Summary of highlights of all oral sessions

VTEC 2018

Florence

Flemming Scheutz, Copenhagen

Phil Tarr, St. Louis

VTEC 2018
Florence

To dare is to lose one's footing momentarily. Not to dare is to lose oneself.

Soren Kierkegaard

TOPICS

A Epidemiology
B Diagnostics, Typing & Phylogenetics
C Genetics & Virulence Factors
D Pathogenesis, Host Response and Animal Models
E Animal Reservoir & Food, Environmental Contamination & Transmission
F Prevention, control and treatment: animal and human

1. STEC Epidemiology & Risk Assessment
2. Experimental models
3. Diagnostics and typing
4. Ecology of STEC and of Stx-Phages
5. STEC Genomics
6. STEC & the agri-food chain
7. Pathogenesis and pathophysiology of STEC HUS
8. Treatment of STEC infections

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*STEC virulence genes – potential for D, BD & HUS**

Level	Trait	Potential for:
1	*stx2a* + *eae* or *aggR*	D/BD/HUS
2	*stx2d* + *eae* (O80:H2)	D/BD/HUS**
3	*stx2c* + *eae*	D/BD
4	*stx1a* + *eae*	D/BD
5	Other *stx* subtypes	D^

*Depending on other factors; eg: host, antibiotic, etc

** Depend on Stx2d variant, strain background, other factors

^ Some subtypes caused BD/HUS on rare occasions; depend on host

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*STEC virulence genes – potential for D, BD & HUS**

Level	Trait	Potential for:
1	*stx2a* + *eae* or *aggR*, LAA, LIC…	D/BD/HUS
2	*stx2d* + *eae* (O80:H2)	D/BD/HUS**
3	*stx2c* + *eae*	D/BD
4	*stx1a* + *eae*	D/BD
5	Other *stx* subtypes	D^
6	*stx2c* + ???	gastroenterologist?

*Depending on other factors; eg: host, antibiotic, etc

** Depend on Stx2d variant, strain background, other factors

^ Some subtypes caused BD/HUS on rare occasions; depend on host

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O26:H11 (*stx2a* highly virulent):

Italy, Ireland, France, Italy, Japan, Latin America, New Zealand, Scotland

O80:H2 *(stx2a, stx2a2d, stx2c2d, stx2d, eae ξ)*

France, Switzerland, Belgium, USA, Germany, Croatia, Denmark

O145:H28 Ireland

O55:H7 South of England

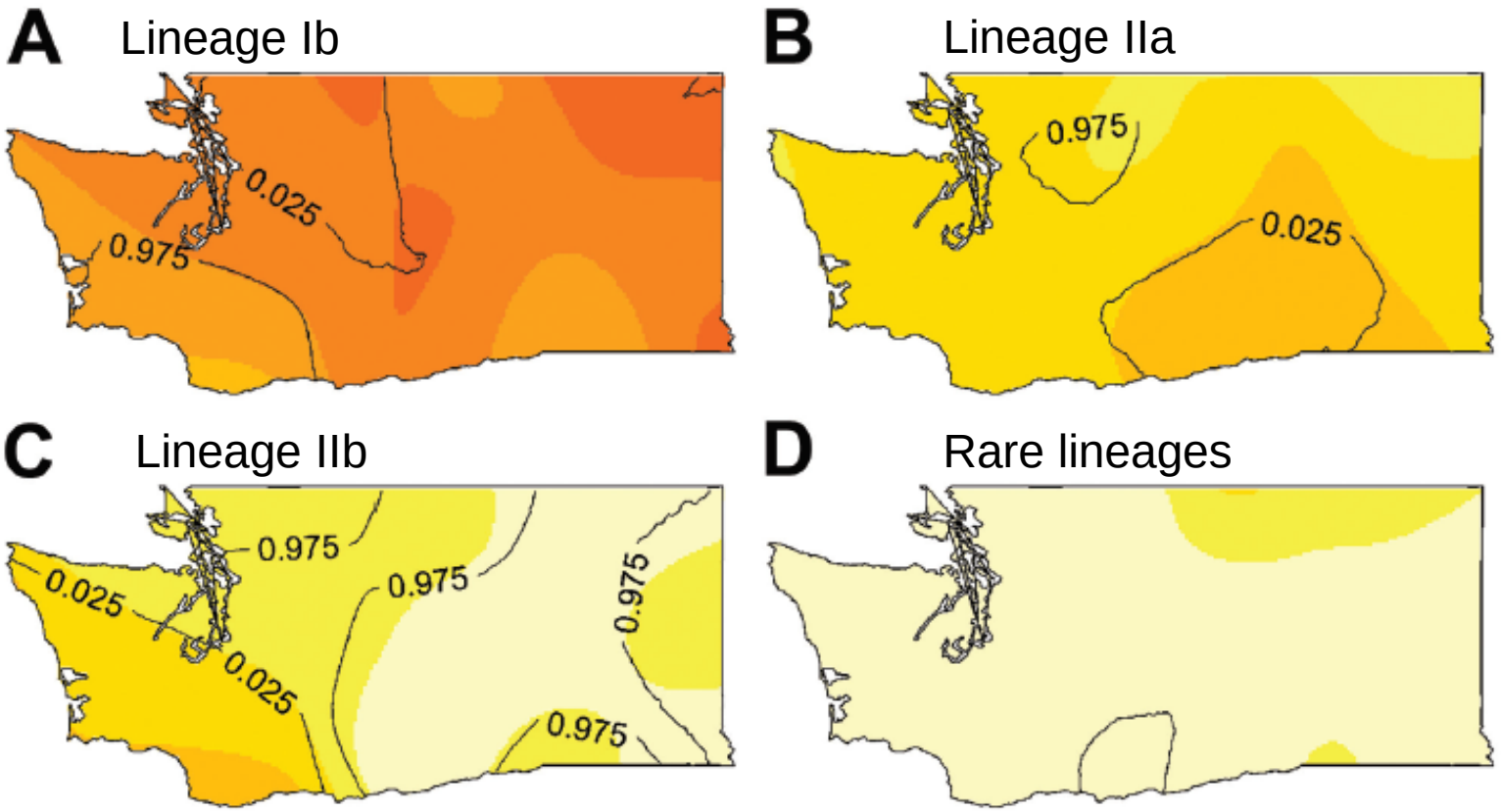

Figure 1. *Escherichia coli* O157:H7 lineage frequency among culture-confirmed human cases reported in Washington, USA, 2005–2014. A) Lineage Ib; B) lineage IIa; C) lineage IIb; D) rare lineages (12 different clinically rare lineages). Lineage-specific probability surfaces were determined by kernel-based estimation of spatial segregation. Darker shading indicates higher risk for that lineage. Contour lines marked 0.025 define areas in which there is a high probability of cases being caused by a given lineage, suggesting spatial segregation. Contour lines marked 0.975 define areas in which there is a low probability of cases being caused by the given lineage.

