


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



Systems Biology: Glycomics of *Campylobacter jejuni*
 Emily Kay

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Talk Outline

- Introduction to project
- Data sources
- Modelling approaches
- Summary

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What is systems biology?

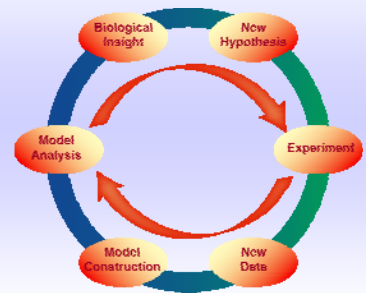
- Systems biology
 - Systems biology is the study of an organism, viewed as an *integrated and interacting network* of genes, proteins and biochemical reactions
 - Currently have a vast amount of 'omics data
 - Genomes
 - Transcriptome
 - Proteome
 - Metabolome
 - Data-rich but information poor

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Systems Biology: An iterative process



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Campylobacter jejuni

- Organism
 - Gram negative, spiral rod-shaped, microaerophilic bacteria
 - Colonize avians
- Disease
 - Leading cause of bacterial diarrhoeal disease
 - Associated with neuropathies (Guillain-Barré syndrome)
 - Transmission often through consumption/handling of contaminated poultry products

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***Campylobacter* resources in post-genome era**

- Small tractable genome (~1600 genes)
- Significant strain variation to infer biologically relevant questions
- Whole genome data from 11 *C. jejuni* strains (5 published)
- Fully annotated and re-annotated genomes (Gundogdu, 2007)
- Access to pan-species *C. jejuni* microarrays including high density arrays for ChIP analysis (<http://www.bugs.sgu.ac.uk>)
- The most comprehensive protein-protein interaction map (Parrish *et al.*, 2007)
- Glycan specific metabolomics data (Soo *et al.*, 2006)
- A bank of over 400 DNA-tagged mutants (<http://www.lshtm.ac.uk/pmbu/crf>)
- Capability for genetic analysis including reporter gene and complementation "tool boxes" (Karlyshev and Wren, 2005)

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Some unanswered *Campylobacter* questions

- Why aren't all *C. jejuni* strains equally pathogenic to humans? What would make a strain avirulent or hypervirulent?
- What makes isolates from various sources (eg chicken, cow, pig, water, human) different?
- Why is *C. jejuni* a commensal in avians, but highly infectious in humans?
- How does *C. jejuni* in some cases perturb the immune system to cause neurological sequelae?
- Answers are likely to lie in glyco-surface structures

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Can systems biology help?

- Can we infer surface structures from genetic data?
- How are glyco-structures synthesised, regulated and modified?
- Can we predict how alterations in surface glycans modify interactions with host cells?

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The 4 *Campylobacter* glycostructures (CLON)

Kelly J, 2006

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Glycostructure questions

- How do we get from sequence to sugar nucleotides?
- How do we get from sugar nucleotides to glycan backbone and full glycan structures?
- How are these regulated?
- How does CLON diversity affect disease potential?

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C. jejuni capsule

- Start with capsule
- Significant strain variation
- Sequences from 11 different strains
- Capsule structure known for 11168 (and others)
- Structural data from 11168 capsule knockouts (Szymanski)

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C. jejuni capsule - EM

Karlyshev et al. 2001

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Structure of capsule in *C. jejuni* 11168

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Data Sources for Modelling

- Microarray data
 - Transcript profiles from capsule mutants
 - Transcript profiles from infection mimic perturbations
 - Data from public repositories
- Metabolomic data
 - Intracellular extract profiles from capsule mutants
 - 1-D ¹H NMR (600 MHz spectrometer)
 - Additionally 2D NMR (800 MHz spectrometer) & UPLC-MS
- Protein-protein interaction data
 - Parrish *et al.* 2007 - <http://proteome.wayne.edu/CampyDescription.html>
- Biochemical network for glycosylation
 - KEGG: www.genome.jp
 - BioCyc: www.biocyc.org
 - Literature

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Modelling objectives

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Modelling approach

- Inductive Logic Programming
 - Given
 - Background knowledge (B): Prolog initial model of network and
 - Empirical observations (E): Microarray data and Metabolomic data
 - Generates
 - Logical hypotheses (H) for missing structures consistent with B and E above.

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Applications of ILP

Source: University of Wales, Aberystwyth

King *et al.*
 Functional genomic hypothesis generation and experimentation by a robot scientist.
Nature. 2004 Jan 15;427(6971):247-52

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Data incorporation

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