Ecology of *Salmonella*

Tim Johnson
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Salmonella evolution

- Evolved over the past 12—160 million years! (split between *E. coli* and *Salmonella*)
- Can infect >100 different species including mammals, birds, reptiles, and insects
- Complex nomenclature:
  - Two major species: *S. enterica* and *S. bongori*
  - Seven subspecies, including *enterica* (I) accounting for >99% of human infection

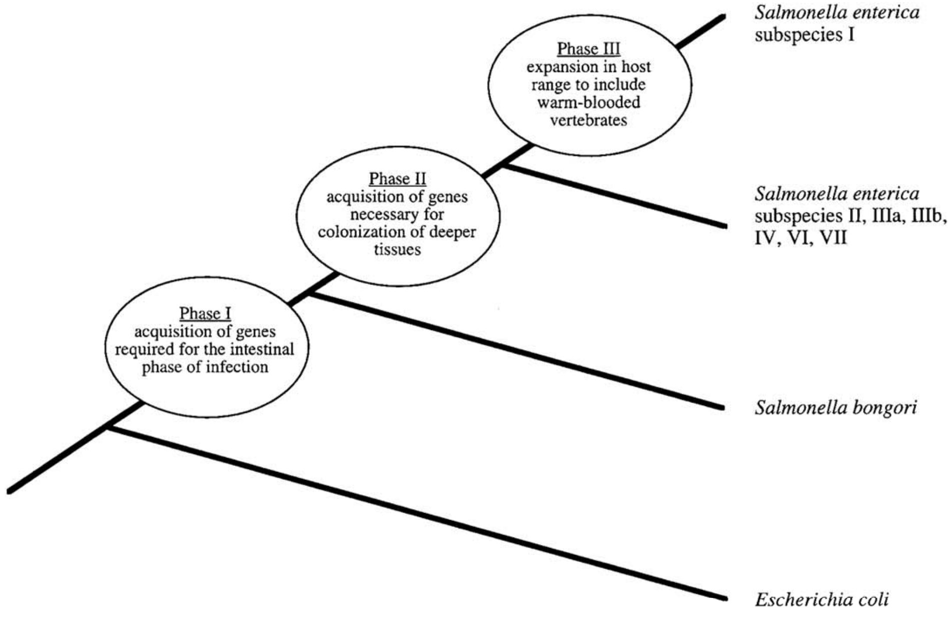
Salmonella evolution

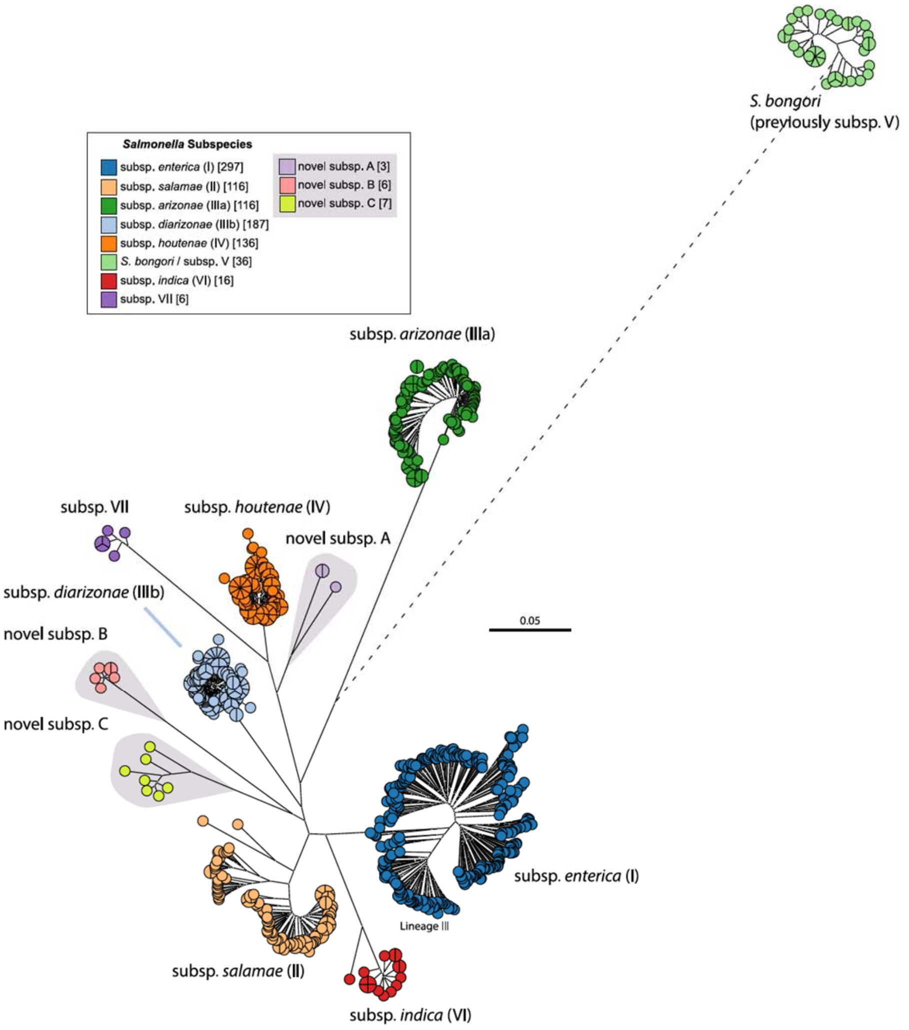
REVIEW

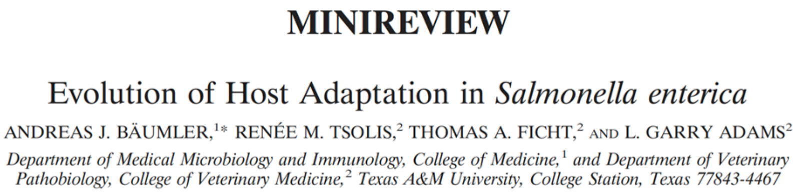
A genomic overview of the population structure of *Salmonella*

Nabil-Fareed Alikhan, Zhemin Zhou, Martin J. Sergeant, Mark Achtman*

Warwick Medical School, University of Warwick, Coventry, United Kingdom







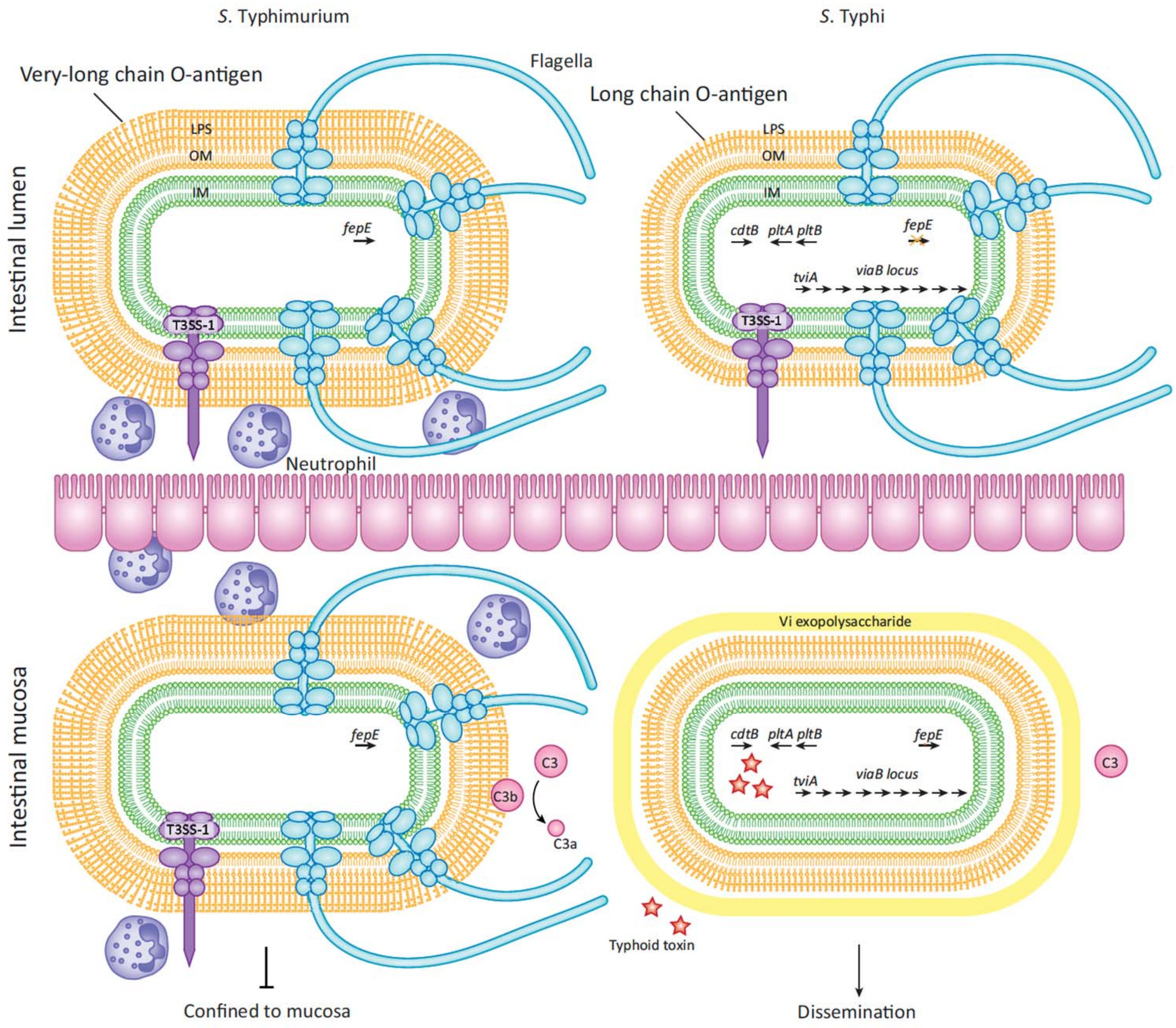
MINIREVIEW

Evolution of Host Adaptation in *Salmonella enterica*

ANDREAS J. BÄUMLER,[1]* RENÉE M. TSOLIS,[2] THOMAS A. FICHT,[2] AND L. GARRY ADAMS[2]

Department of Medical Microbiology and Immunology, College of Medicine,[1] and Department of Veterinary Pathobiology, College of Veterinary Medicine,[2] Texas A&M University, College Station, Texas 77843-4467

Salmonella evolution



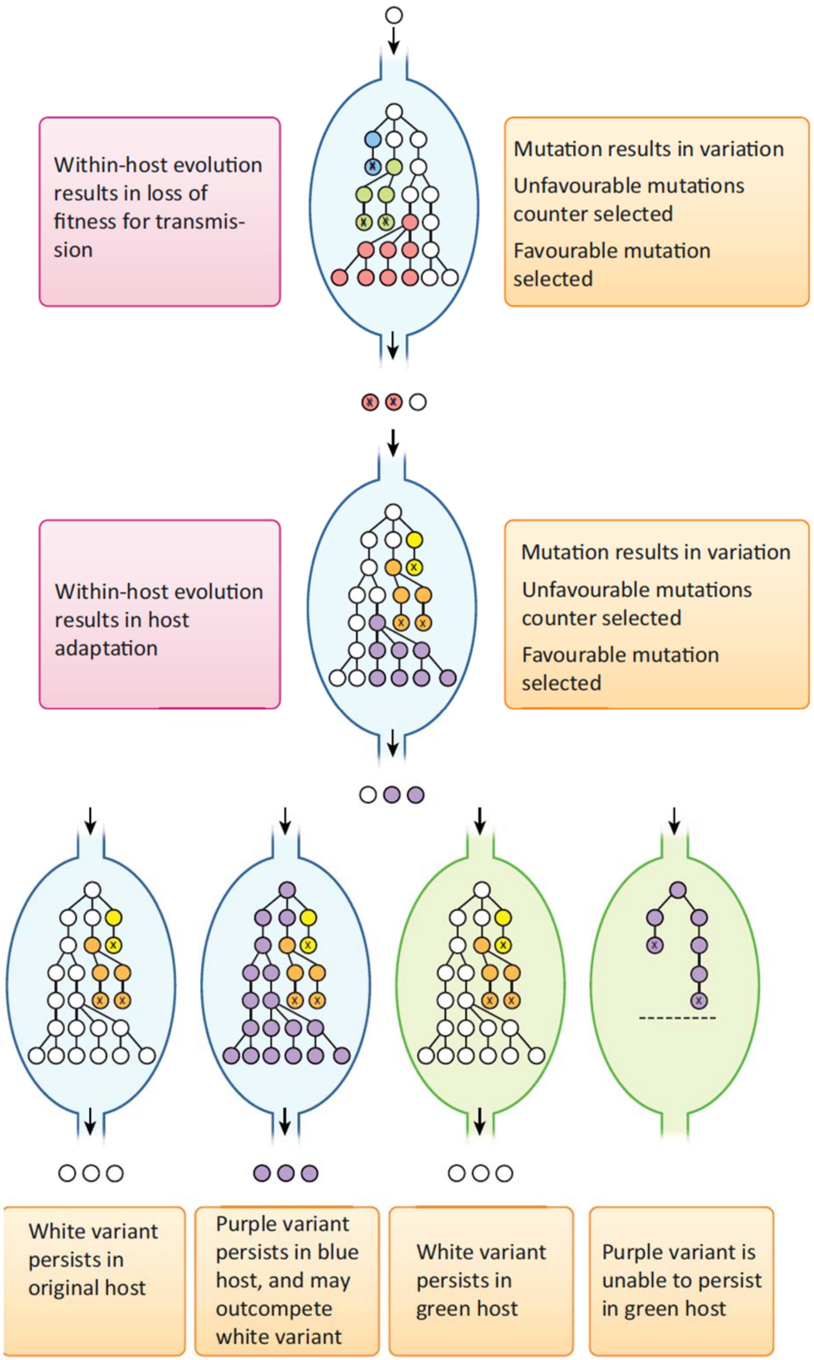
Trends in Microbiology

Review

Evolution of *Salmonella* within Hosts

Jennifer R. Tanner[1] and Robert A. Kingsley[1,*]