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Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 24, No. 1, January 2018

Geogenomic Segregation and Temporal Trends of Human Pathogenic *Escherichia coli* O157:H7, Washington, USA, 2005–2014[1]

Gillian A.M. Tarr, Smriti Shringi, Amanda I. Phipps, Thomas E. Besser, Jonathan Mayer, Hanna N. Oltean, Jon Wakefield, Phillip I. Tarr, Peter Rabinowitz

Bacteriophages

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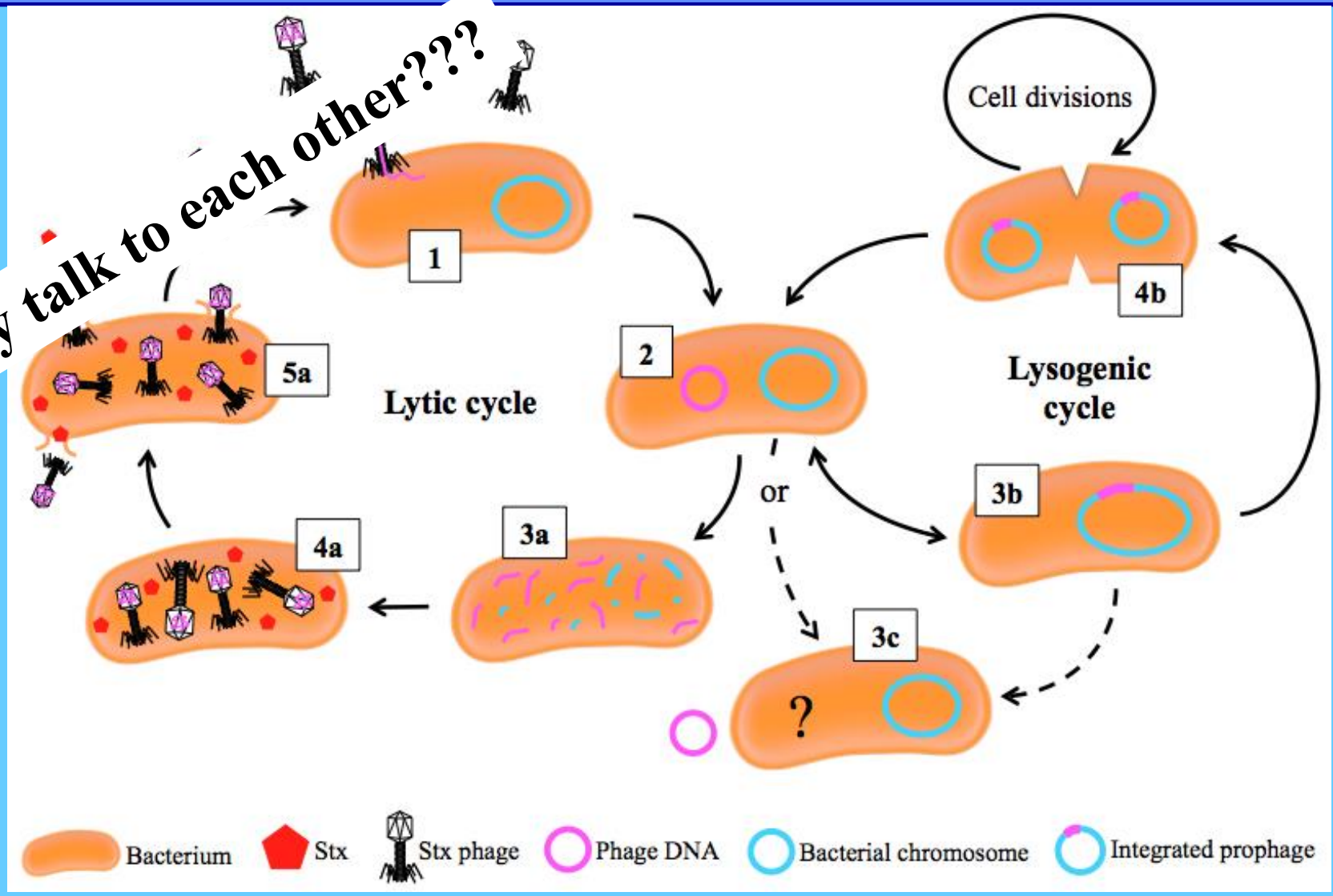
Stx2f bacteriophage has gone into tEPEC O63:H6, O128:H2 ….

..,. and it is having a party!

Stx phage life cycles



Why does *E. coli* accumulate so many prophages? Why these differences?

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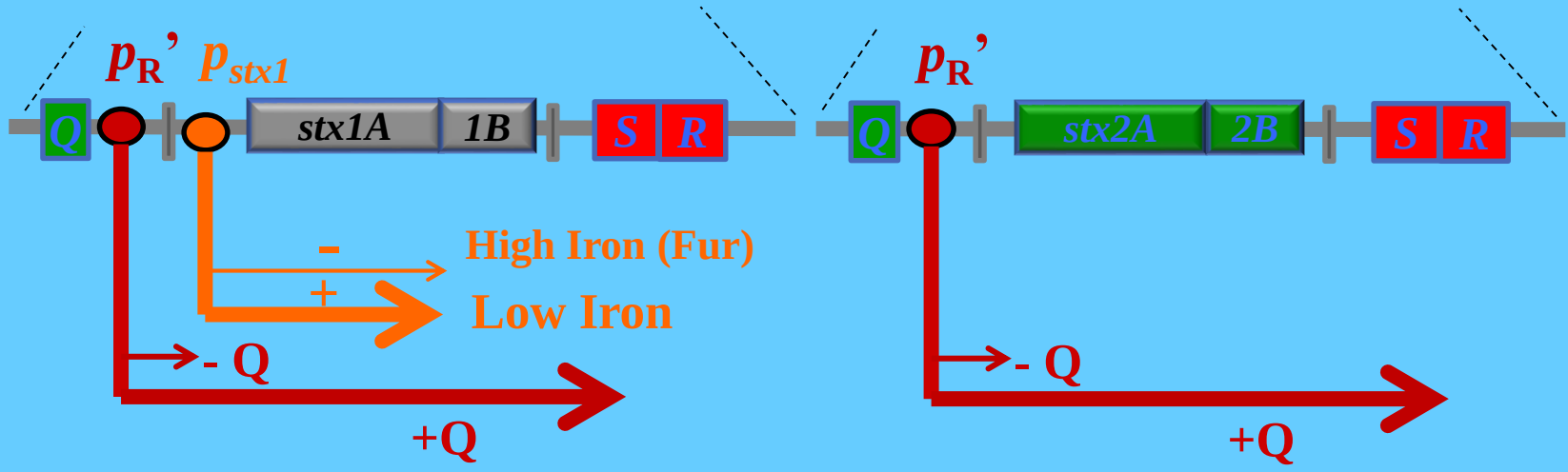
Stx1- and Stx2-encoding phages display some differences



