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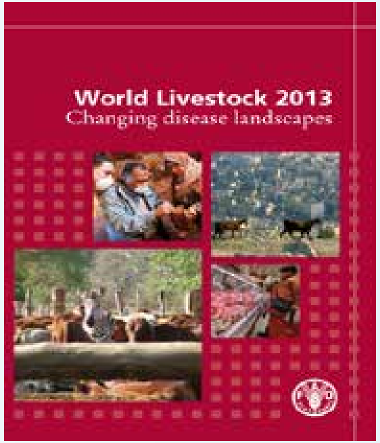
ANIMAL HEALTH: The potential of molecular biotechnology to improve disease control

Prof Robin Skuce

Why is animal health important?

- Globally - by 2030 we need 50% more food (FAO)
- Industry driving to improve efficiency and productivity
- Livestock diseases reduce efficiency of animal production by 20% (FAO/OIE)
- Significant economic and animal welfare impact
- An animal health problem is a production problem


World Livestock 2013
Changing disease landscapes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GOING FOR
GROWTH

Challenges in disease control

- AFBI key role
- **Epizootic risk** – introduction – emergency response capability
  - HPAI, BTV8, FMD etc
- **New and emerging risks**
  - "New" pathogens - especially viruses
    - Schmallenberg, PMWS (PCV2)
  - 60% of all known pathogens and 75% of emerging pathogens are zoonotic in nature
  - Pathogens with increased "virulence", recombination, jumping species etc

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Challenges in disease control

- **Public health and food safety**
  - One Health - Antimicrobial resistant (AMR) bacteria
    - *"…global action is needed to tackle the catastrophic effect of antimicrobial resistance, which in 20 years could see any one of us dying following minor surgery"*
      - CMO Annual Report 2011
- Climate change and changing vector patterns allowing disease introduction and spread
- **Endemic disease**
  - Bovine TB
    - £317M in 15 years NI

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Molecular biology - DNA

- The heritable genetic code of life – written in chemical letters
  - Specifies the traits of animals, microorganisms etc
- Revolutionary new discipline – **molecular biology**
- **How AFBI deploys these technologies**
- Future potential - **genomics** and bioinformatics (data)
  - The genome – the genetic code of an animal or microbe etc

FMD virus genome	8.5 thousand letters
TB bacterium genome	4.4 million letters
Cow genome	3 billion letters

Drivers - enabling technologies

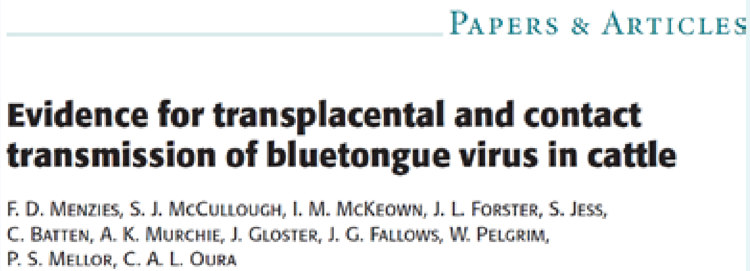
- **DNA sequencing**
  - Reading the genetic code of animals and pathogens
  - Very labour-intensive and expensive…
- **Game-changer – ‘next-generation’ DNA sequencing**
  - Facilitates whole-genome sequencing (WGS) of animals and pathogens
  - Facilitates high-density and high-throughput genotyping of animals and pathogens
- **DNA amplification**
  - Extremely sensitive and specific detection
- Transforming how we do microbiology and genetics

Applications:
Virus detection, characterisation and tracking

- Classical virology
- Revolutionised by molecular biology
- PCR now key AFBI technology
    - Detect important viral pathogens - HPAI, BTV etc
    - Partial sequence to characterise AI – H1N1, H5N8 etc
    - Animal health schemes – BVD
- Rapid global sharing of epidemiological, clinical, geographic data eg GISAID