Tradeoffs for host range versus host adaptation



Within-host evolution results in loss of fitness for transmission

Mutation results in variation

Unfavourable mutations counter selected

Favourable mutation selected

Within-host evolution results in host adaptation

Mutation results in variation

Unfavourable mutations counter selected

Favourable mutation selected

White variant persists in original host

Purple variant persists in blue host, and may outcompete white variant

White variant persists in green host

Purple variant is unable to persist in green host

Trends in Microbiology

Review

Evolution of *Salmonella* within Hosts

Jennifer R. Tanner[1] and Robert A. Kingsley[1,*] Review

Evolution of *Salmonella* within Hosts

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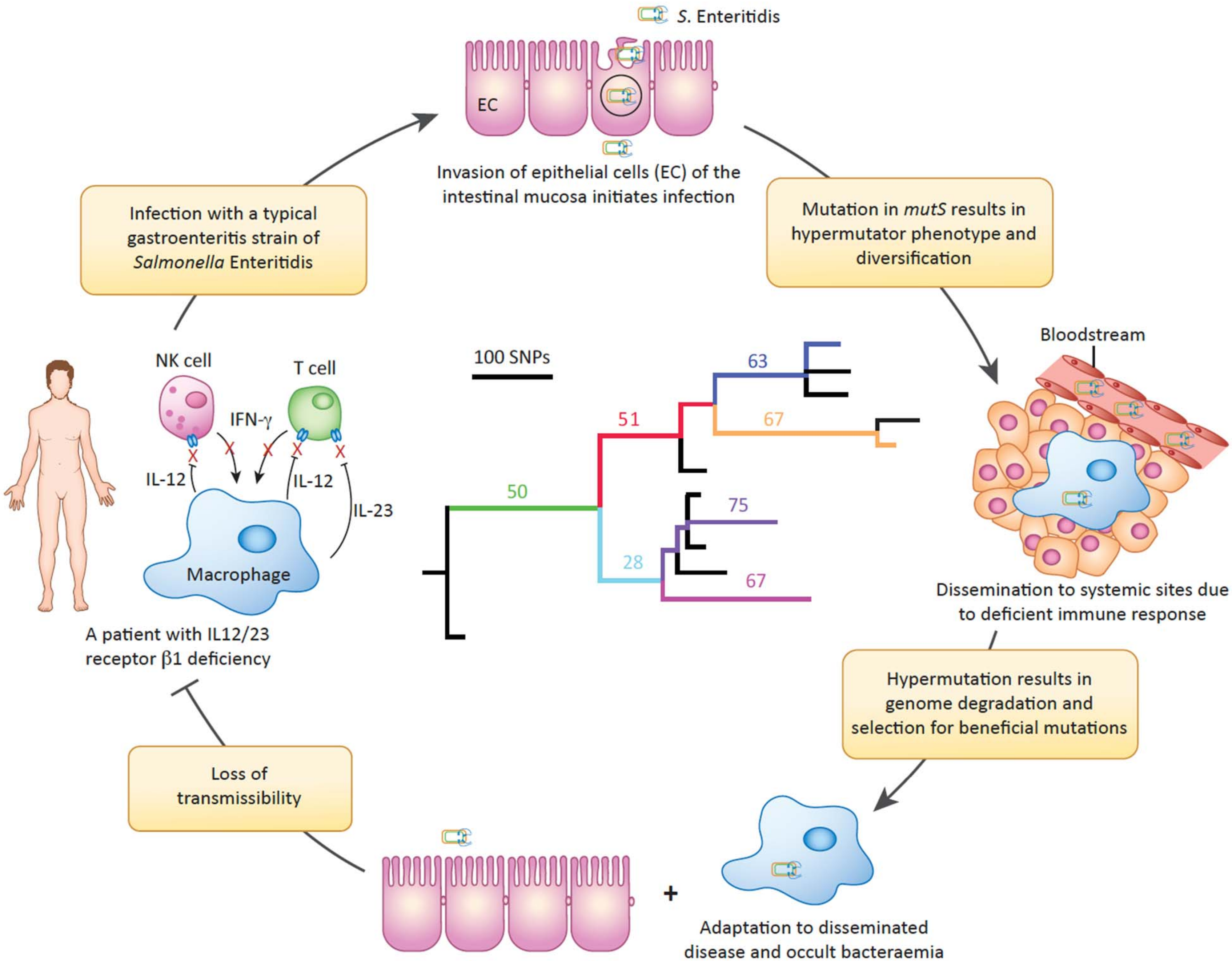


Invasion of epithelial cells (EC) of the intestinal mucosa initiates infection

Mutation in *mutS* results in hypermutator phenotype and diversification

Dissemination to systemic sites due to deficient immune response

Hypermutation results in genome degradation and selection for beneficial mutations

Adaptation to disseminated disease and occult bacteraemia

+

Attenuated intestinal virulence

Loss of transmissibility

A patient with IL12/23 receptor β1 deficiency

Infection with a typical gastroenteritis strain of *Salmonella* Enteritidis

Trends in Microbiology

Salmonella typing

- Kauffmann-White serotyping scheme give the serovars their names
    - LPS (O) antigen
    - H1 and H2 flagellar antigens
    - Capsular antigen
- O antigen divides into 6 serogroups: A, B, 1, C2, D, E
- >2,300 servars

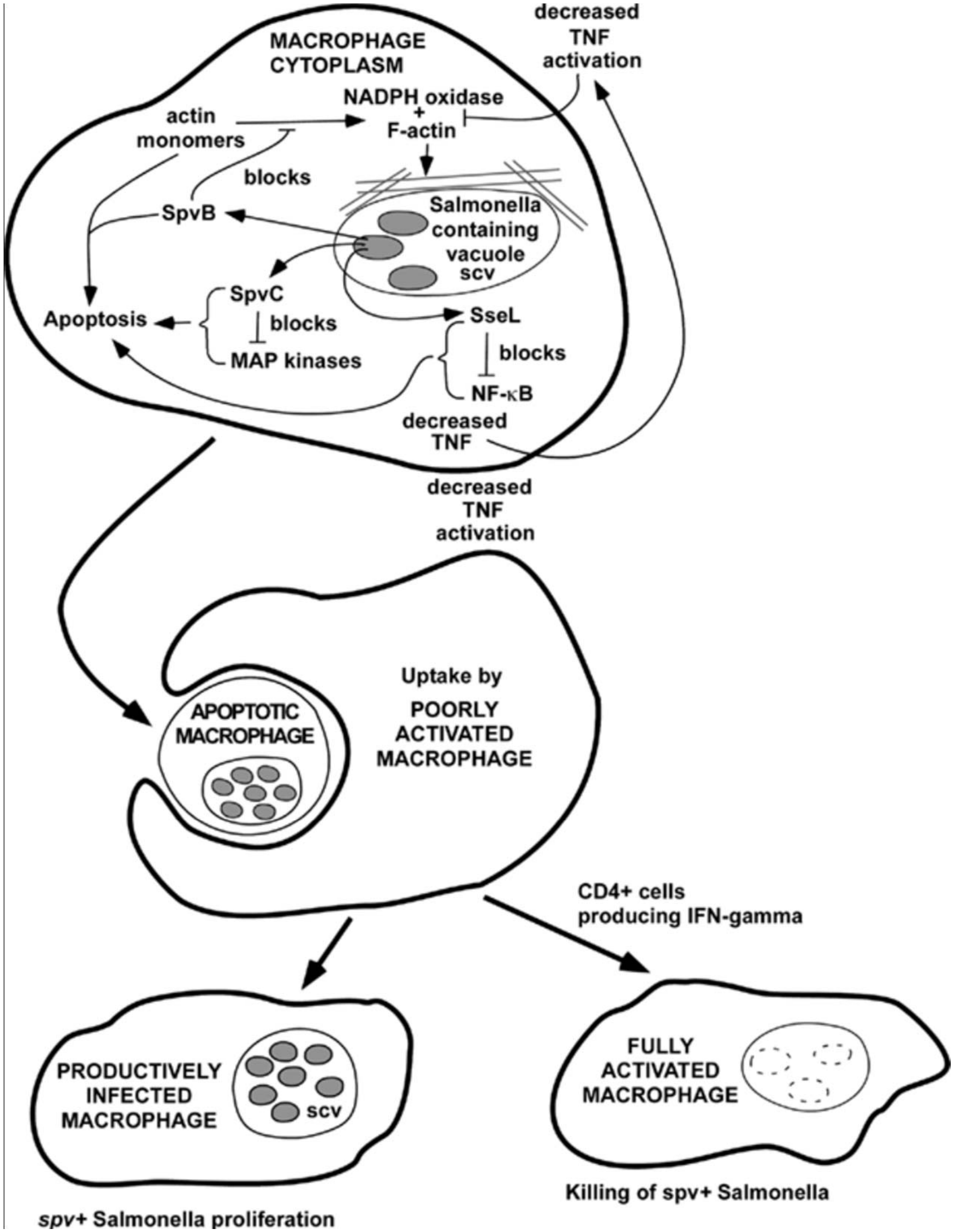
Factors involved in host range

- Colonization
  - SPI-3, SPI-4
  - Numerous fimbrial operons (*agf*, *sef*, *pil*, *lpf*, *pef*)
- Persistence
  - LPS
- Invasion
  - Exotoxins and enterotoxins
  - SPI-1, SPI-5
- Intracellular survival
  - SPI-2 through SPI-6
  - Virulence plasmid (*spv*)
- Phase variation in flagella expression

Plasmids

- Often ignored in outbreak investigations
- They provide critical hints about host source and host range
- They can encode for multidrug resistance
- They can encode for enhanced virulence
- They can enable enhanced fitness

