NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

Whole Genome Sequencing – Science going Global

The next global machine:
The Global Microbial Identifier: GMI

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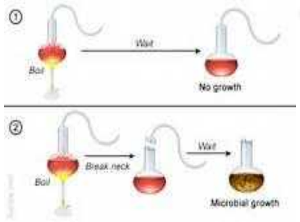
Whole Genome Sequencing (WGS) - The next Milestone

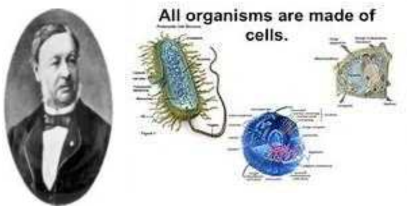
Leeuwenhook 1676 Bacteria/Microscopy



Pasteur 1861 Proves Germ Theory

Invents pure culture technique ***(+ Koch)***

2005 Next Generation Sequencing (NGS) of microorganisms



Schwann 1839 Cell Theory

Fleming 1928 Discovers Antibiotics

NOTEWORTHY MILESTONES IN MICROBIOLOGY

Finally

We are getting to

The Blueprint

Of Life

"There is a pathway from good science to publication to evidence, and to programs that work. In this way research becomes an inherent part of problem-solving and policy implementation"

Julio Frenk

Former Mexican Minister of Health

Former Assistant Director General WHO

Dean, Harvard School of Public Health

At a time of growing protectionism it is more important than ever to reassert the value of sharing scientific data.

Since scientific evidence grows out of shared data, sharing DNA sequence data provides global advantage for all

– a point which needs emphasizing at a time when introversion in science and protection of industrial data could be on the rise

– *and WGS has just given us the perfect tool in microbiology*

Paradigm Shift

from Pasteur and Koch to Watson and Crick

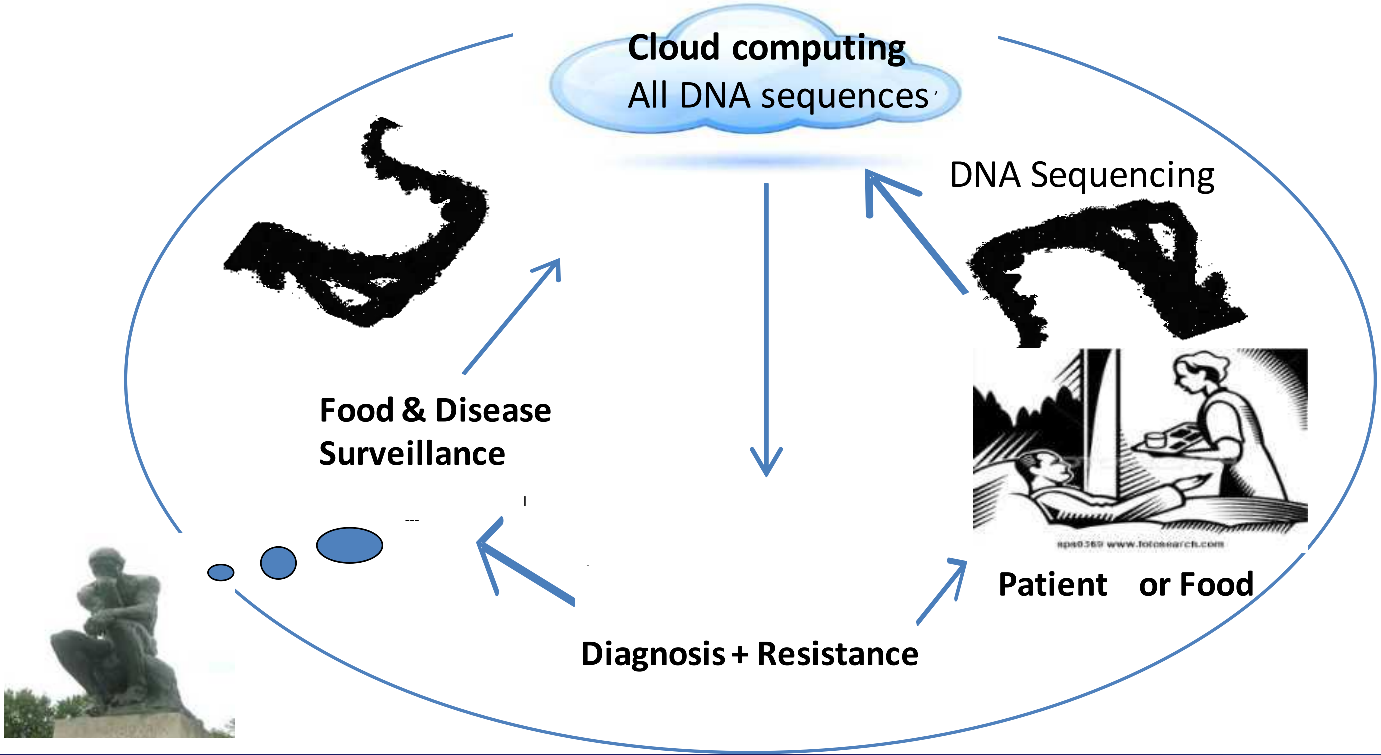
“In the future all microbiological labs will have a DNA sequencer. Whole bacterial genomes might be less than 50 EURO”