Initial incursion of pandemic (H1N1) 2009 influenza A virus into European pigs

M. D. Welsh, P. M. Baird, M. P. Guelbenzu-Gonzalo, A. Hanna, S. M. Reid, S. Essen, C. Russell, S. Thomas, L. Barrass, F. McNeilly, J. McKillen, D. Todd, V. Harkin, S. McDowell, B. Choudhury, R. M. Irvine, J. Borobia, J. Grant, I. H. Brown



Papers & Articles

Evidence for transplacental and contact transmission of bluetongue virus in cattle

F. D. Menzies, S. J. McCullough, I. M. McKeown, J. L. Forster, S. Jess, C. Batten, A. K. Murchie, J. Gloster, J. G. Fallows, W. Pelgrim, P. S. Mellor, C. A. L. Oura

Genomics and virus discovery

- Classical virus discovery methods
- NGS is entirely changing the field of virus discovery
  - Unidentified cattle disease in Germany and Netherlands 2011
  - NGS clinical samples - Schmallenberg virus
  - Isolated from blood of affected animals
  - Rapidly developed novel tests and diagnostics

- NGS increasingly utilised as part of horizon scanning for the emergence of new virus threats
- Non-selective NGS for virus discovery

Schmallenberg Virus: First case in Northern Ireland confirmed

31 October 2012 | Northern Ireland

Animal vaccines

- Continue to have major impact on animal health
- Classical approach
  - Specialist virus isolation, inactivation or attenuation
- **2 world-leading AFBI successes by this approach**
  - *Circovac* – global sales ~$3bn
  - Salmon pancreas disease virus - multi-million vaccine doses annually
- Genomics – attenuation?
- Genome sequence comparison enables
  - Sub-unit vaccines
  - Reverse genetics - rationally-attenuated vaccines
  - Potential multi-valent, chimaeric vaccines
  - DIVA vaccine strategies
  - Marked vaccines

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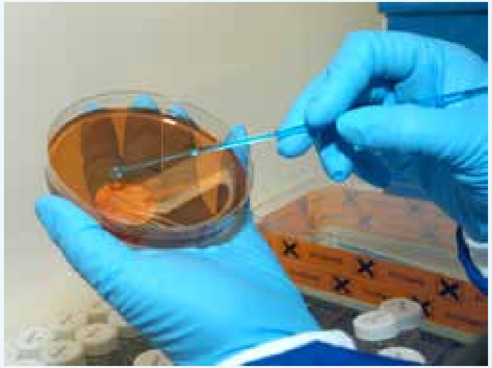
Pathogenic bacteria

- Currently, isolate bacteria on specialised media – phenotyping
  - Time consuming, labour intensive and expensive, challenging in inter-laboratory comparisons
- From phenotyping to genotyping
  - TB confirmation includes a molecular test
- Bacterial WGS has the potential to replace such tests
- Detection can be specific/selective or non-selective
- Output data are digital, portable and can be compared against international databases



Genomics and AMR

- AMR bacteria could kill 10 million people a year by 2050 - at a potential cost of £790bn
    - UK O’Neill Report 2016

- Currently concerned about:
    - LA-MRSA, mono-phasic *S. Typhimurium*, ESBL *E. coli*, other MDR *S. enteriditis* with high impact in public health
- Pathogen WGS – identity, susceptibility and AMR mutations
- International efforts to index AMR mutations by WGS
- ‘Meta-genomics’ and comparative genomics could help identify the next generation of antibiotics and antimicrobials

Molecular typing – bovine TB

- AFBI genome-enabled tools to investigate TB evolution, epidemiology and outbreaks
- Deep ancestry shows UK and Ireland dominated by their own TB strain family (EU1)
- TB strains - striking local geographical clustering
  - **Locally-driven epidemic: a series of local micro-epidemics**
  - Valuable for tracing locally, nationally and internationally
- Cattle and badger TB strains associated at regional level
- Lacking direct genetic evidence of transmission chains linking cattle and badgers at farm scale

