

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

OspG a versatile type III effector protein
From genomic to cellular microbiology
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Enterohemorrhagic *E. coli* (EHEC) : a major foodborne pathogen

The reservoir of EHEC is cattle and other ruminants

Worldwide outbreaks
USA 1982
France 1992
Scotland 1996
Germany 1996
Japan 1996
etc..

Major EHEC serogroup: O157, O111, O103, O26

Shiga-toxin + type III effector proteins

Systemic circulation

Hemorrhagic colitis

Hemolytic and Uremic Syndrome (HUS)

Kaper et al. 2004

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A genomic approach of EHEC virulence

Non pathogenic *E. coli* K-12 (4.6 Mb) vs EHEC O157 Sakai (5.5 Mb)

O157-specific regions (Sp3 to Sp17)

Phage Backbone Exchangeable Effector Loci

Tobe et al. 2006

The pathogenicity of EHEC strains requires specific genes present on mobile genetic elements (phages, PAIs, plasmids...)

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The gene of a *Shigella* type III effector is present in the genome of EHEC

other effector, other gene, K12 conserved, unknown, IS, gene on IS

EHEC 11128 (O111:H-) vs *Yersinia enterocolitica* 8081 vs *Shigella flexneri* pWR100

In *Shigella*, OspG is a type III effector protein

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Type III secretion system (T3SS)

Host cell

Host cell plasma membrane, Bacterial outer membrane, Periplasmic space, Bacterial inner membrane, Outer pore, Inner pore, Outer channel, Inner channel, ATPase

Garmendia et al. 2005

Type III effector proteins are injected into the host cell by a molecular syringe

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EHEC ospG is injected into host cell via EHEC T3SS

WT vs ΔescN (ΔT3SS)

TEM vs ospG-TEM

No fluorescence vs Green fluorescence vs Blue fluorescence

Charpentier and Oswald, 2004

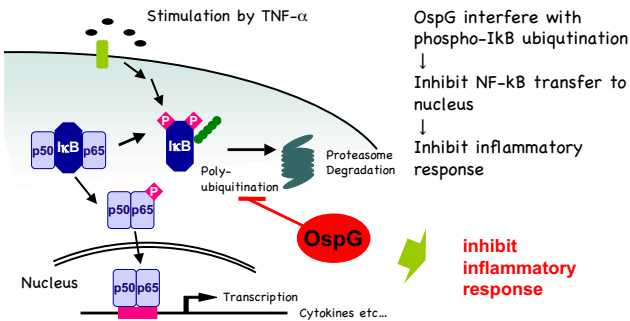
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OspG a versatile type III effector protein

Rika Nobe, INRA, France



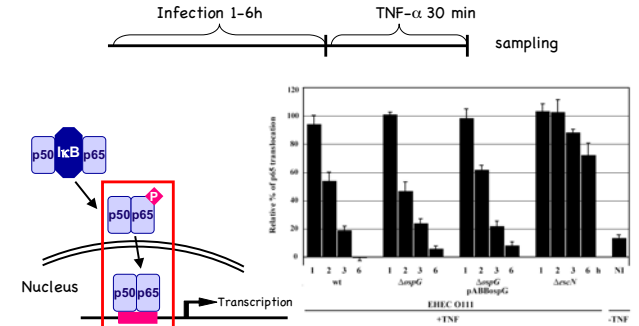
OspG reduces the inflammatory response in *Shigella* infections



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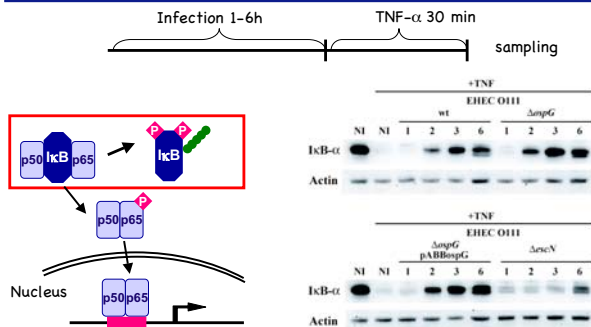
EHEC ospG is not involved in the inhibition of NF- κ B p65 transfer to nucleus



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EHEC ospG is not required to inhibit I κ B degradation

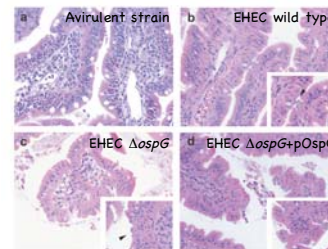


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EHEC ospG does not affect inflammatory response *in vivo*

Rabbit ileal loop experiment



- 1) some mild lesions of congestion
- 2) oedema of the submucosa
- 3) infiltration of lymphocytes and/or granulocytes in all layers of the wall, more especially in the mucosa and submucosa

Inflammatory lesions of similar intensity were observed in all samples

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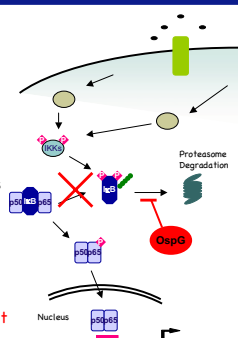
Conclusion

OspG genes are present in EHEC, *Shigella* and *Yersinia* strains. *OspG* is injected into host cells via T3SS.

Infection of host cells with EHEC O111 inhibited NF- κ B-dependent innate immune response via a T3SS-dependant mechanism.

However, an *ospG* mutant of EHEC O111 is still able to inhibit NF- κ B p65 transfer to nucleus in infected human cells and no difference in the inflammatory response was observed between wild-type EHEC O111 and the isogenic *ospG* mutant in the rabbit model.

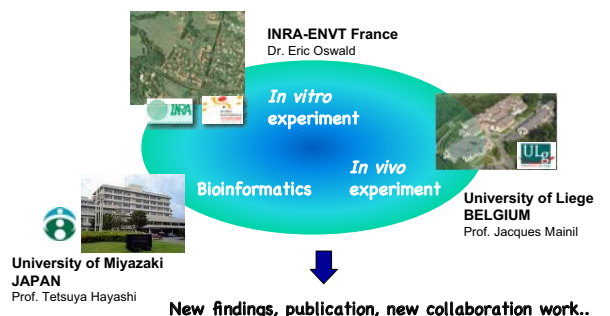
Another EHEC T3SS effector inhibits the NF- κ B signaling pathway.
 What is the role of *OspG* when EHEC strains infect the human gut?



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Collaboration



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