The capacity to exchange/manage large data quantities over the web now enables the creation of global databases of DNA-codes of all relevant microbiological strains”

Statement, Expert Meeting Microbiological Genomic Systems, Bruxelles (2011) – GMI 1

GMI - Global Microbial Identifier <u>the Idea</u>

1st global tool to identify all Microorganisms and Antimicrobial Resistance



<u>Global Microbial Identifier: GMI</u>

A global system enables 3 lines of action:

- Simple identification of all microorganisms through faster, cheaper, more correct characterization + antimicrobial resistance pattern

- A DNA database of all microbiological strains globally, enabling <u>real-time</u> global (*and national*) surveillance of disease and AMR

- A DNA database enabling a **<u>giant ressource for genomic knowledge</u>** about all microorganisms – global scientific collaboration

Virus Bacteria Parasites

Same – Same

www.globalmicrobialidentifier.org

GMI

Global Microbial Identifier

Moving on *each meeting approx. 100-400 participants*

"GMI" 1-4, USA & Europe 2011-12	Initiating discussions
GMI 5, Copenhagen, *Feb 2013*	Preparing a Road Map
GMI 6, California, *Sep 2013*	Agreeing a Charter
GMI 7, York UK, *Sep 2014*	Constructing an Organization
GMI 8, Beijing, *May 2015*	Moving on
GMI 9, Rome, May 2016	Including developing countries
GMI 10, Cabo San Luca, May 2017	Strengthening health involvement
GMI 11, Geneva, May 2018	Involving Governmental Entities

GMI 12, Singapore, June 12-14 2019 – preparing for global agreement

? GMI 13, ??, May 2020 – a global resolution (World Health Organization)

GMI achievements

Epidemiological metadata in NCBI using GMI/NCBI minimum epi data requirements (FDA GenomeTrakr and CDC use these fields)

Three GMI Lab Proficiency Tests assessing DNA sequencing procedures and output (support from USFDA and WHO Coll. Centre (Tech Uni DK)

Letter sent to 192 Governments (Ministries of Health and Agriculture), suggesting that these countries support international WGS discussions

NGS leap-frog potential in developing countries:

NGS-based diagnostic microbiology avoids need for specialized training and labs (testing for Salmonella and Norovirus the same)

New diagnostic systems reaching further

with real-time characterization of microorganisms
incl. Metagenomics, i.e. without culture step, just sequence
in decentralized labs w sequencers + internet

NGS enables uniform, global lab-based <u>*surveillance systems*</u>

Same-same for humans & animals - **One Health**

Bigger picture   multiple facets

Clinical – the patient will survive only if we have the sequence in our database

Clinical – metagenomic analysis for pathogen identification and AMR

Surveillance – microbial metagenomics in sewage

One Health – linking human and animal pathogens and AMR

Food Safety, outbreaks – much earlier, much more efficient

Food Safety, source attribution – which types of food are responsible for sporadic foodborne cases

Historical investigation – new understanding – new potential for prevention

Four examples   revolutionary change

1) Foodborne disease source attribution

2) Historical analysis of spread of pathogens

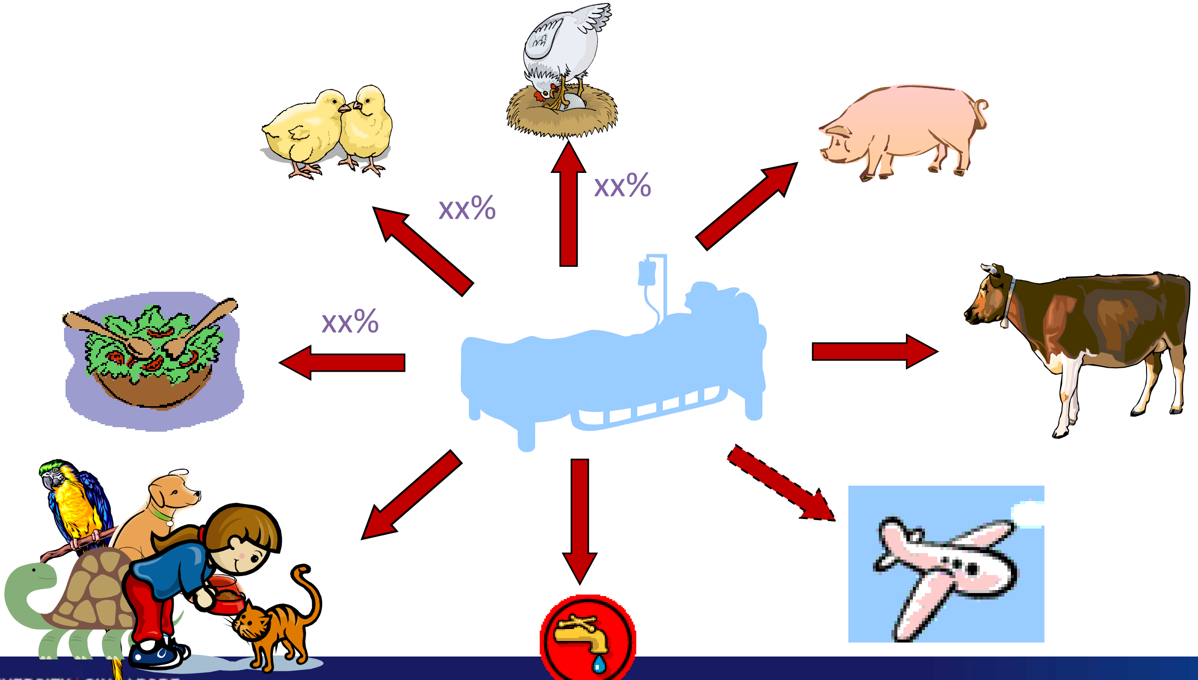
3) Metagenomic analysis and prediction of AMR

