typhimurium* 2h at MOI50 (killed and live)



RNA

→ amplification →




aRNA

↓

Affymetrix GeneChips® Array (36)


↓

PLIER



Raw image

→



Normalised image

• statistical analysis ANOVA, t-test

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DIFFERENTIALY EXPRESSED GENES

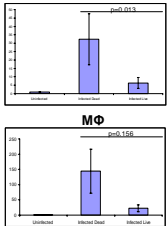
Striking differences between DC and M Φ response

Cell type	Comparison	↑ genes	↓ genes
M Φ	Noninf. vs killed	110	5
	Noninf. vs live	140	71
DC	Noninf. vs killed	32	1
	Noninf. vs live	5	0

FDR ≤ 0.05

MEFV

Novel link

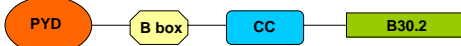


- MEFV is upregulated upon *Salmonella* infection
- Higher upregulation of MEFV after stimulation with **killed** bacteria


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MEFV (Mediterranean fever) = PYRIN

- Mutations in this gene are associated with **Mediterranean fever** –
 - a hereditary periodic fever syndrome
 - autoinflammatory disorder
 - short recurrent bouts of fever
 - 50 mutations have been identified
- This gene encodes a protein that is a modulator of innate immunity
- Expressed in neutrophils, eosinophils, monocytes, DC and M Φ



PYD domain also in NOD Like Receptors (NODs)






CONCLUSIONS

- MΦ and DC differ in the resting state
- Different response of MΦ and DC to *Salmonella*
- Some of the genes overlap between the treatments
- *Salmonella* upregulates expression of Pypin
- **NOVEL** link between Pypin and *Salmonella*

FUTURE PERSPECTIVES

Functional analysis of Pypin



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