Stx1 phages

Stx2 phages

Stx1 could be expressed by phage induction or independently by iron depletion

Stx2 could ONLY be expressed by phage induction

Calderwood and Mekalanos, 1987. J. Bact; Neely and Friedman, 1998. Mol.Micro; Grau-Leal et al., 2015. Environ Microbiol

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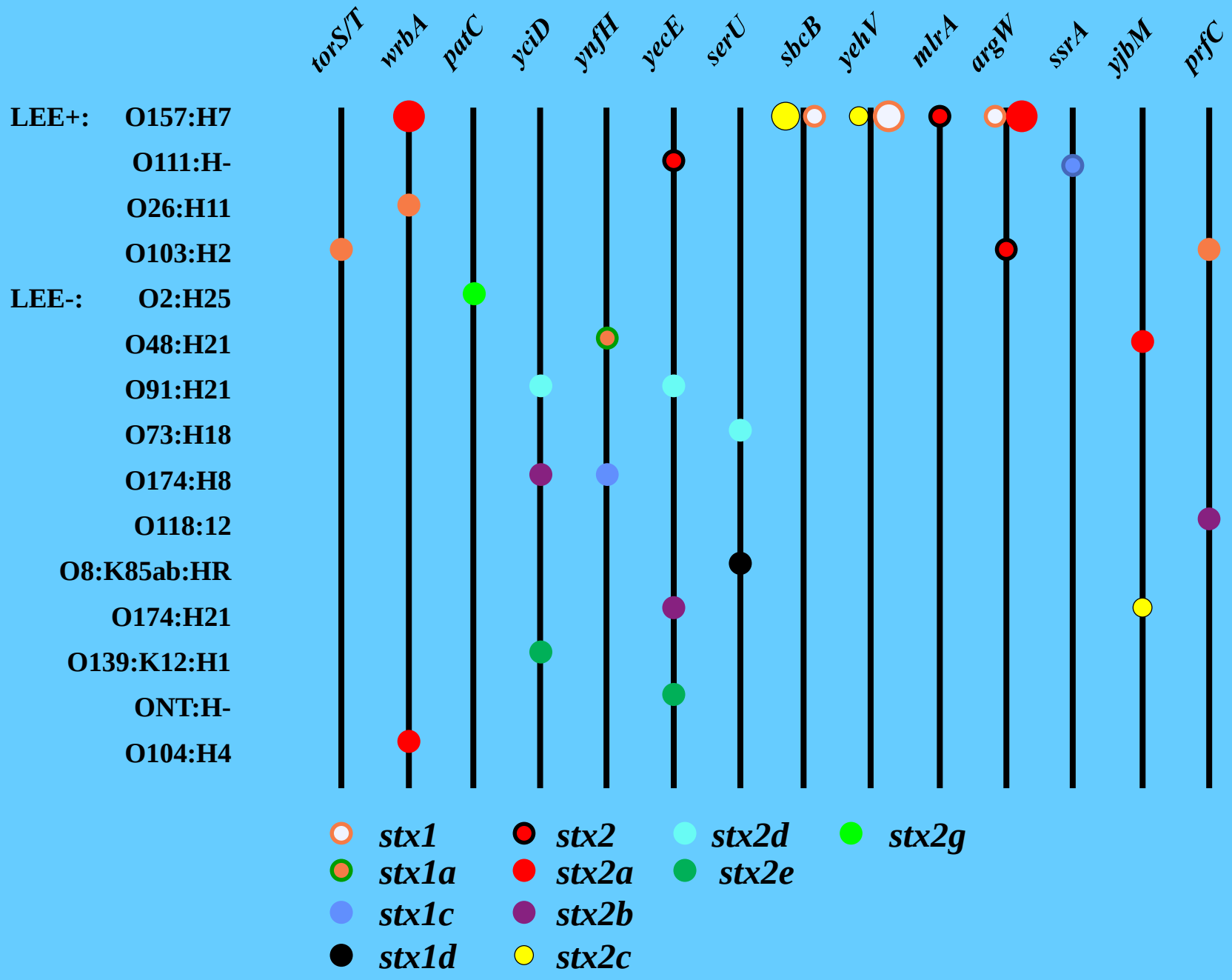
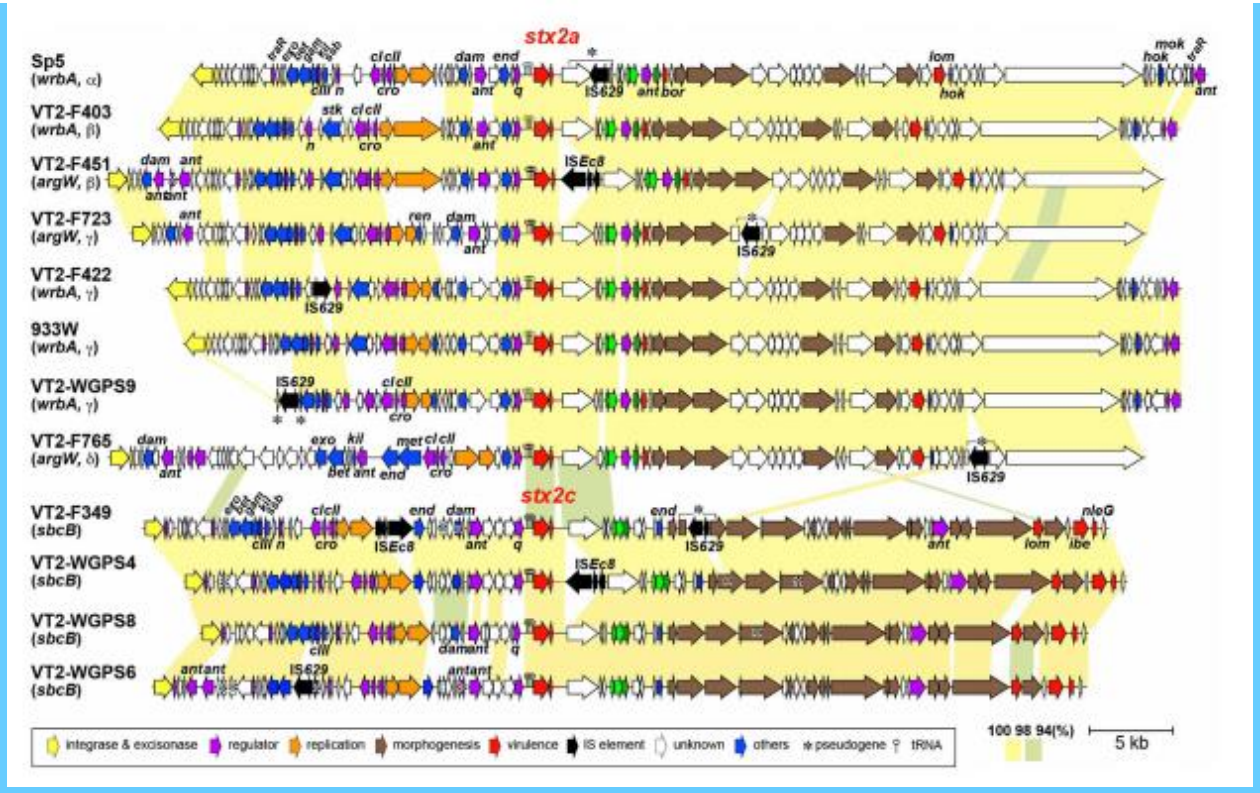