Plasmids – virulence plasmid

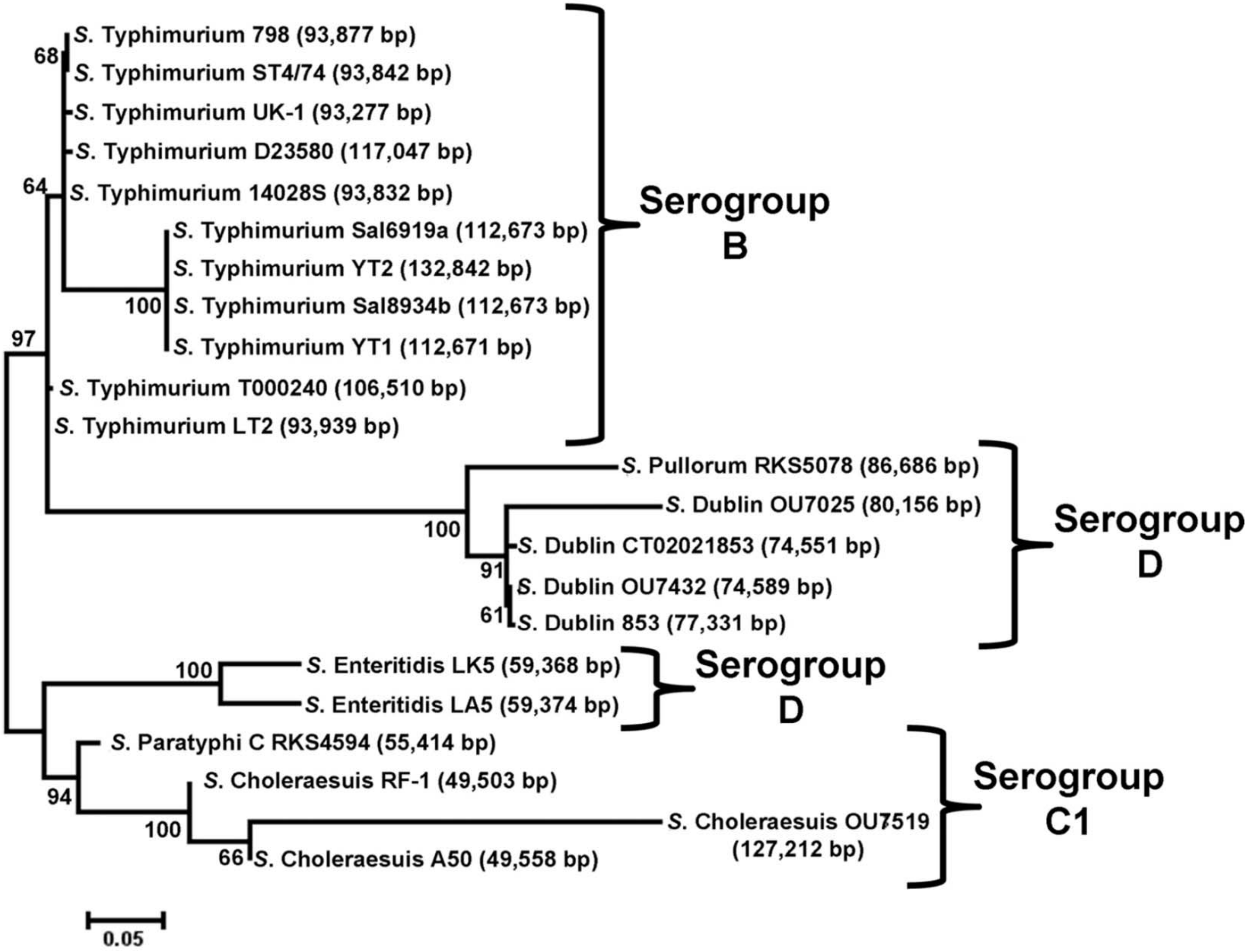


The role of the *spv* genes in *Salmonella* pathogenesis

Donald G. Guiney[1]* and Joshua Fierer[1,2]

[1] Department of Medicine, University of California San Diego School of Medicine, La Jolla, CA, USA

[2] Veterans Administration Medical Center, La Jolla, CA, USA

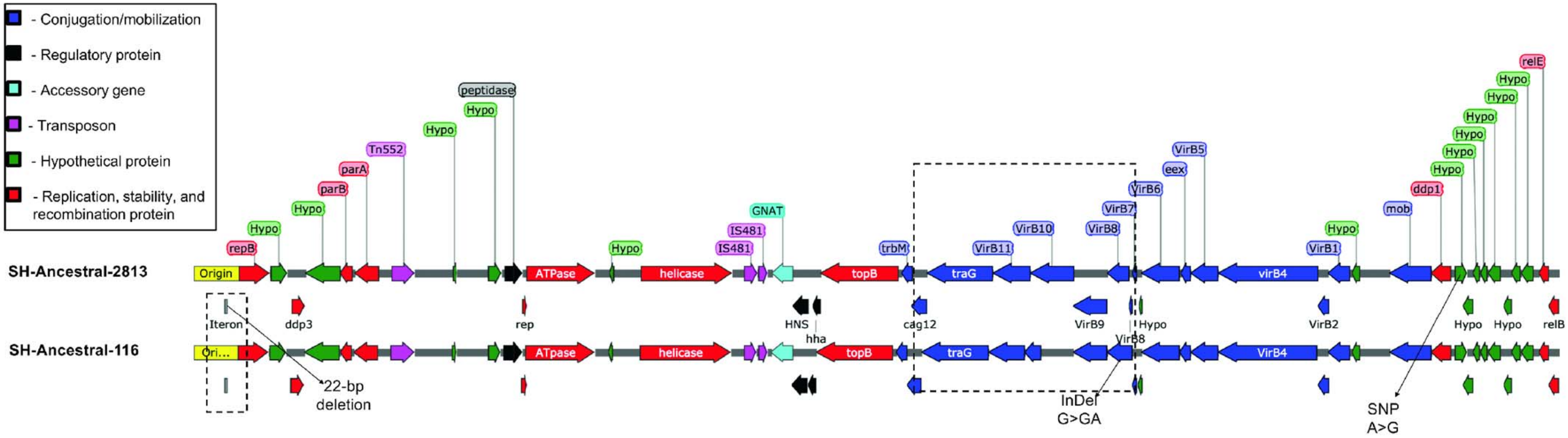


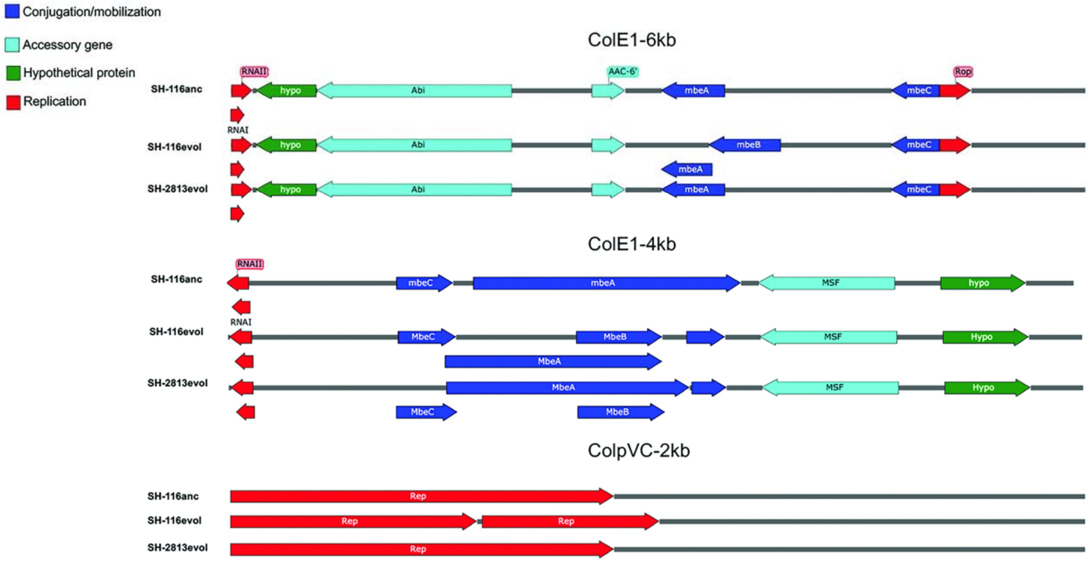
Salmonella Pathogenicity and Host Adaptation in Chicken-Associated Serovars

Steven L. Foley,[a] Timothy J. Johnson,[b] Steven C. Ricke,[c] Rajesh Nayak,[a] Jessica Danzeisen[b]

Division of Microbiology, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, Arkansas, USA[a]; Department of Veterinary and Biomedical Sciences, University of Minnesota, Saint Paul, Minnesota, USA[b]; Center for Food Safety and Department of Food Science, University of Arkansas, Fayetteville, Arkansas, USA[c]

Plasmids – IncX and Col plasmids



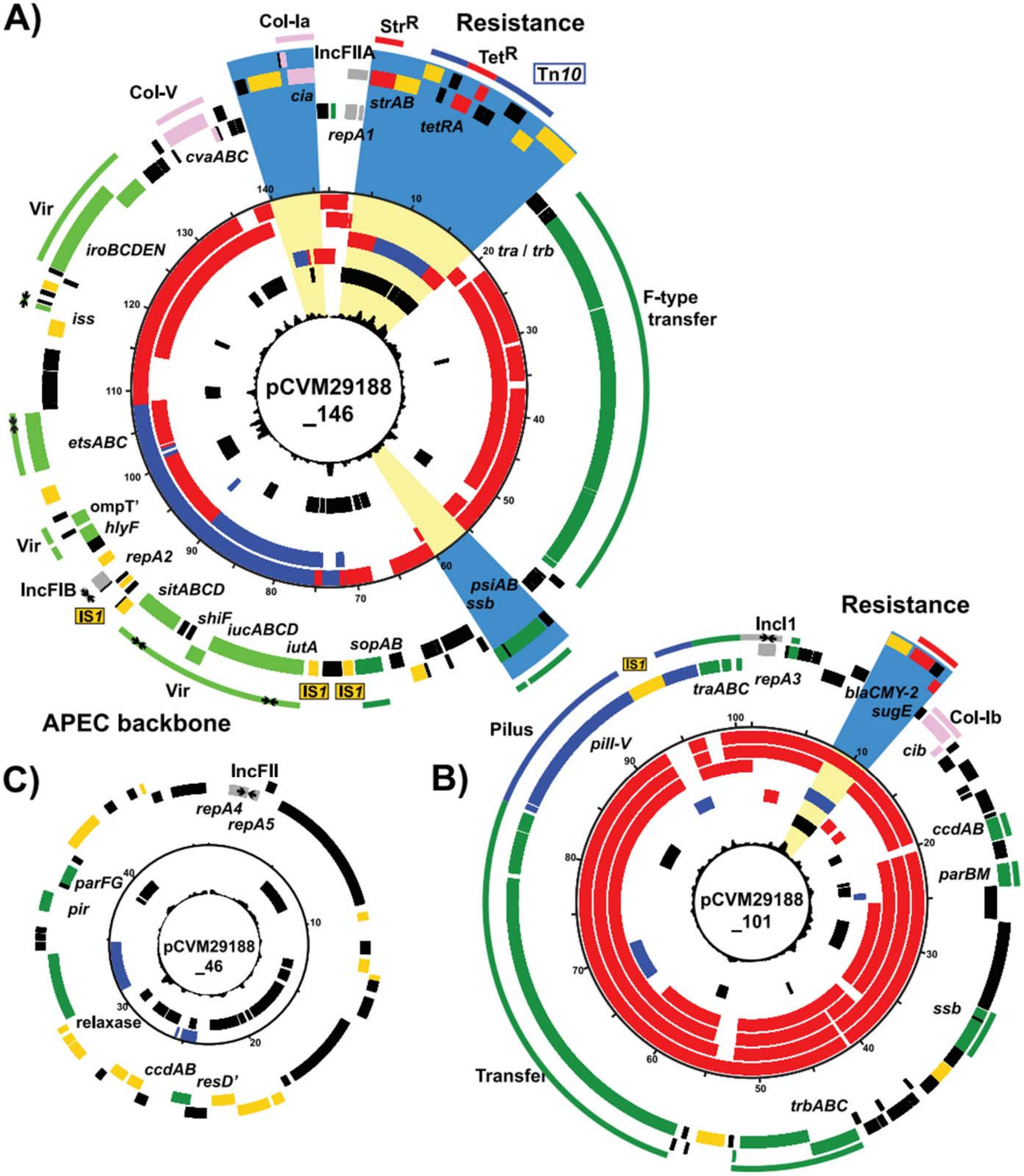


RESEARCH ARTICLE

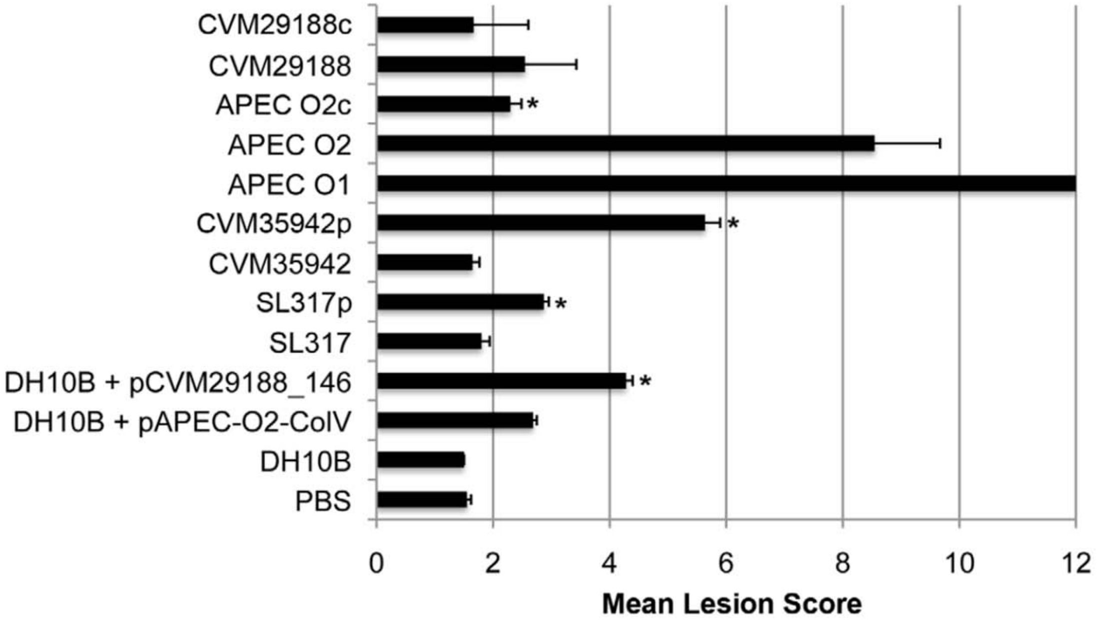
Hotspot mutations and ColE1 plasmids contribute to the fitness of *Salmonella* Heidelberg in poultry litter