4) Positive microbiology – Revelations from the gut!

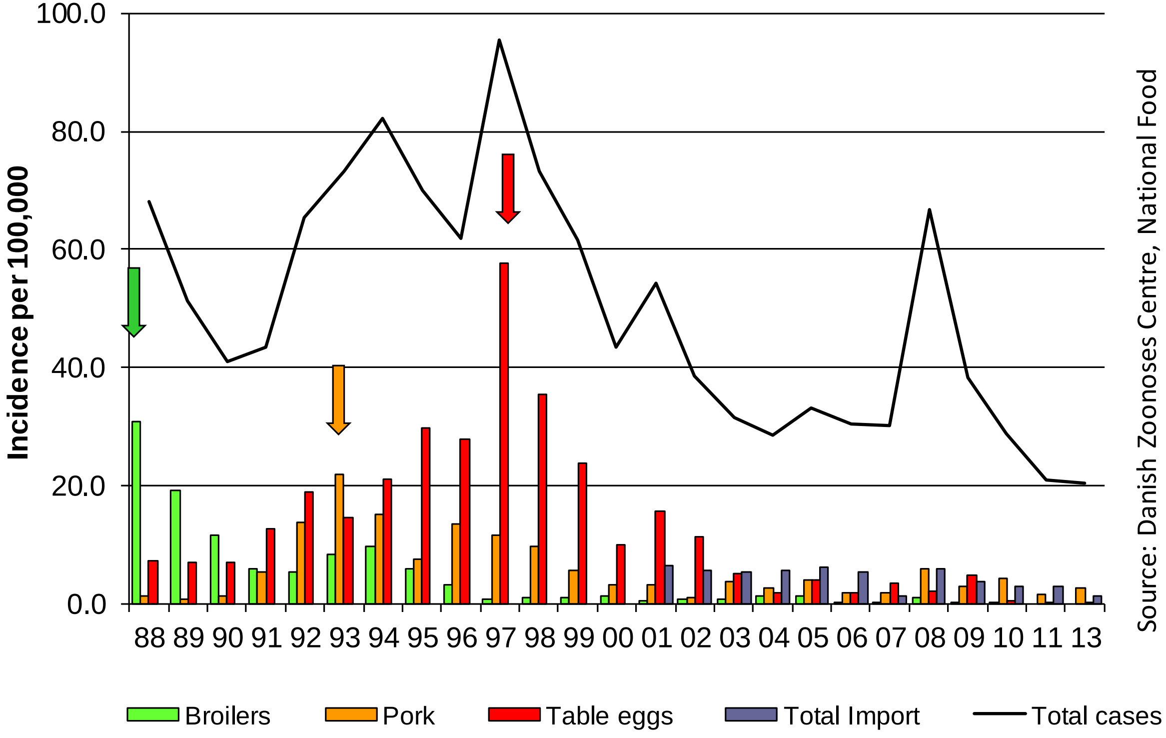
1) Linking disease and food

Before WGS: only Salmonella – After WGS: all pathogens

Source attribution - partitioning human disease burden to specific food sources (Pires et al., 2009).



