

# Towards a Systems Biology Approach: Comparative studies of *Salmonella enterica* serotype Newport strains from the US and the UK to understand the emergence of multi-drug resistant (MDR) strains

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## Background:

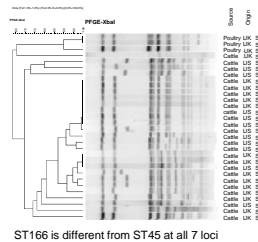
### US MDR S. Newport

- Rapidly became epidemic in North America
- Caused serious diseases in animals and people
- Restricted treatment options as they are resistant to 7-13 antimicrobial agents, esp. carry the resistance to the 3<sup>rd</sup> generation of cephalosporins mediated by *bla*<sub>cmv-2</sub>

### UK S. Newport

- Cause mild disease
- MDR strains were only found in poultry
- Not resistant to the 3rd generation of cephalosporins

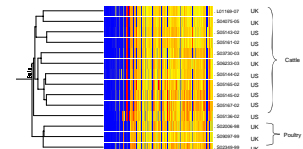
## PFGE and MLST Typing



ST166 is different from ST45 at all 7 loci

- The UK poultry isolates are evolutionarily distinct from the cattle isolates
- The UK and US cattle isolates have the same evolutionary origin based on the MLST results
- Some UK and US cattle isolates are indistinguishable by PFGE

## Comparative genomic hybridisation



Orange or yellow indicates a gene is present. Blue indicates a gene is absent. Grey or different shades of green indicate divergent or partial identity

- Extra phage-related elements were identified in the US strains by CGH Microarray
- Phage related elements were also identified in the US strains by DART (diversity array)
- Pertussis-like (*artAB*) toxin genes were found in the US MDR strains by DART

## Optical Genome Mapping



Cells gently lysed to release genomic DNA



DNA captured in parallel arrays of long single DNA molecules using a microfluidic device

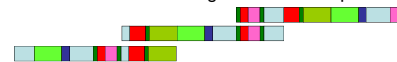


Restriction enzymes cleave the DNA at specific sites

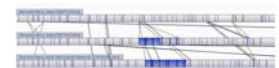
Gaps in the DNA indicate location of cut sites



The DNA is stained with fluorescent dye and image analysis measures the size and order of each fragment to create "Single Molecule Maps".

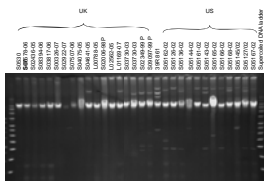


Overlapping single molecule maps are aligned to produce a map assembly covering an entire chromosome.



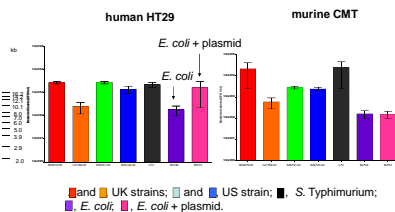
- Figure showing region of Gifsy-2 phage present in US wild type strain and US sequenced strain (lower two maps) but absent in UK strain (top map).
- Genes *sodC*, *pepN*, *pyrD*, *fabA*, *mgsA*, *ompA* and *yccS* in US strains only and may contribute to the virulence

## Plasmid profiling



The MDR S. Newport strains contain more plasmids

## Invasion study

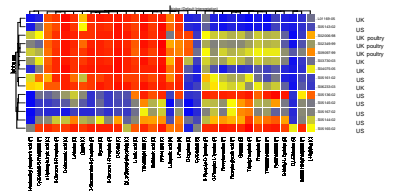


- The invasiveness of the UK and US strains were comparable to S. Typhimurium
- The MDR large plasmid may have increased the invasiveness of the *E. coli* strain.

## Phenotypic Microarray



Can measure about ~2000 metabolic properties



The colour spectrum in this figure represents the respiratory activities generated by each compound where the maximum value was set at 300 (red), middle point at 150 (yellow) and minimal at 0 (blue). Un-labelled strains were all from cattle.

- Only poultry strains can use D-tagatose
- Metabolic differences among the UK strains were relatively small
- There are considerable metabolic differences among the MDR US Newport strains suggesting rapid evolution of the MDR US S. Newport

## Summary:

- S. Newport are polyphyletic and cannot be treated as one group
- The UK and US cattle isolates have the same evolutionary origin and some are genetically similar
- The MDR US strains carry a large MDR plasmid and extra phage elements, and may harbour extra virulence genes
- The MDR strains are genetically and metabolically diverse and rapidly evolving.

## Acknowledgements:

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