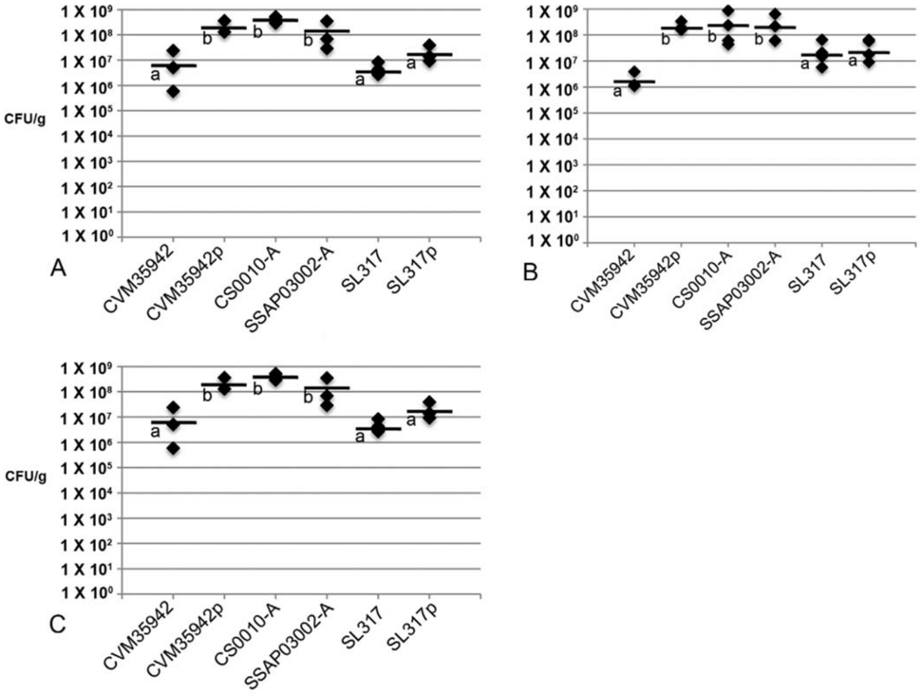
Adelumola Oladeinde[1☯]*, Kimberly Cook[1☯], Alex Orlek[2☯], Greg Zock[1‡], Kyler Herrington[3‡], Nelson Cox[4‡], Jodie Plumblee Lawrence[1‡], Carolina Hall[1‡]

Plasmids – ColV plasmid



Plasmids – ColV plasmid

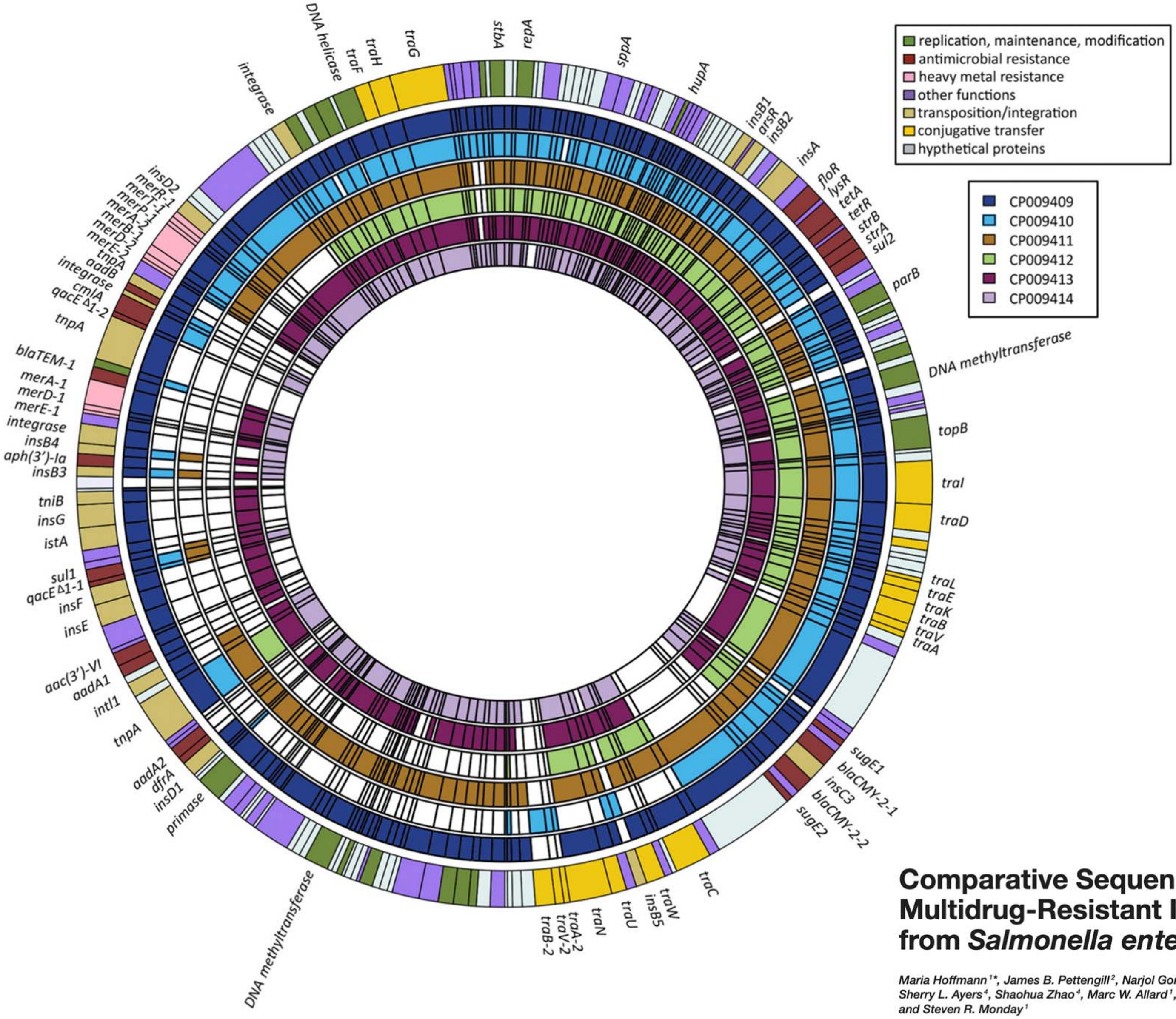




Horizontal Gene Transfer of a ColV Plasmid Has Resulted in a Dominant Avian Clonal Type of *Salmonella enterica* Serovar Kentucky

Timothy J. Johnson[1]*, Jessica L. Thorsness[1], Cole P. Anderson[2], Aaron M. Lynne[2], Steven L. Foley[3], Jing Han[3], W. Florian Fricke[4], Patrick F. McDermott[5], David G. White[5], Mahesh Khatri[1], Adam L. Stell[1], Cristian Flores[1], Randall S. Singer[1]

Plasmids – IncA/C plasmid



Comparative Sequence Analysis of Multidrug-Resistant IncA/C Plasmids from *Salmonella enterica*

Maria Hoffmann[1], James B. Pettengill[2], Narjol Gonzalez-Escalona[1], John Miller[2,3], Sherry L. Ayers[4], Shaohua Zhao[4], Marc W. Allard[1], Patrick F. McDermott[4], Eric W. Brown[1] and Steven R. Monday[1]*

Plasmids – IncA/C plasmid

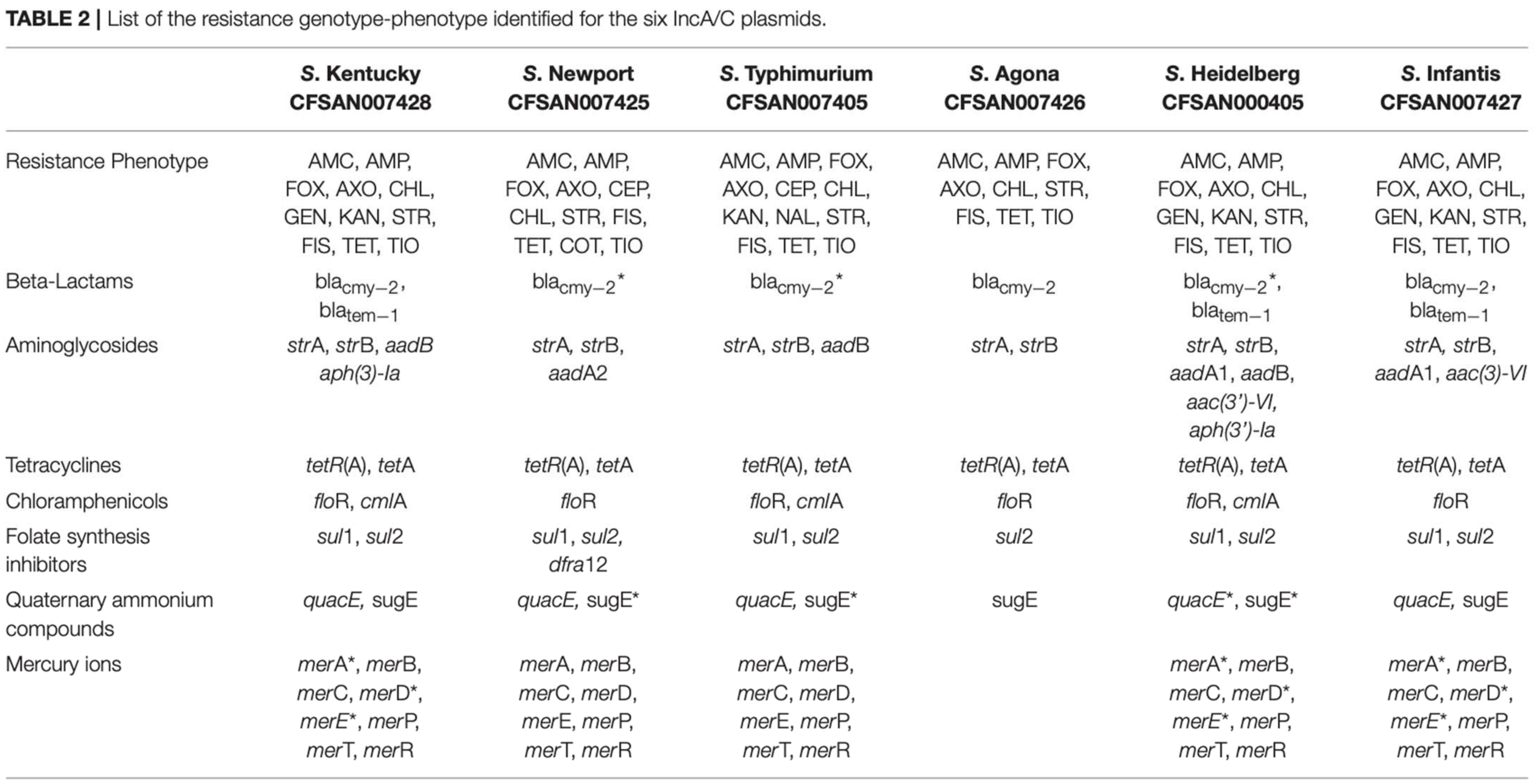
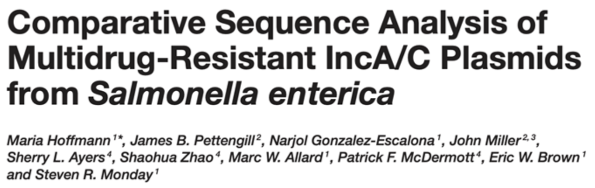


TABLE 2 | List of the resistance genotype-phenotype identified for the six IncA/C plasmids.