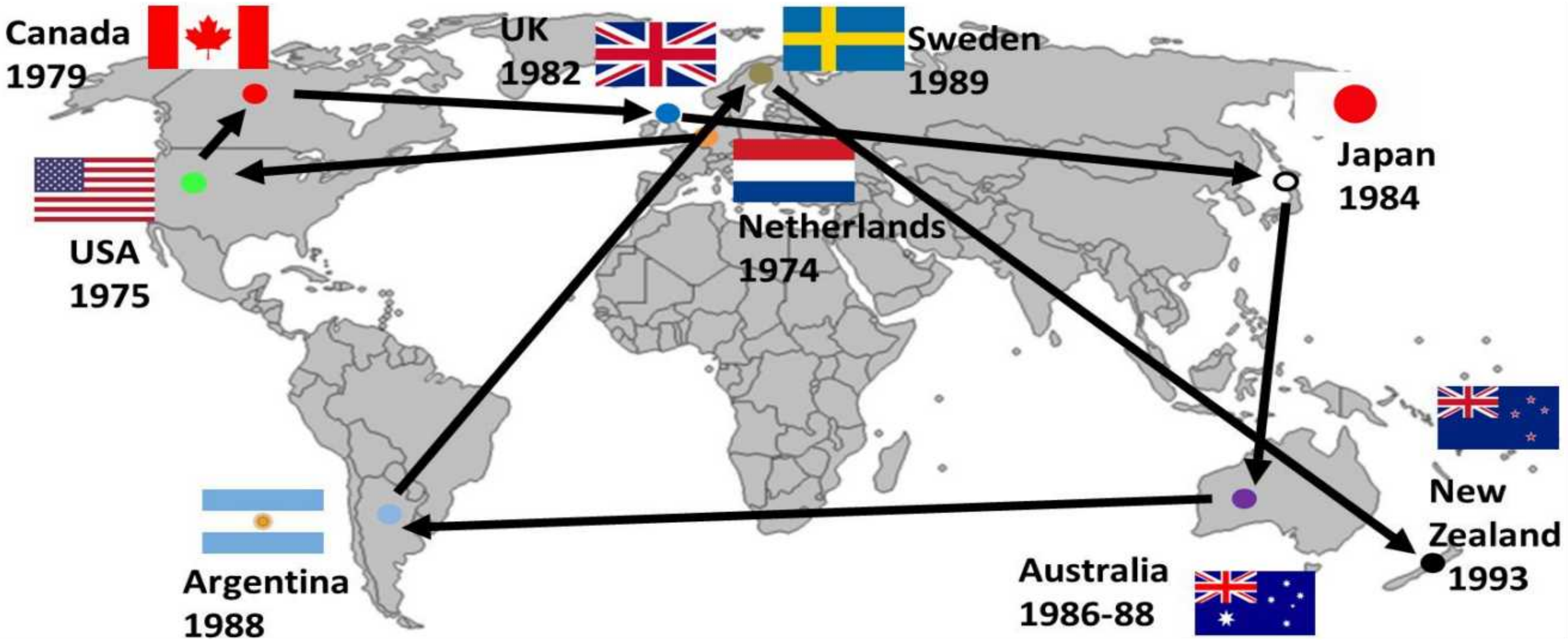
Source attribution to guide policy intervention Salmonellosis in Denmark, 1988-2013



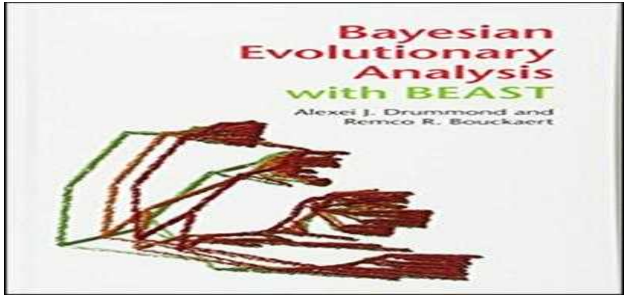
Arrows indicate implementation of sector-specific intervention