torS/T
wrbA
pagC
yciD
ynfH
yecE
serU
sbcB
yehV
mlrA
argW
ssrA
yjbM
prfC
LEE+:
O157:H7
O111:H-
O26:H11
O103:H2
LEE-:
O2:H25
O48:H21
O91:H21
O73:H18
O174:H8
O118:12
O8:K85ab:HR
O174:H21
O139:K12:H1
ONT:H-
O104:H4
stx1
stx1a
stx1c
stx1d
stx2
stx2a
stx2b
stx2c
stx2d
stx2e
stx2g

Stx2 subtype	Integration site	No. of strains*									
		Clade 1	Clade 2	Clade 3	Clade 4/5	Clade 6	Clade 7	Clade 8	Clade 9	Untypeable	Total
stx2a	*wrbA*	4 (4)	11 (7)	20 (19)	0	0	0	0	0	4 (4)	39 (34)
	argW	0	0	0	0	0	2 (0)	8 (0)	0	0	10 (0)
stx2c	*sbcB*	0	0	0	1 (0)	2 (0)	56 (23)	0	0	0	59 (23)
stx2a + *stx2c*	*argW* & *sbcB*	0	0	0	1 (1)	4 (0)	6 (0)	4 (0)	0	0	15 (1)
total		4 (4)	11 (7)	20 (19)	2 (1)	6 (0)	64 (23)	12 (0)	0	4 (4)	123 (60)

Table 1. Phylogenetic clades and stx2 subtypes of strains used in this study. *The number of strains that have the *stx1* gene is indicated in parenthesis.



STEC Genomics

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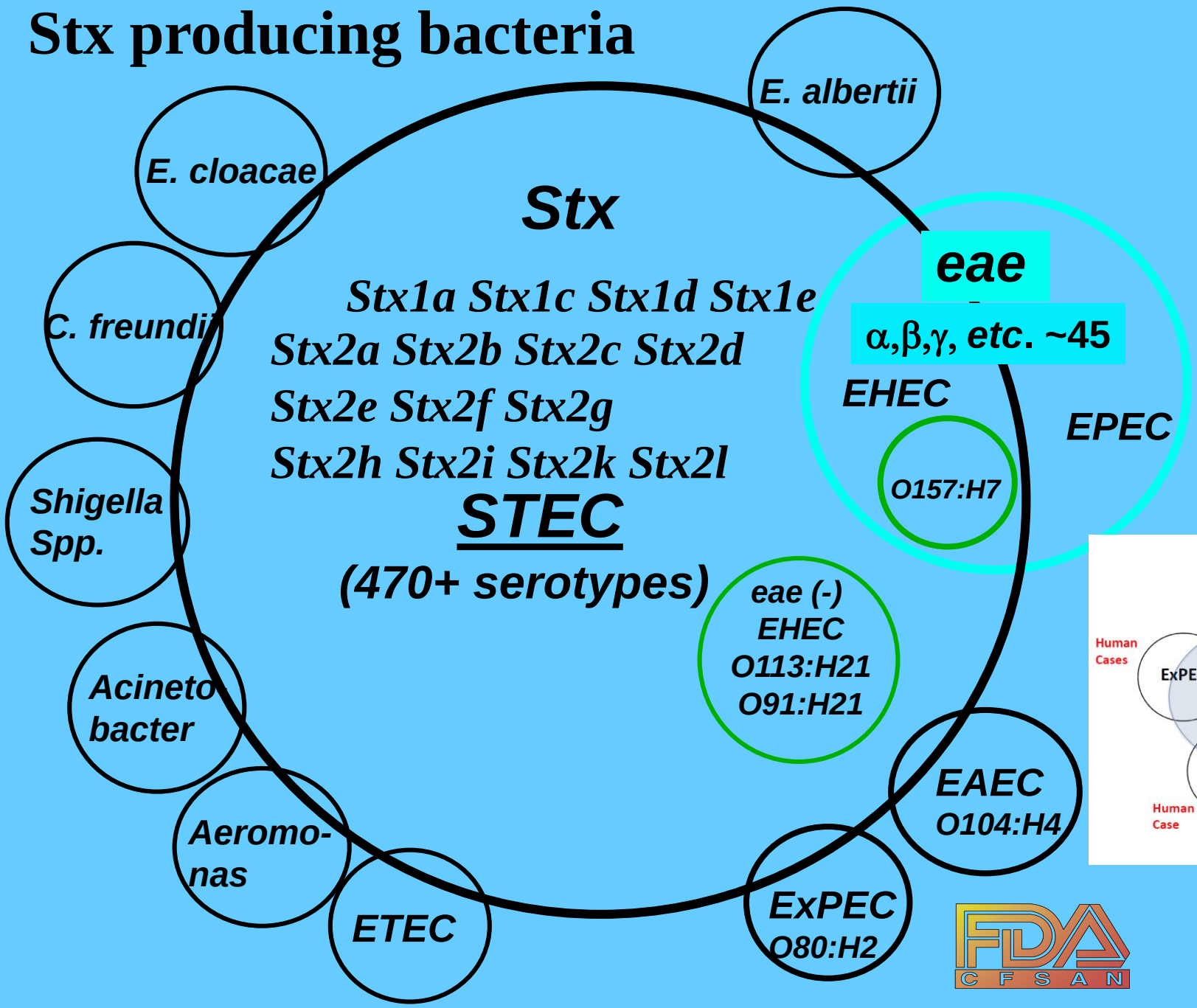
- **Identification signatures of hypervirulent Stx producers provide attractive targets for improved biosurveillance, risk assessment and development of novel therapeutic anti-Stx suppression strategies**
- **Genotype not always phenotype**

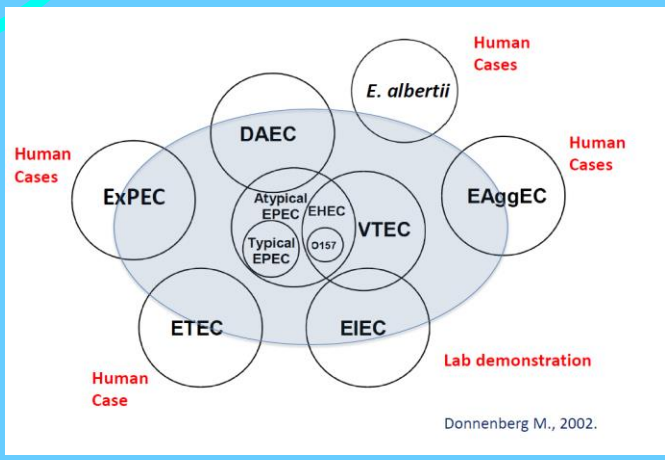
O26:H11

415 years ago but entry of *stx2a* only during the past 60 years!