	S. Kentucky CFSAN007428	**S. Newport CFSAN007425**	**S. Typhimurium CFSAN007405**	**S. Agona CFSAN007426**	**S. Heidelberg CFSAN000405**	**S. Infantis CFSAN007427**
Resistance Phenotype	AMC, AMP, FOX, AXO, CHL, GEN, KAN, STR, FIS, TET, TIO	AMC, AMP, FOX, AXO, CEP, CHL, STR, FIS, TET, COT, TIO	AMC, AMP, FOX, AXO, CEP, CHL, KAN, NAL, STR, FIS, TET, TIO	AMC, AMP, FOX, AXO, CHL, STR, FIS, TET, TIO	AMC, AMP, FOX, AXO, CHL, GEN, KAN, STR, FIS, TET, TIO	AMC, AMP, FOX, AXO, CHL, GEN, KAN, STR, FIS, TET, TIO
Beta-Lactams	bla$_{cmy-2}$, bla$_{tem-1}$	bla$_{cmy-2}^{*}$	bla$_{cmy-2}^{*}$	bla$_{cmy-2}$	bla$_{cmy-2}^{*}$, bla$_{tem-1}$	bla$_{cmy-2}$, bla$_{tem-1}$
Aminoglycosides	strA, strB, aadB aph(3)-Ia	strA, strB, aadA2	strA, strB, aadB	strA, strB	strA, strB, aadA1, aadB, aac(3')-VI, aph(3')-Ia	strA, strB, aadA1, aac(3)-VI
Tetracyclines	tetR(A), tetA	tetR(A), tetA	tetR(A), tetA	tetR(A), tetA	tetR(A), tetA	tetR(A), tetA
Chloramphenicols	floR, cmlA	floR	floR, cmlA	floR	floR, cmlA	floR
Folate synthesis inhibitors	sul1, sul2	sul1, sul2, dfra12	sul1, sul2	sul2	sul1, sul2	sul1, sul2
Quaternary ammonium compounds	quacE, sugE	quacE, sugE*	quacE, sugE*	sugE	quacE*, sugE*	quacE, sugE
Mercury ions	merA*, merB, merC, merD*, merE*, merP, merT, merR	merA, merB, merC, merD, merE, merP, merT, merR	merA, merB, merC, merD, merE, merP, merT, merR		merA*, merB, merC, merD*, merE*, merP, merT, merR	merA*, merB, merC, merD*, merE*, merP, merT, merR



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Restricted versus non-restricted host range

- Those dominating human infection tend to have broad host range
  - Typhimurium, Enteritidis, Newport, Heidelberg
- Others have restricted host range
  - Typhi, Paratyphi, Gallinarum, Pullorum, Choleraesuis, Dublin
- When spillover of restricted serovars occurs, they tend to be more invasive
- Most of the host-adapted serovars have tendency to accumulate pseudogenes

Host species	Disease	*S. enterica* subspecies I serotype(s) most frequently encountered	Most susceptible age groups	Typical symptoms or sign(s) of disease	Reference
Humans	Salmonella enteritis	Typhimurium, Enteritidis	Children (<4 yr)	Diarrhea, dysentery, fever	78
	Typhoid fever	Typhi[c]	Children and adults	Septicemia, fever[a]	78
	Paratyphoid fever	Sendai; Paratyphi A, B, and C[c]	Children and adults	Septicemia, fever[a]	78
Cattle	Salmonellosis	Typhimurium	Calves (<8 wk)	Diarrhea, dysentery, septicemia, fever	104
		Dublin	Calves and adult cattle	Diarrhea, dysentery, septicemia, abortion, fever	99, 104
Poultry	Pullorum disease	Pullorum[c,d]	Newly hatched birds	Diarrhea, septicemia	27
	Fowl typhoid	Gallinarum[c,d]	Growing stock and adults	Diarrhea, comb discoloration, septicemia	27
	Avian paratyphoid	Enteritidis, Typhimurium	Newly hatched birds	Diarrhea, septicemia	27
Sheep	Salmonellosis	Abortusovis[c]	Adult sheep	Septicemia, abortion, vaginal discharge	90
			Lambs	Diarrhea, dysentery, septicemia	90
		Typhimurium	Lambs	Diarrhea, dysentery, septicemia	90
Pigs	Pig paratyphoid	Choleraesuis[c]	Weaned and adult pigs	Skin discoloration, septicemia, fever[b]	106
	Salmonellosis	Typhimurium	Weaned pigs (<4 mo)	Diarrhea	106
	Chronic paratyphoid	Typhisuis		Intermittent diarrhea	7
Horses	Salmonellosis	Abortusequi[c]	Adult horses	Septicemia, abortion	110
			Foals	Diarrhea, septicemia	110
		Typhimurium	Foals	Diarrhea, septicemia	110
Wild rodents	Murine typhoid	Typhimurium, Enteritidis		Septicemia, fever	28

MINIREVIEW

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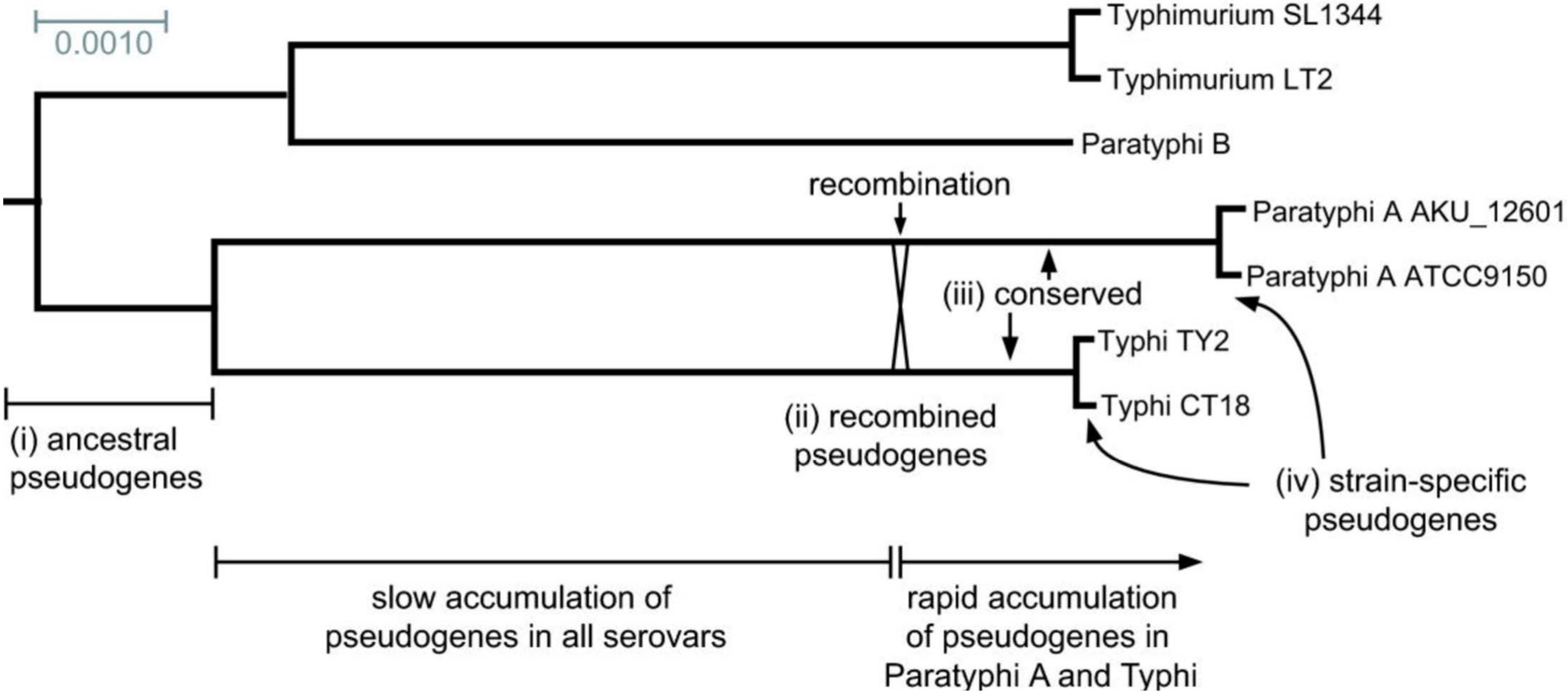
Department of Medical Microbiology and Immunology, College of Medicine,[1] and Department of Veterinary Pathobiology, College of Veterinary Medicine,[2] Texas A&M University, College Station, Texas 77843-4467

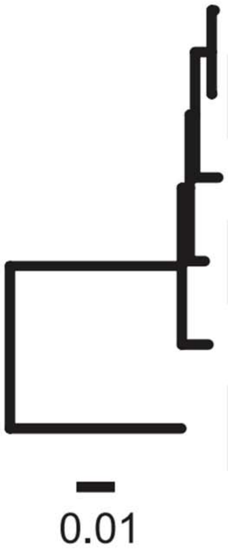
Pseudogene formation in *Salmonella*



Pseudogene accumulation in the evolutionary histories of Salmonella enterica serovars Paratyphi A and Typhi

Kathryn E Holt ✉, Nicholas R Thomson, John Wain, Gemma C Langridge, Rumina Hasan, Zulfiqar A Bhutta, Michael A Quail, Halina Norbertczak, Danielle Walker, Mark Simmonds, Brian White, Nathalie Bason, Karen Mungall, Gordon Dougan and Julian Parkhill