2) Brief global history of E.coli O157 infections

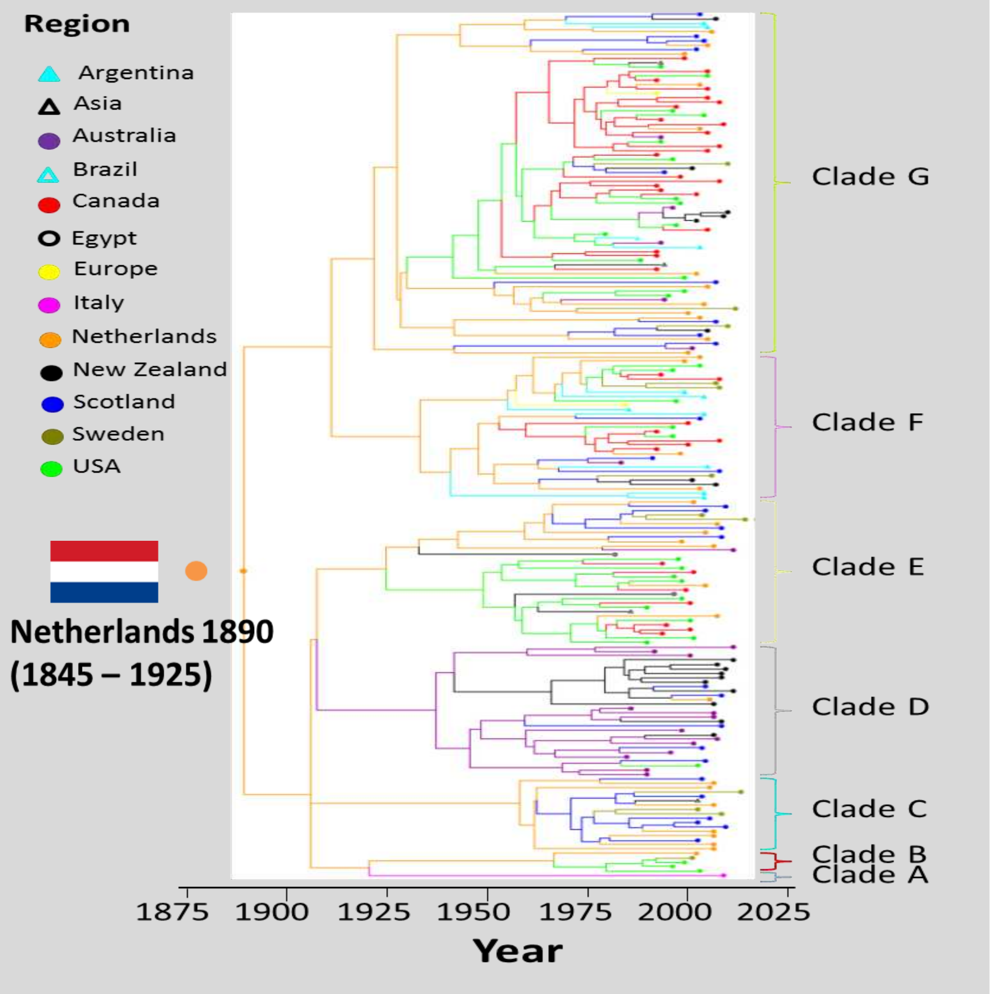
From Eelco Franz, RIVM, NL, GMI11 presentation, 2018