HARMONIZATION!

Stx producing bacteria





Tozzoli 2014

Continuous changes

Pathogen

Disease

Environment

Host

STEC Cattle reservoir

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Suppression of immunity after the first infection is making cattle more prone to persistent colonization after re-infection

***In vivo* local administration of lactoferrin at the recto-anal junction was capable of completely clearing *E. coli* O157:H7**

Proposed that insect, especially house fly management should be incorporated into pre- and postharvest food safety strategies to minimize the public health risk

STEC human reservoir?

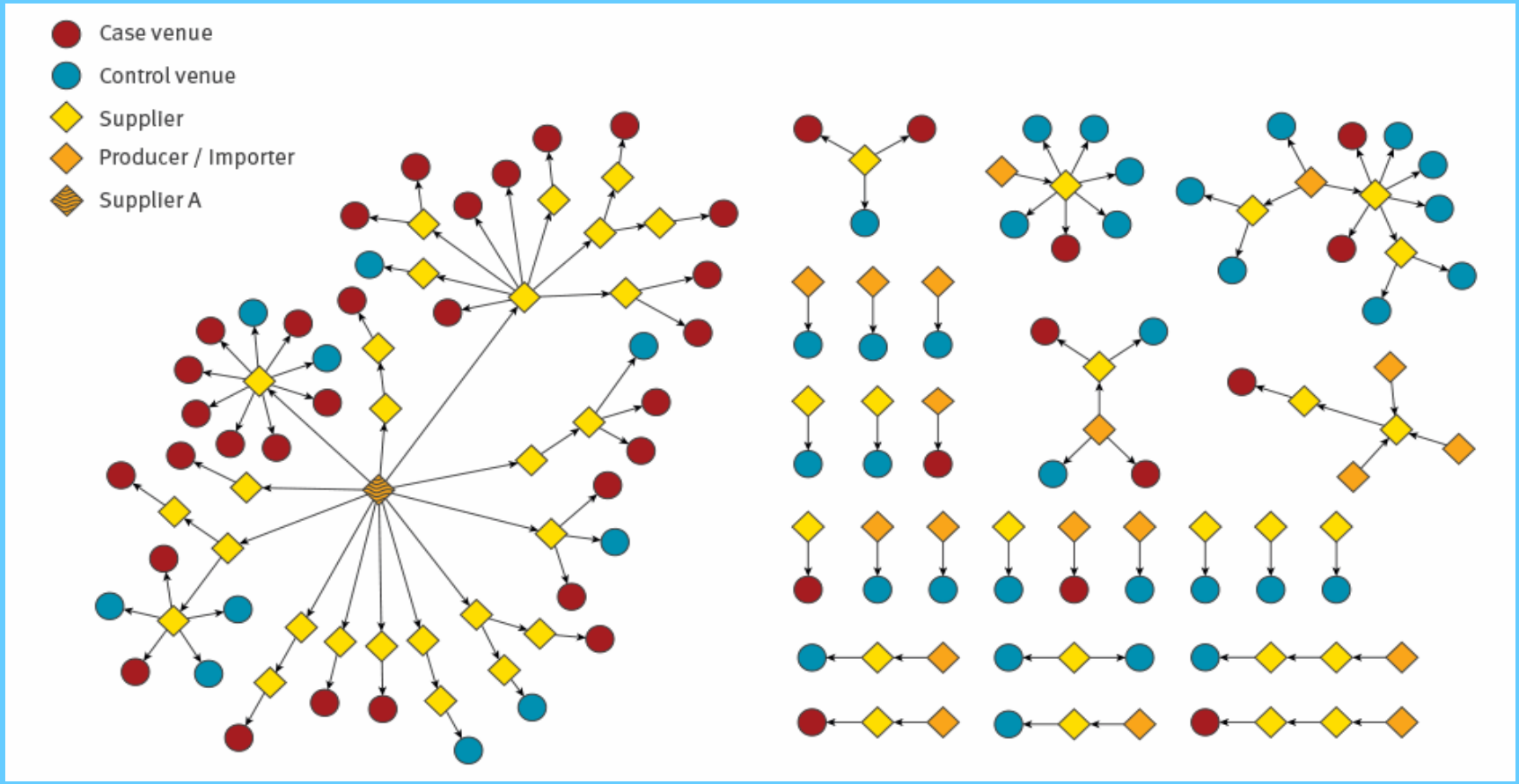
- **tEPEC O63:H6, O128:H2 Stx2f**
- **O55:H7 NSF but beta-glucuronidase positive**
- **O104:H4 EAEC-STEC**

The environment
Increasingly not meat-borne

FLOUR??