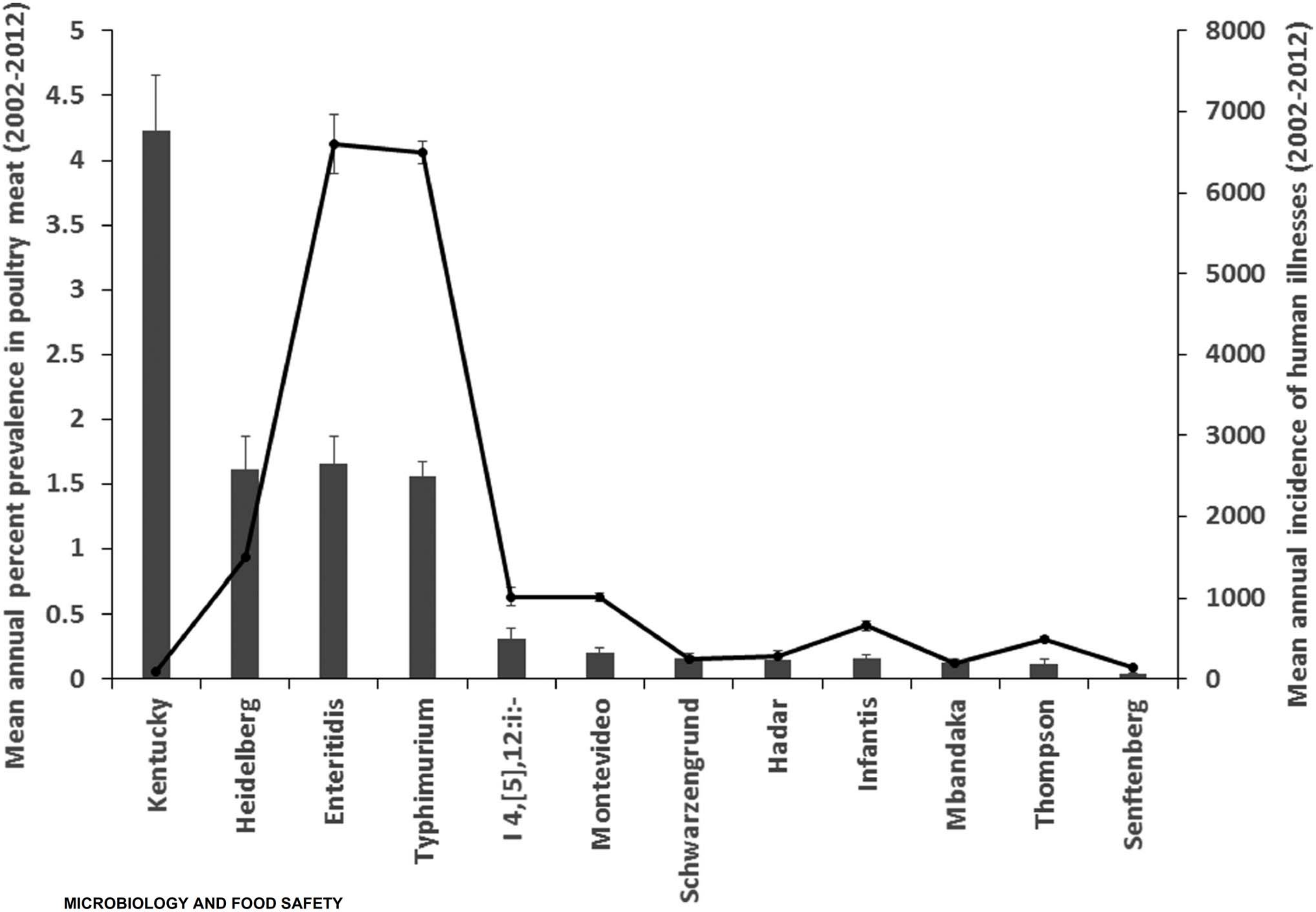
Pseudogene formation in *Salmonella*



	Number of protein-coding genes	Genome-wide K_a / K_s ratio	Number of pseudogenes classified by the number of inactivating mutations		
			1	2	3+
Gallinarum	3,965	0.100	141	4	2
Enteritidis	4,206	0.098	21	–	–
Choleraesuis	4,413	0.102	81	9	3
Typhimurium	4,423	0.097	13	–	–
Typhi	4,395	0.100	90	8	6
S. enterica subsp. *arizonae*	4,498	–	–	–	–

The Extinction Dynamics of Bacterial Pseudogenes

Chih-Horng Kuo¤, Howard Ochman*
Department of Ecology and Evolutionary Biology, University of Arizona, Tucson, Arizona, United States of America

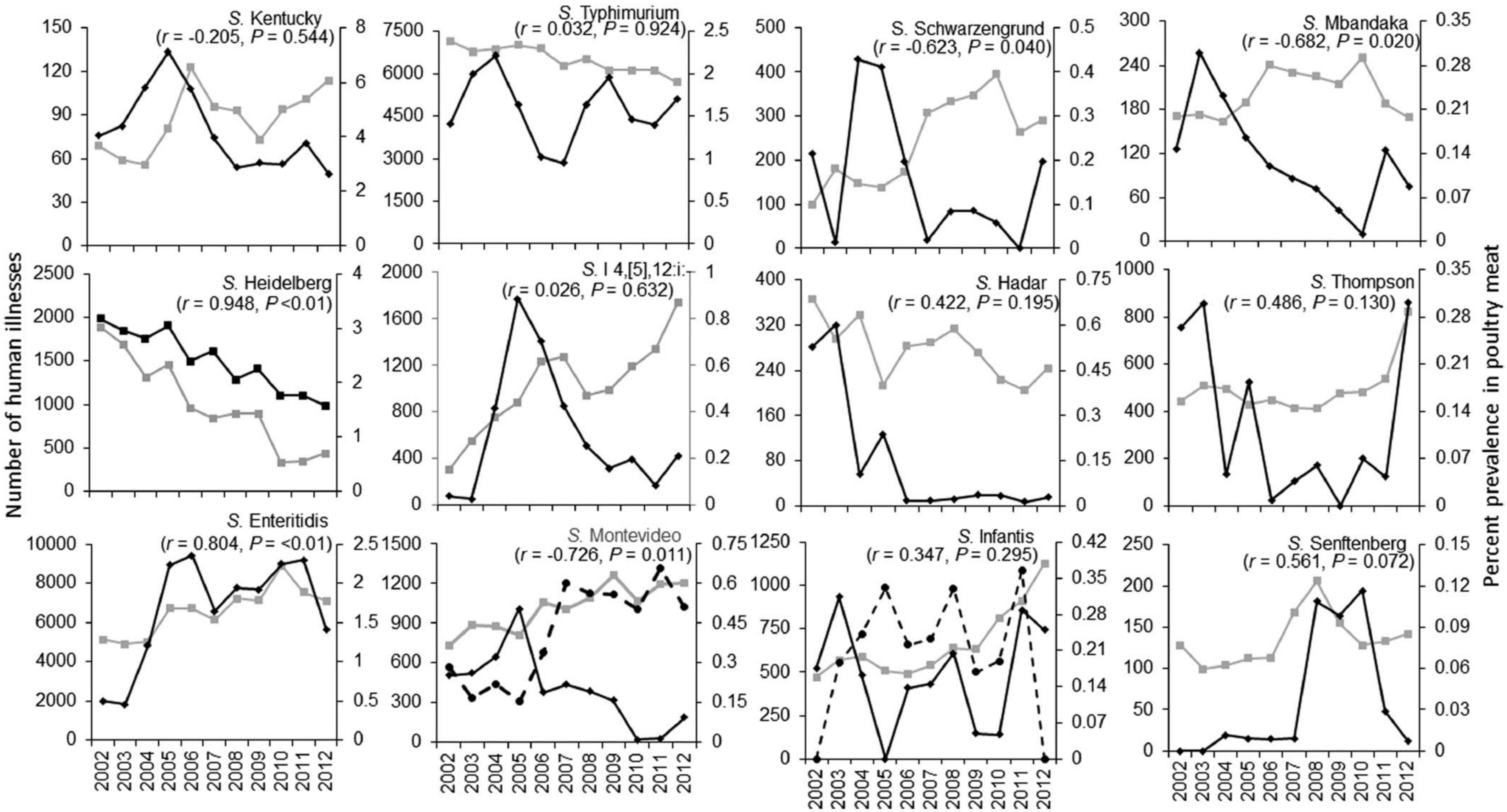


MICROBIOLOGY AND FOOD SAFETY

Population dynamics and antimicrobial resistance of the most prevalent poultry-associated *Salmonella* serotypes

Devendra H. Shah,[*,1] Narayan C. Paul,[*] Willium C. Sischo,[†] Rocio Crespo,[*] and Jean Guard[‡]

[*] *Department of Veterinary Microbiology and Pathology;* [†] *Department of Veterinary Clinical Sciences, Washington State University, Pullman, WA 99164-7040; and* [‡] *Egg Quality and Safety Research Unit, United States Department of Agriculture, Atlanta, GA 30605, USA*



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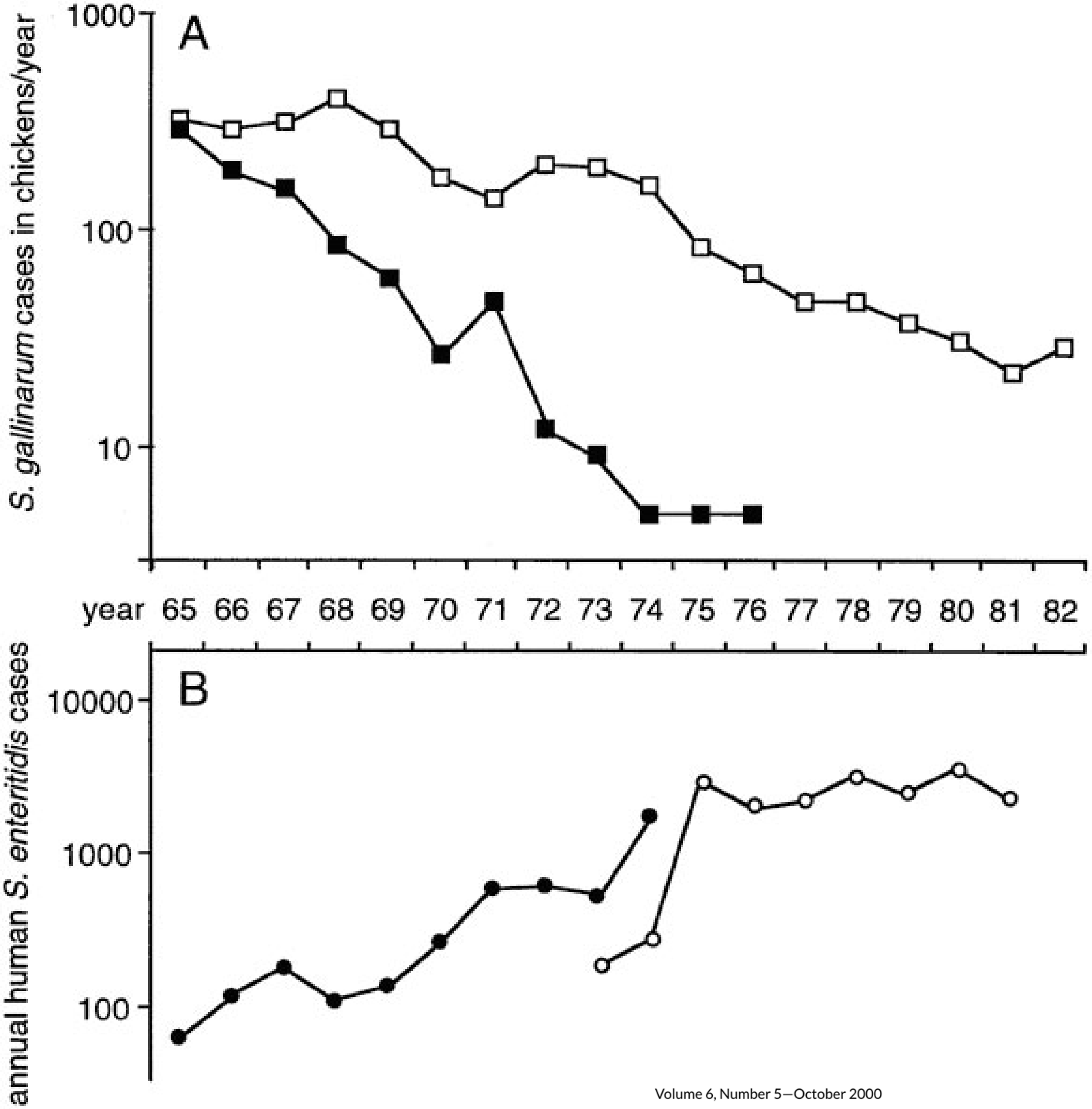
Washington State University, Pullman, WA 99164-7040; and [‡]*Egg Quality and Safety Research Unit,*
United States Department of Agriculture, Atlanta, GA 30605, USA

Niche replacement

- Principle of competitive exclusion applies to Salmonella
- Example: *Salmonella* Gallinarum, Pullorum, and Enteritidis
  - All are O9 antigen
  - Gallinarum and Pullorum were deadly to poultry and were eradicated
  - Enteritidis now occupies that niche
  - Enteritidis has tropism for the reproductive tract of the chicken
  - Spillover into table eggs occurs more frequently then pre-eradication of Gallinarum/Pullorum