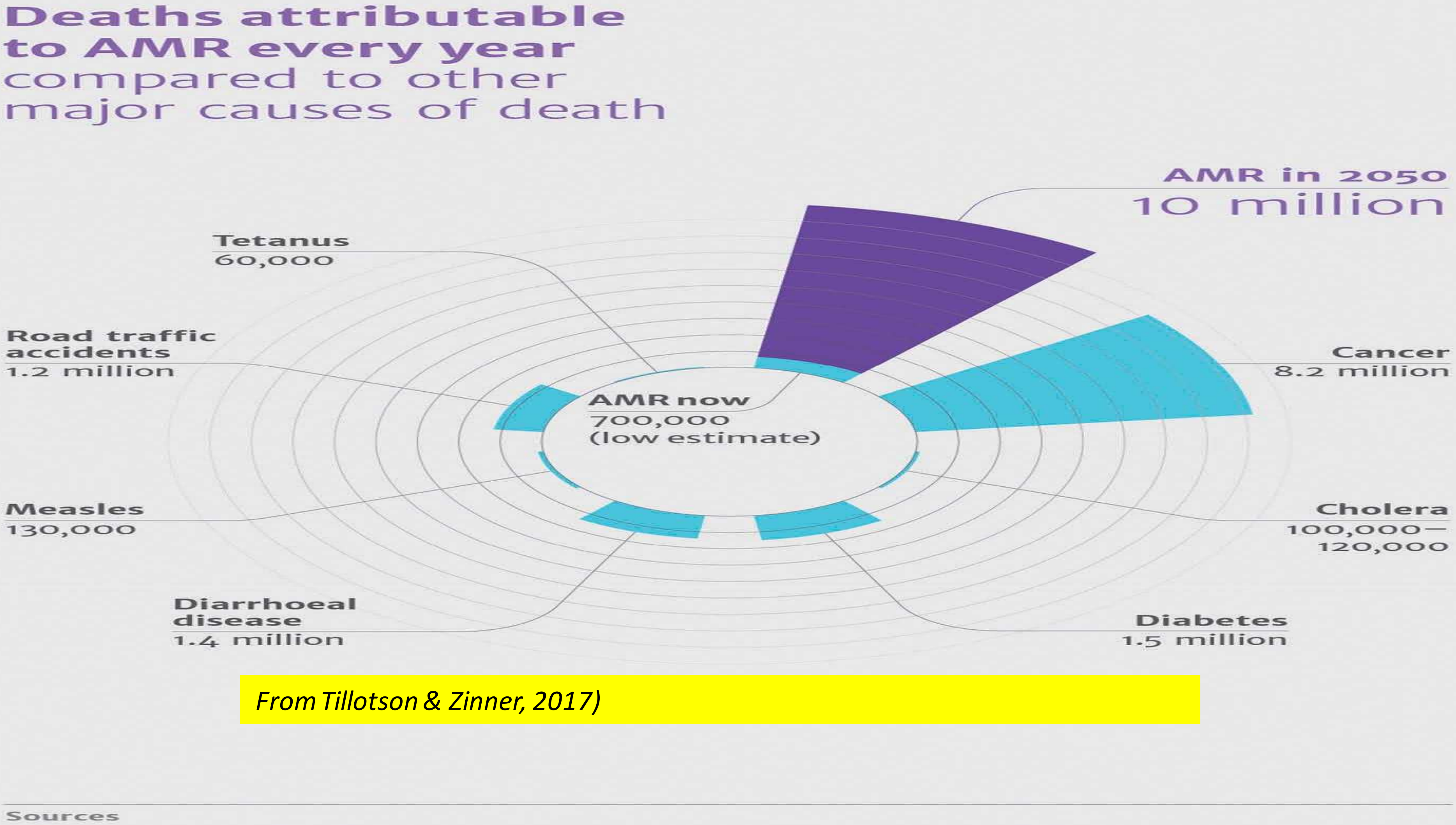


Timed phylogeny unravels emergence and spread



Common ancestor current strain set is from The Netherlands around 1890





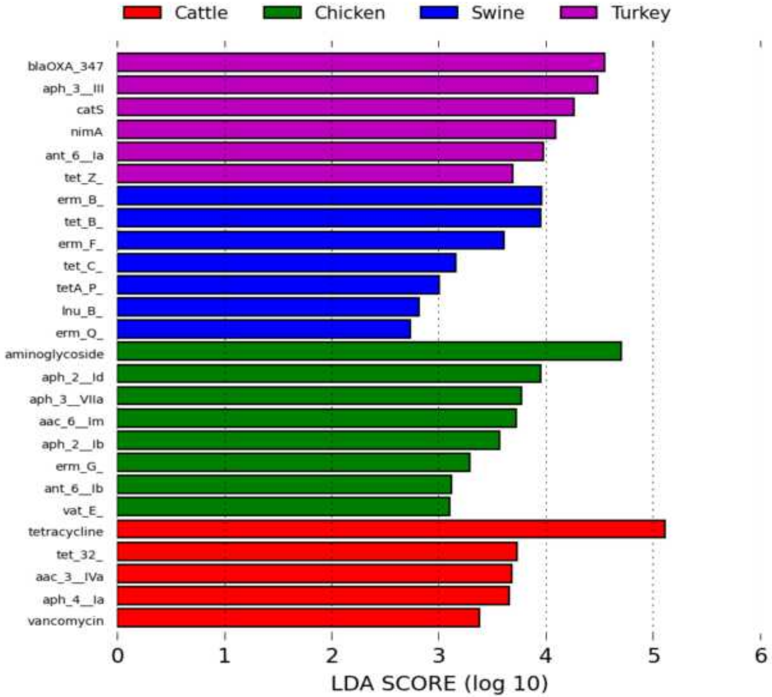
From Tillotson & Zinner, 2017)

Predicting resistance from WGS data

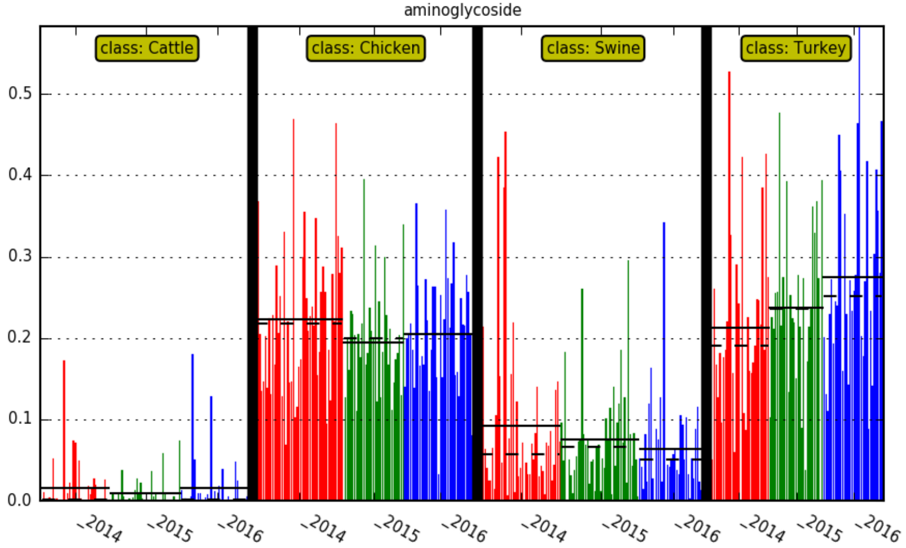
From Pat McDermott, CVM, USFDA, GMI 11, 2018