Complexity of supply chains

Traceback outbreaks



1st Food Safety Law in America

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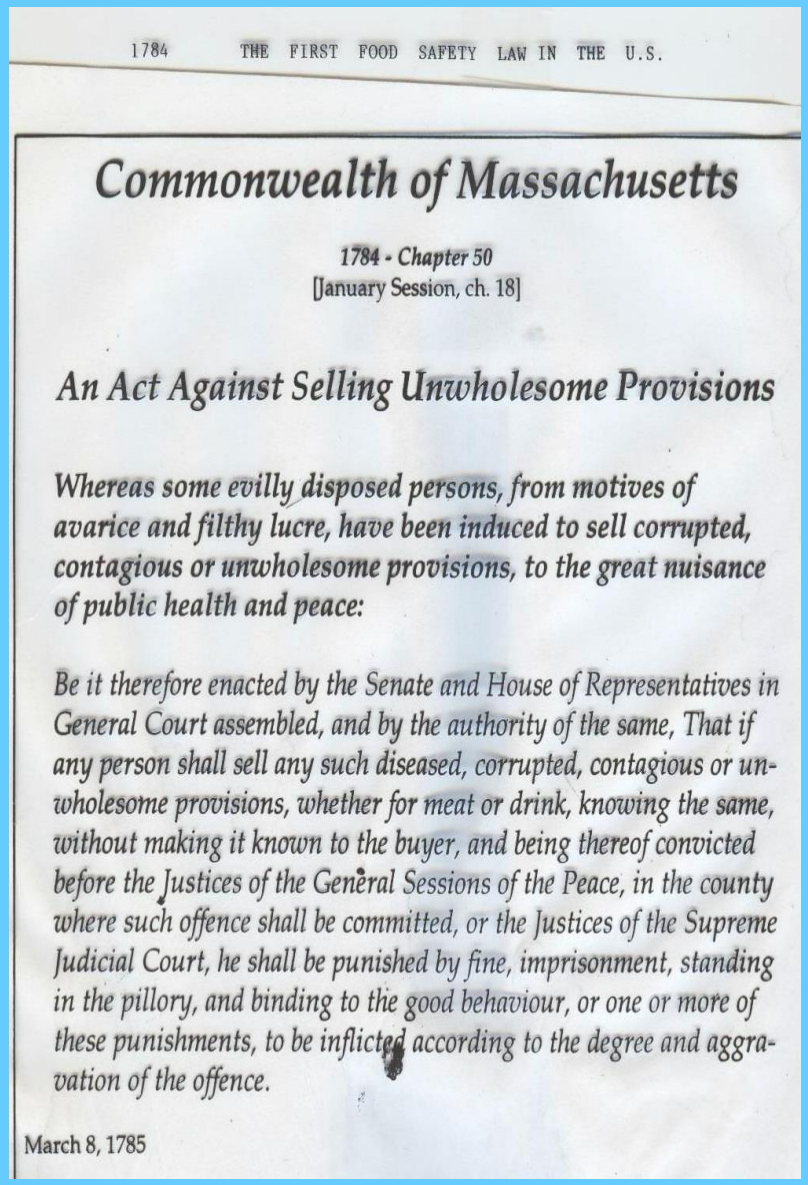
1784 - State of MA: "..against...sell...diseased, corrupted, contagious or un-wholesome provisions…"

- ***"….punishment by fine, imprisonment, standing in the pillory….."***



1784 THE FIRST FOOD SAFETY LAW IN THE U.S.

Commonwealth of Massachusetts

1784 - Chapter 50
[January Session, ch. 18]

An Act Against Selling Unwholesome Provisions

Whereas some evilly disposed persons, from motives of avarice and filthy lucre, have been induced to sell corrupted, contagious or unwholesome provisions, to the great nuisance of public health and peace:

Be it therefore enacted by the Senate and House of Representatives in General Court assembled, and by the authority of the same, That if any person shall sell any such diseased, corrupted, contagious or unwholesome provisions, whether for meat or drink, knowing the same, without making it known to the buyer, and being thereof convicted before the Justices of the General Sessions of the Peace, in the county where such offence shall be committed, or the Justices of the Supreme Judicial Court, he shall be punished by fine, imprisonment, standing in the pillory, and binding to the good behaviour, or one or more of these punishments, to be inflicted according to the degree and aggravation of the offence.