Volume 6, Number 5—October 2000

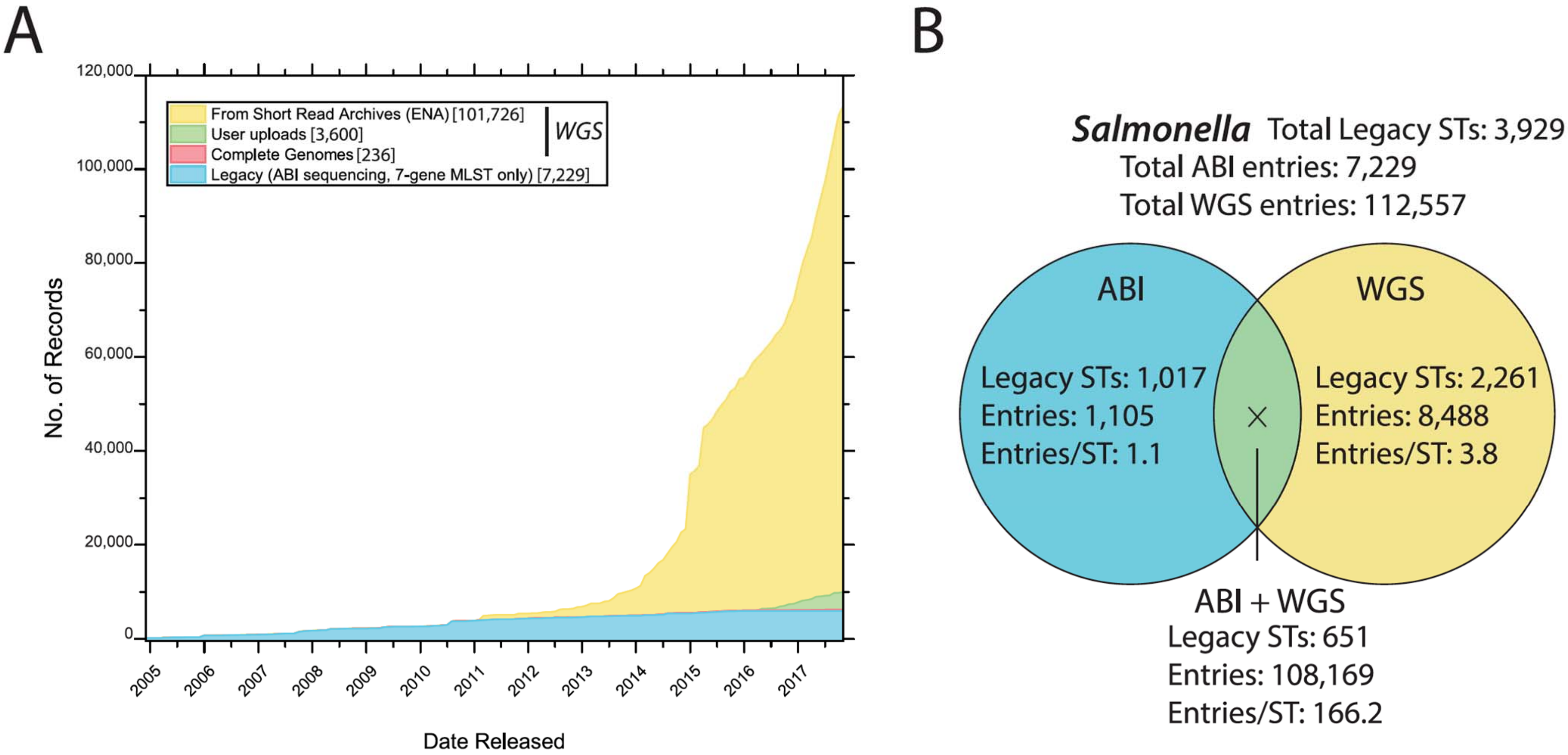
Perspective

Competitive Exclusion of *Salmonella* Enteritidis by *Salmonella* Gallinarum in Poultry

Wolfgang Rabsch*, Billy M. Hargis†, Renée M. Tsolis†, Robert A. Kingsley†, Karl-Heinz Hinz‡, Helmut Tschäpe*, and Andreas J. Bäumler†✉

Author affiliations: *Robert Koch Institute, Wernigerode, Germany; †Texas A&M University, College Station, Texas, USA; ‡School of Veterinary Medicine, Hanover, Germany

Whole genome sequencing is here!



REVIEW

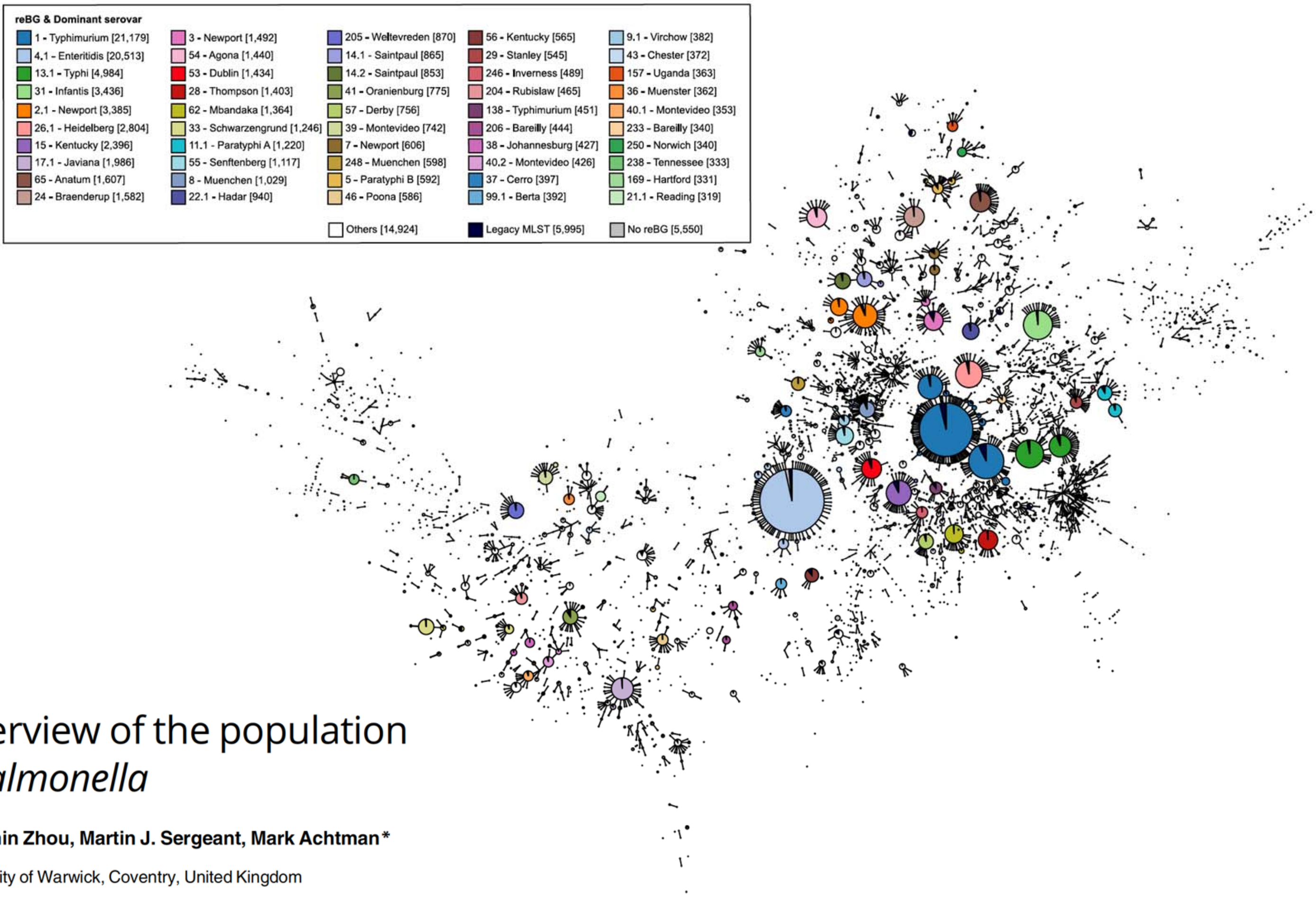
A genomic overview of the population structure of *Salmonella*

Nabil-Fareed Alikhan, Zhemin Zhou, Martin J. Sergeant, Mark Achtman*

Warwick Medical School, University of Warwick, Coventry, United Kingdom

Table 1. ***Salmonella*** **MLST genotyping schemes offered by EnteroBase (1 November, 2017).**

Legacy MLST	rMLST	cgMLST	wgMLST
7 Loci	51 Loci	3,002 Loci	21,065 Loci
Conserved housekeeping genes	Ribosomal genes	A soft subset of core genes from wgMLST	All pan-genomic coding sequences from 537 completed/ representative genomes
Conserved low resolution	Highly conserved medium resolution	Variable high resolution	Ultravariable extreme resolution
Different scheme for each species	Single scheme across tree of life	Different scheme for each genus	Different scheme for each genus
STs: 3,929 eBGs: 360	rSTs: 5,454 reBGs: 337	cgSTs: 96,108	wgSTs: 112,409



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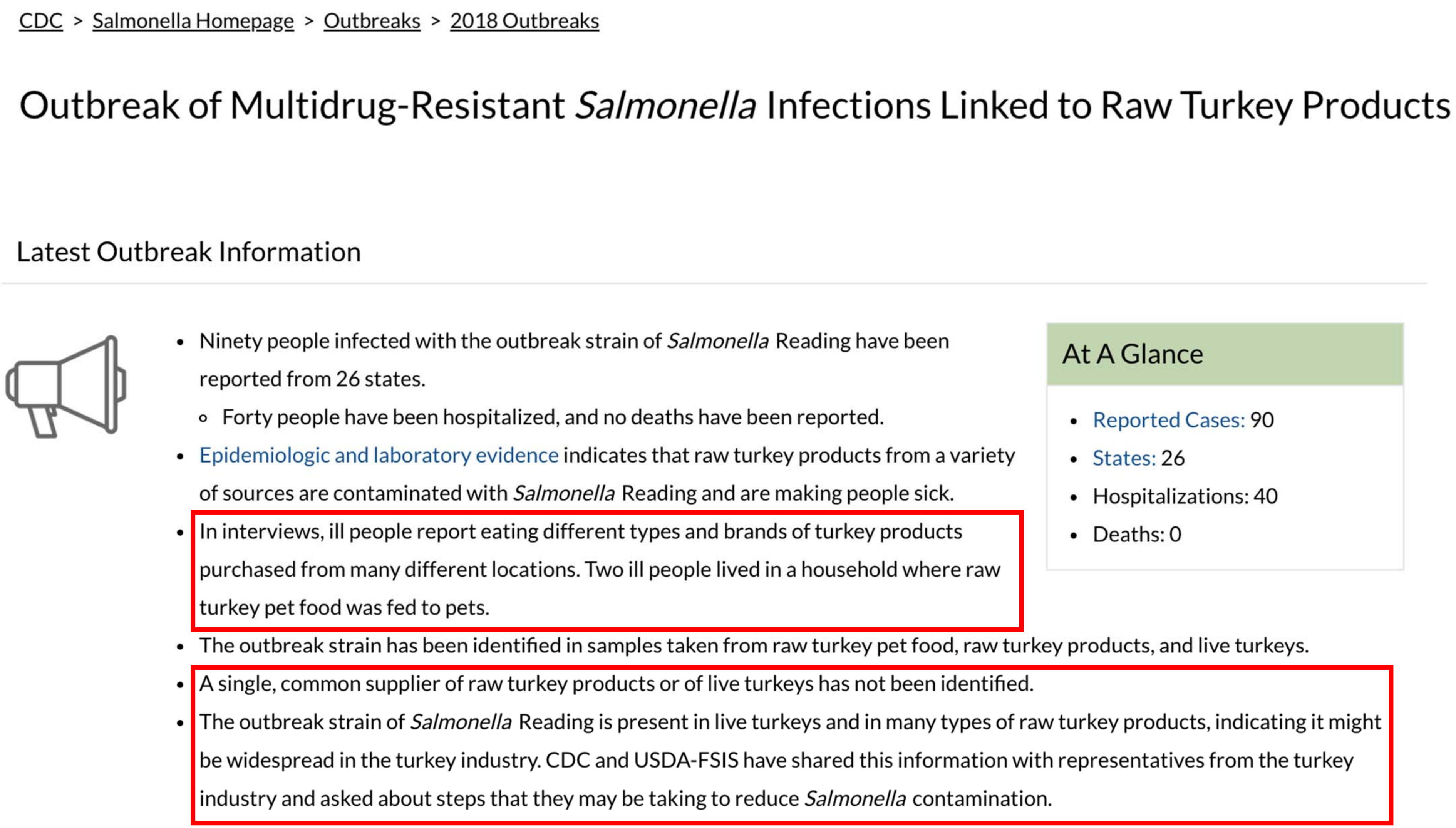


CDC > Salmonella Homepage > Outbreaks > 2018 Outbreaks

Outbreak of Multidrug-Resistant *Salmonella* Infections Linked to Raw Turkey Products