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Pathogen WGS – bovine TB

- **Genomic epidemiology** – target one strain
  - Molecular typing, **bacterial WGS** and mathematical modelling (Glasgow)
  - ***"First direct evidence of <u>ongoing</u> TB transmission between cattle and badgers at the individual farm level"***
  - **Also signals of cattle-cattle spread (amplification) within some study herds**
- AFBI research providing insights into disease transmission dynamics which were previously unattainable

Genomics – cattle resistance to bovine TB

- Parallel genetics studies identified heritable genetic variation in risk of TB – exploitable via **selective breeding**
- Industry-led national genetic and genomic evaluations (EBVs) for TB resistance in dairy cows (SRUC and *AHDBDAIRY)*
- ***<u>TB Advantage</u>***: new genetic selection trait launched January 2016 – a world first
- NI data being included in EBV estimates. AFBI key role

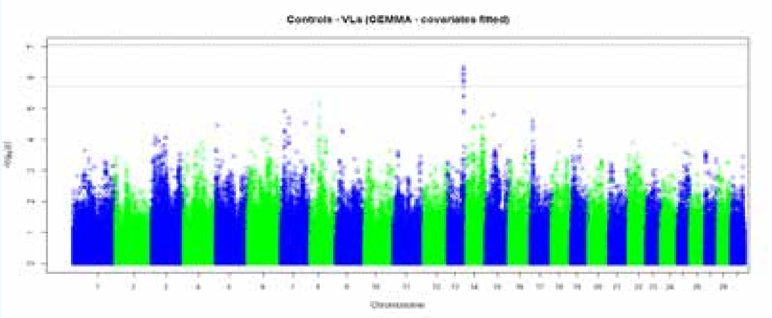
PROCEEDINGS OF THE ROYAL SOCIETY B BIOLOGICAL SCIENCES

Bovine tuberculosis: the genetic basis of host susceptibility

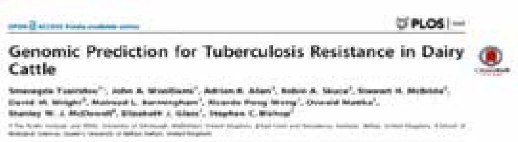
A. R. Allen, G. Minozzi, E. J. Glass, R. A. Skuce, S. W. J. McDowell, J. A. Woolliams and S. C. Bishop

Proc. R. Soc. B 2010 **277**, 2737-2745 first published online 2 June 2010
doi: 10.1098/rspb.2010.0830

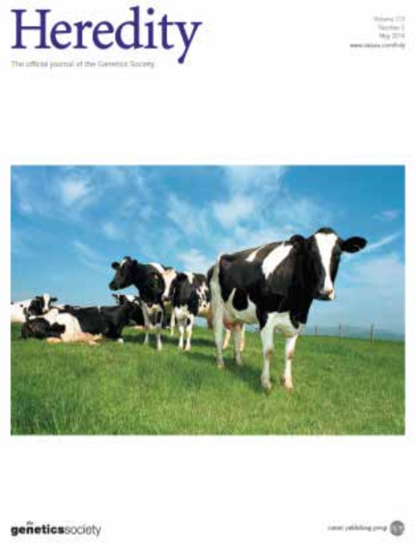
Genomics – cattle resistance to bovine TB



- NI case-control genetic association study estimated heritability of **0.23**
- Mapped genetic variants associated with TB disease trait
- Demonstrated that **genomic prediction/selection** was feasible for the TB resistance trait


PLOS

Genomic Prediction for Tuberculosis Resistance in Dairy Cattle



- Disease genetics in the future?
  - Only some diseases amenable
  - Exciting new opportunities to exploit genetic variation in new traits

Key points

- Advances in ‘Ag-bio’ science allow AFBI to undertake things that were inconceivable just a few years ago
- New tools and evidence-based approaches allow AFBI to help solve some of society’s biggest real-world problems
- DNA technology is revolutionising human medicine – personalised medicine agenda
- Similar advances already rapidly changing the way AFBI diagnoses and understands animal disease
- AFBI contributing to improved and more sustainable control of infectious diseases in livestock - supporting local food production and livestock trade

Building on our inheritance
Genomic technology in healthcare

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