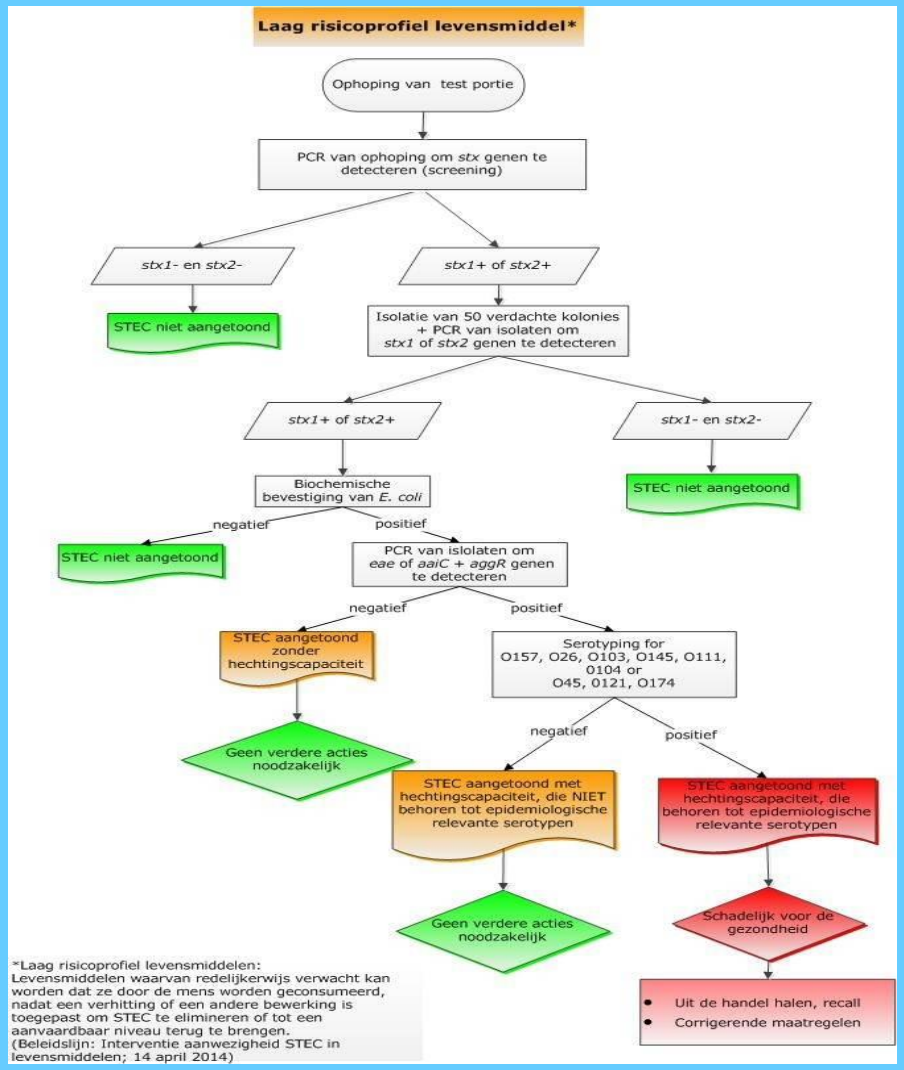
March 8, 1785

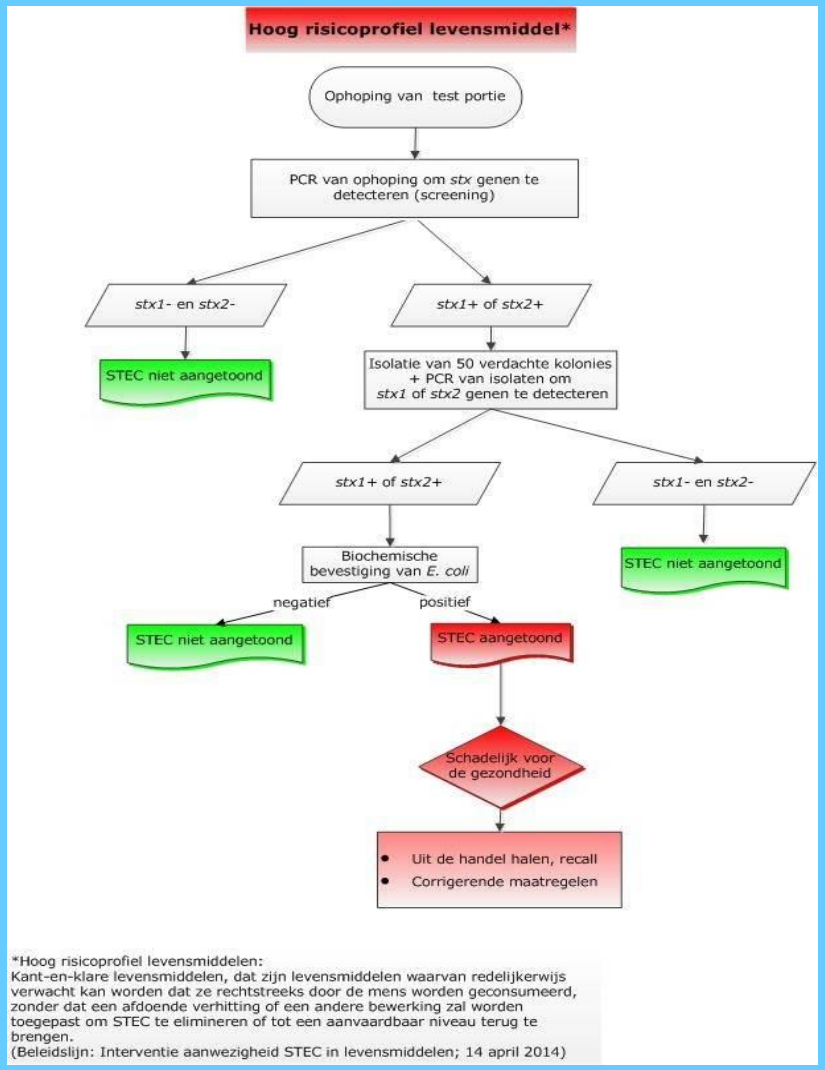
FDA CFSAN

Japan

Lessons from the 1996 outbreak were used to overcome jurisdictional challenges between prefectures

The Netherlands enforcement policy





Bioinformatics – Reg. application

- ***Raw goat's milk cheese -*** *stx1, eae.* ***stx1a, γ-eae, O111:H8*** *(big 6; HC, HUS)* ***high risk***
- ***Baby red romaine lettuce -*** *stx1, eae.* ***stx1a, α-eae, O98:H21*** *(no severe illness).* ***low risk***
- ***Raw goat's milk cheese -*** *stx1,stx2.* ***stx1a, stx2b, O91:H14*** *(no severe illness)* ***low risk.***
- ***Microgreen -*** *stx2.* ***stx2a, O91:H21*** *(HC, HUS)* ***high risk***
- ***Pea protein pellets -*** *stx1, eae.* ***stx1a, ε-eae, O103:H2*** *(big 6; HC)* ***high risk***
- ***Flour.*** *stx2.* ***stx2a, O8:H19*** *(HUS in EU but strain was* ***stx2f + eae****).* ***low risk*** *(serotype not = pathotype)*