Bacterium	Gen/Phe correlation	Reference
Salmonella enterica	**99.70%**	Zankari et al., 2013, J Antimicrob Chemother
	99.00%	McDermott et al., 2016, Antimicrob Agents Chemother
Escherichia coli	**97.10%**	Stoesser et al., 2013, J Antimicrob Chemother
	98.50%	Tyson et al 2015., J Antimicrob Chemother
Campylobacter spp.	**99.20%**	Zhao et al 2015., J Antimicrob Chemother
Staphylococcus aureus	**98.80%**	Gordon et al 2014., J Antimicrob Chemother
Pneumococcus	**98.00%**	Metcalf et al 2016, Clin Microbiol Infect
Enterobacteriaceae (B-lacs)	**100.00%**	Shelburne et al, 2017 Clin Infect Dis
Mycobacterium	**95.30%**	Phelan et al 2016. Genome Med
	92.30%	Walker et al 2015. Lancet Infect Dis

Metagenomic surveillance of resistance genes by animal origin

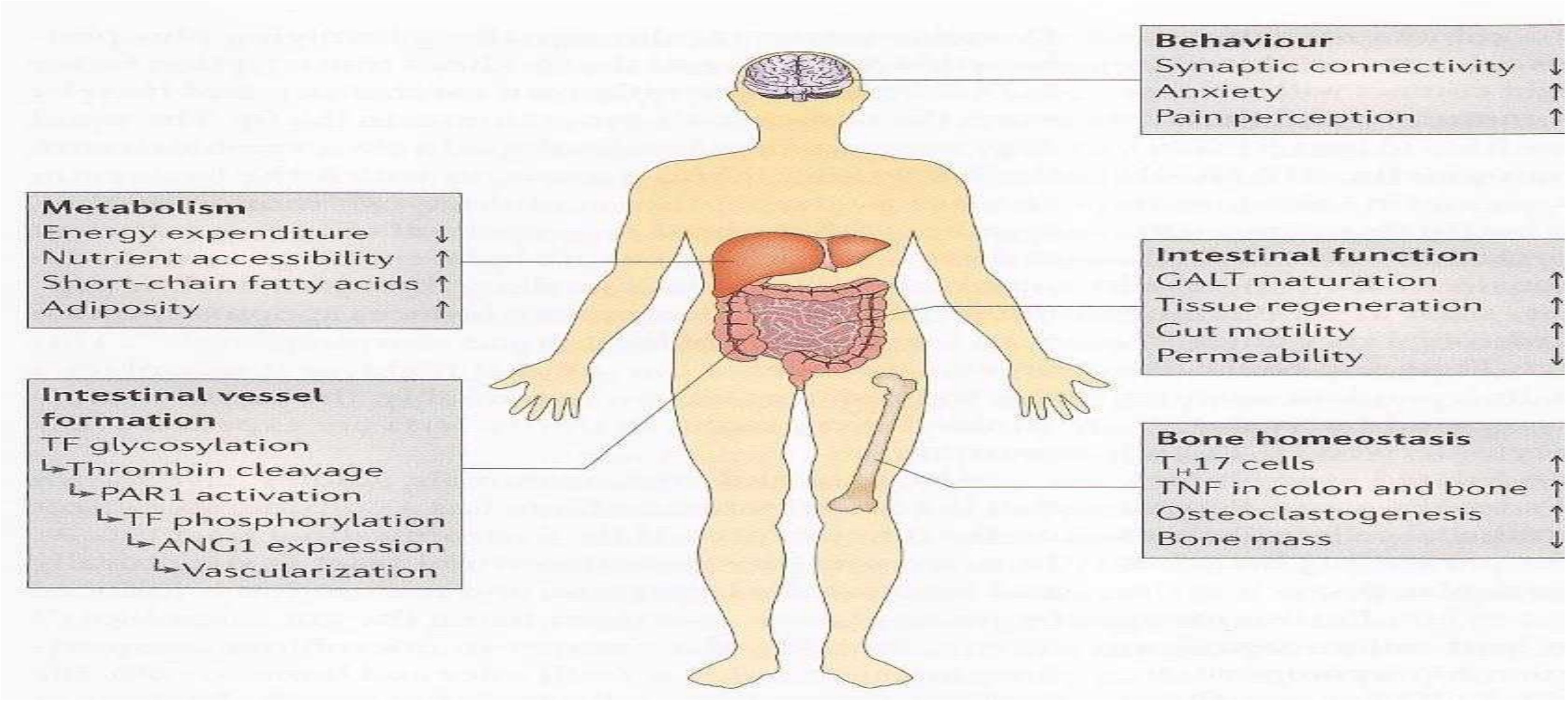


- Total cecal samples received = 20,000
- Total cecal samples DNA extracted = 16,864
- Total with completed analysis = 1,400
- Total processed by the end of 2018 = 25,000