Scientific decision – subjective & case-by-case basis

FDA CFSAN

STEC Epidemiology & Risk Assessment

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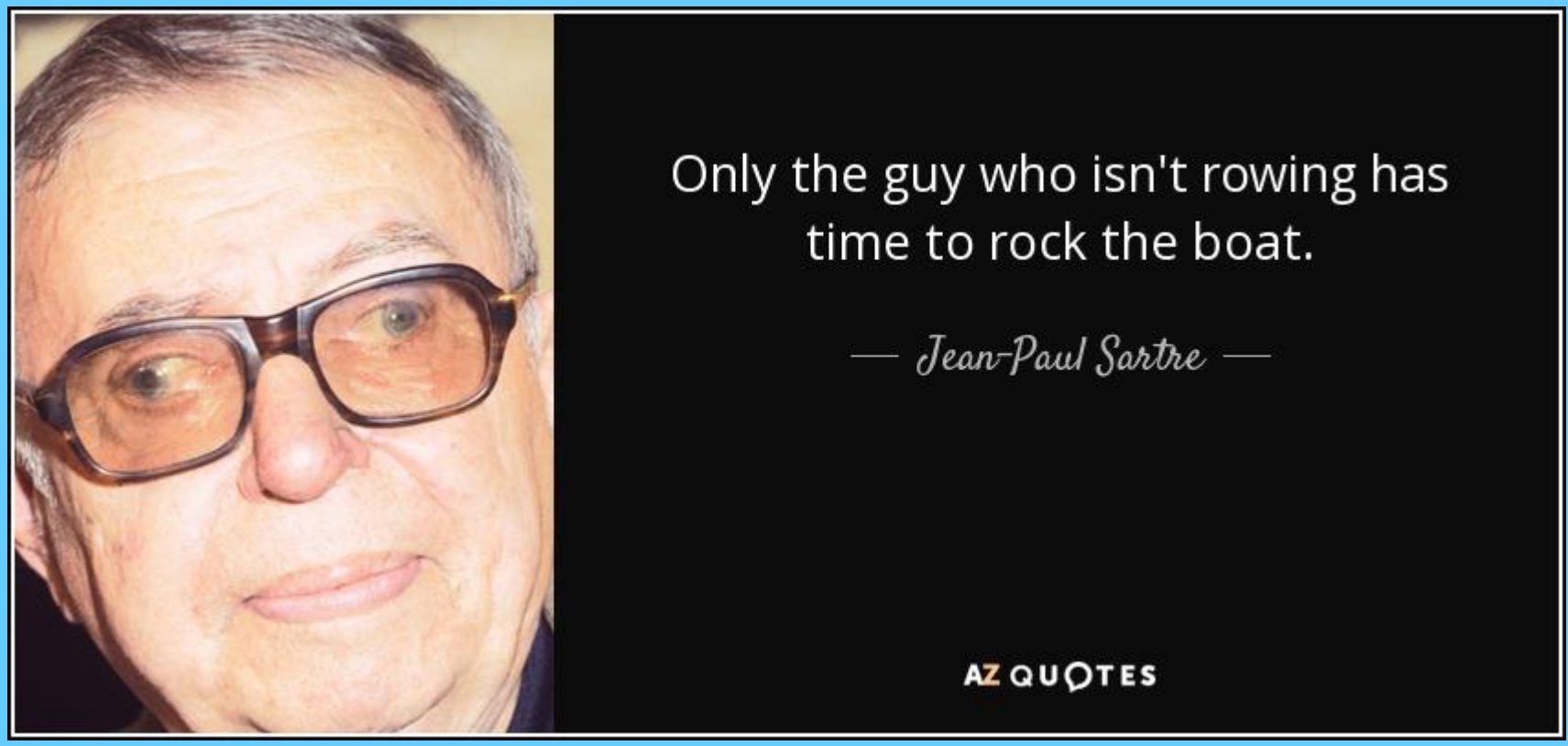
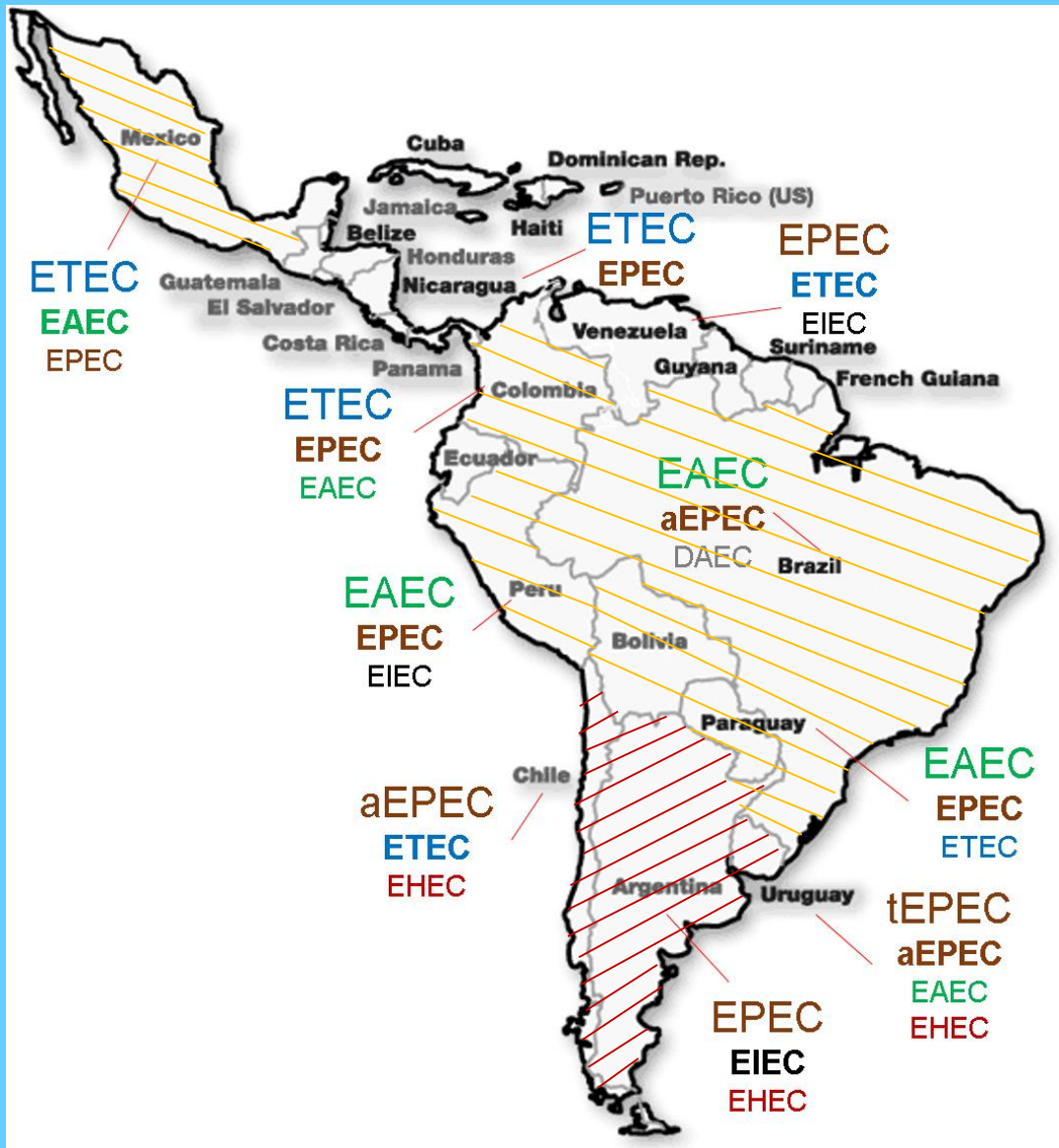
1. Lanark Blue Cheese Batch E24, ONT:H20 *stx2d* ST1308
2. Corra Linn Cheese Batch F27A, O8:H9 *stx2e* ST23
3. Corra Linn Cheese Batch E23A, ONT:H14 *stx2b* ST7010
4. Corra Linn Cheese Batches H1A, G7A, G20A, G25A, O157:H42 *stx not detected* ST7077
5. Corra Linn Cheese Batch B17A, O153-O178:H7 *stx1c* ST278
6. Raw milk bulk tank: O15:H16; *vtx2g*, STa ST325
7. Raw milk: O150:H2; *vtx1a vtx2a, eae* P3223


Only the guy who isn't rowing has time to rock the boat.
— Jean-Paul Sartre —
AZ QUOTES

Mission and philosophical underpinning

Provide a multidisciplinary forum for exchanging information, disseminating new knowledge, and highlighting state-of-the art scientific advances within a collegial atmosphere;
Striving to achieve a synthesis between art, science, culture, and humanity

Prevalence of diarrheagenic *Escherichia coli* in Latin America

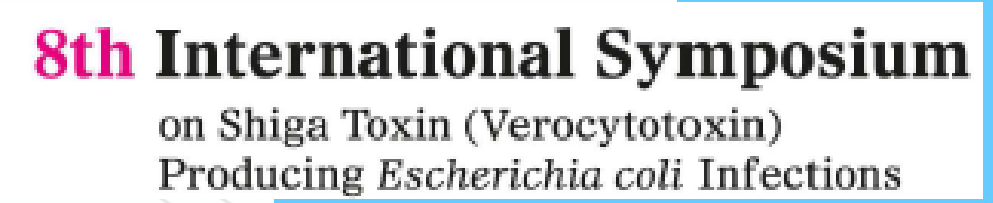


ETEC: Enterotoxigenic *E. coli*
EPEC: Enteropathogenic *E. coli*
EAEC: Enteroaggregative *E. coli*
EIEC: Enteroinvasive *E. coli*
EHEC: Enterohemorrhagic *E. coli*

STEC animals, sporadic human cases
EHEC/HUS cases, STEC in animals

Torres AG. Pathog Dis. 2017; 75(2)
Torres AG. PLoS Pathog. 2017;13:e1006047

Time for contemplation

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