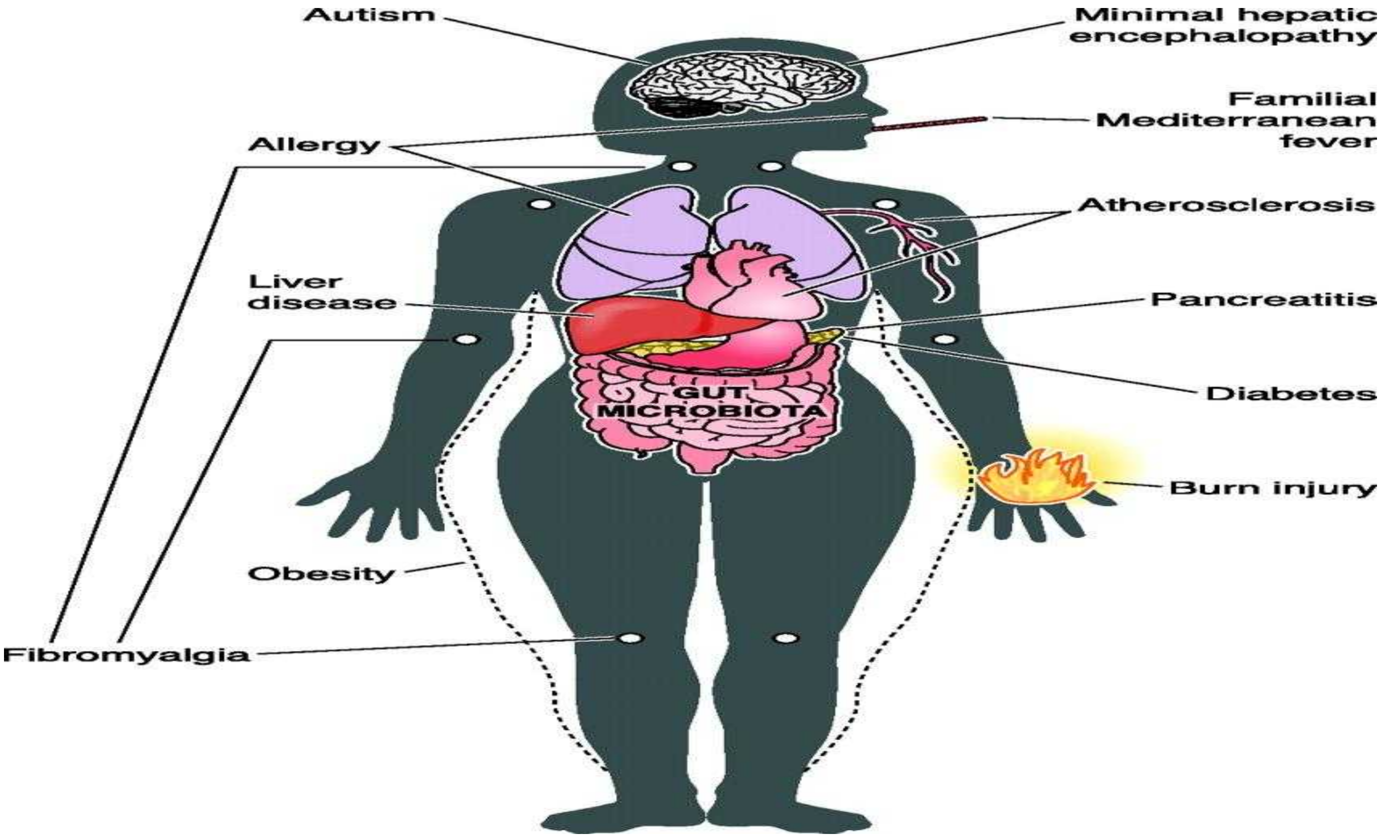
LDA: Linear Discriminant Analysis detecting resistance genes with statistically significant difference in abundance among different sources

The gut microbiota – masters of host development and physiology – investigated through NGS



Sommer and Backhed, 2013, Nature Reviews, Microbiology, 11:227

Association of gut microbiota with diseases outside of the gastrointestinal tract.



Inna Sekirov et al. Physiol Rev 2010;90:859-904

Data sharing - in my opinion a public good:

In the future sharing of NGS data will occur, no matter what

The most damage (in relation to health, but also politically) is done when data is concealed as part of a cover-up

Experience shows that (even dangerous) data always gets out

There is so much to gain (in relation to health, food safety, but also to economy) if we share data

Refusing global sharing – why?

- Concerns about national security and safety *(deliberate enhancement)*
- Concerns about international decision making overruling national decisions
- Institutional and management barriers, *including Nagoya Protocol*
- Outbreak situation, *full data not fully public - ? potential for prosecution*
- Potential misuse by others, including IP-related risks *(drugs, vaccines)*
- “My scientific publication more important than principle of sharing”

Global problems

Global solutions

– with open source datasharing

www.globalmicrobialidentifier.org

GMI

Global Microbial Identifier