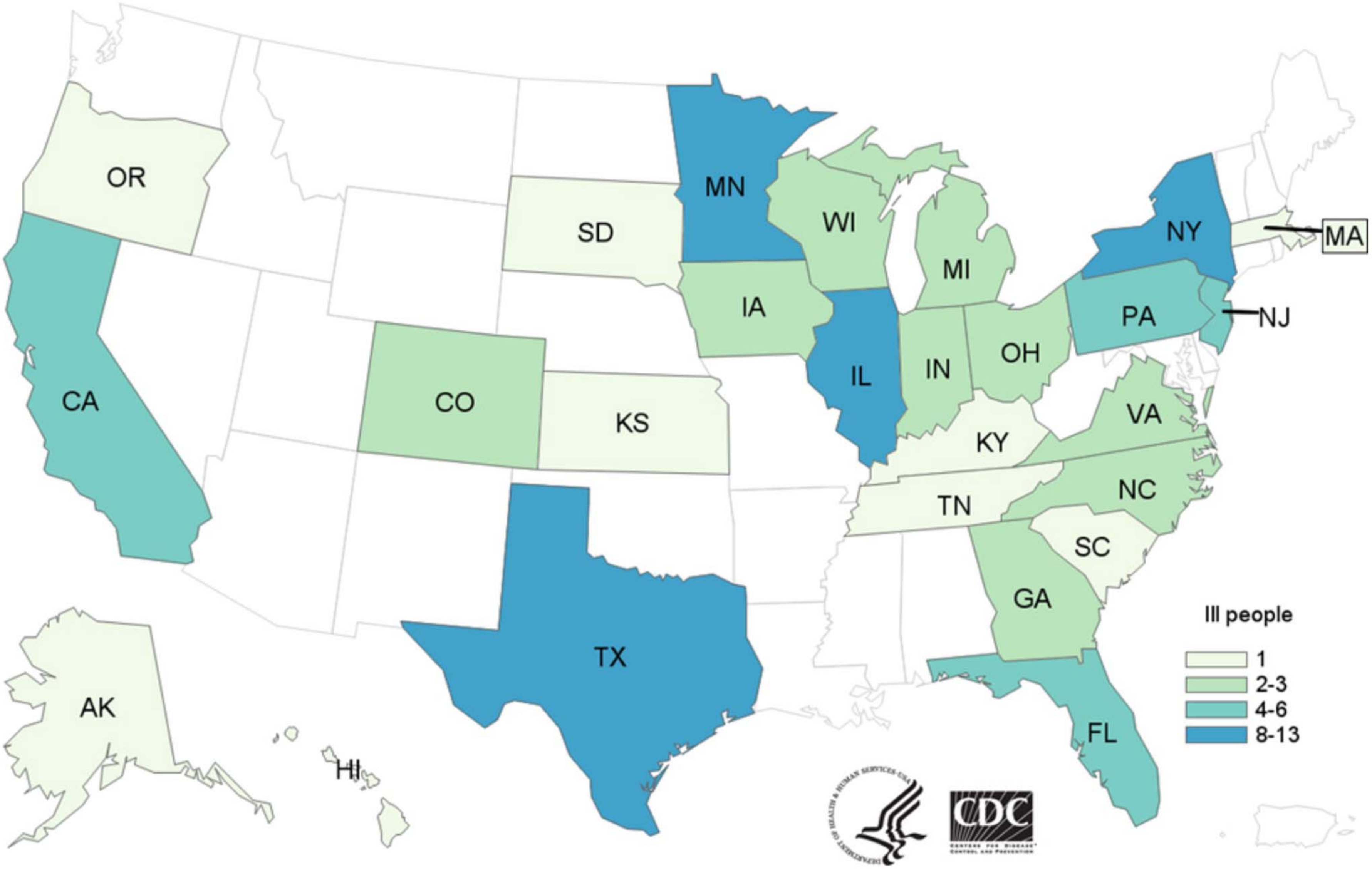
Latest Outbreak Information

- Ninety people infected with the outbreak strain of *Salmonella* Reading have been reported from 26 states.
    - Forty people have been hospitalized, and no deaths have been reported.
- Epidemiologic and laboratory evidence indicates that raw turkey products from a variety of sources are contaminated with *Salmonella* Reading and are making people sick.
- In interviews, ill people report eating different types and brands of turkey products purchased from many different locations. Two ill people lived in a household where raw turkey pet food was fed to pets.
- The outbreak strain has been identified in samples taken from raw turkey pet food, raw turkey products, and live turkeys.
- A single, common supplier of raw turkey products or of live turkeys has not been identified.
- The outbreak strain of *Salmonella* Reading is present in live turkeys and in many types of raw turkey products, indicating it might be widespread in the turkey industry. CDC and USDA-FSIS have shared this information with representatives from the turkey industry and asked about steps that they may be taking to reduce *Salmonella* contamination.

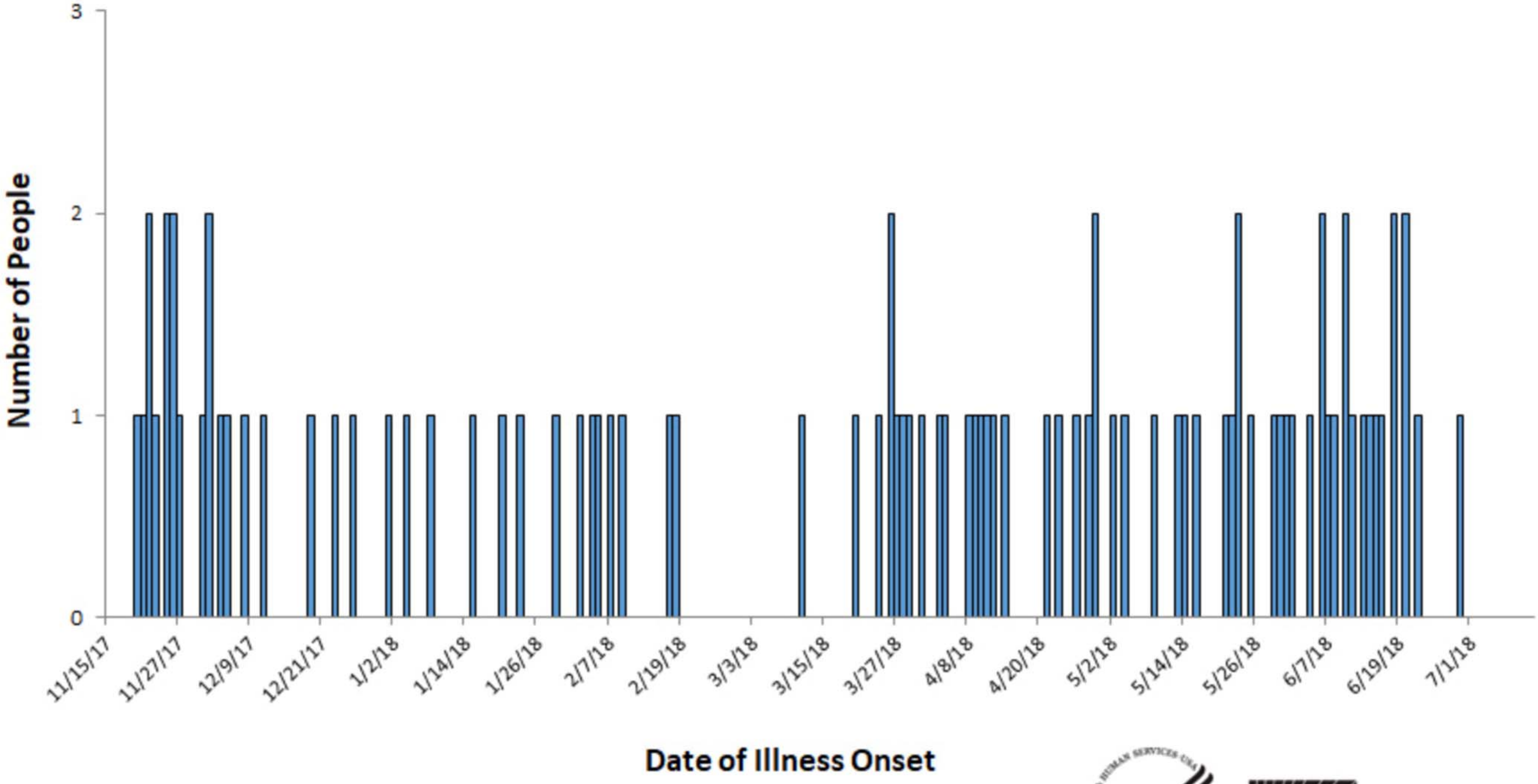
At A Glance

- Reported Cases: 90
- States: 26
- Hospitalizations: 40
- Deaths: 0

People infected with the outbreak strain of *Salmonella* Reading, by state of residence, as of July 11, 2018 (n=90)

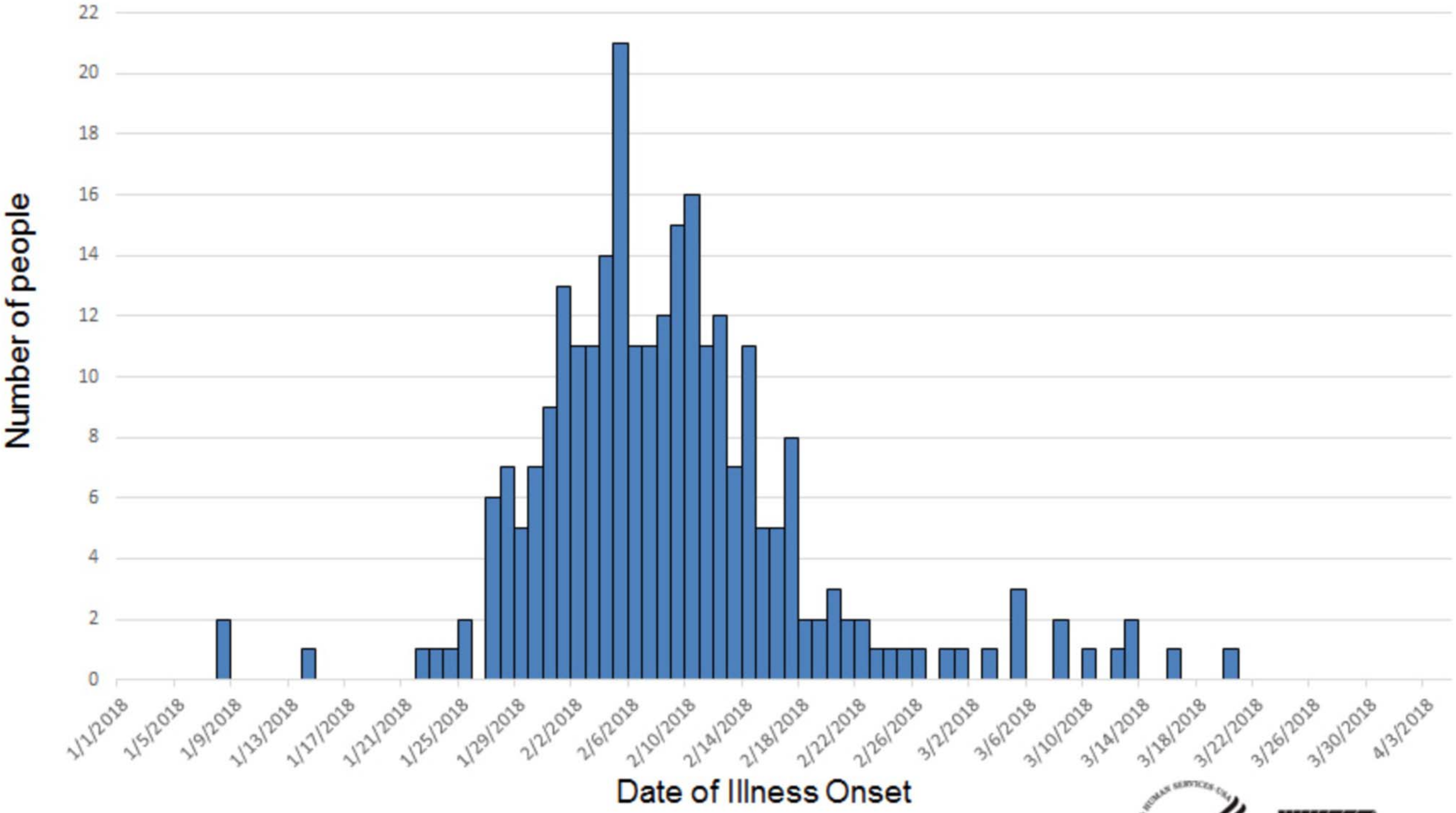


People infected with the outbreak strain of *Salmonella* Reading, by date of illness onset*

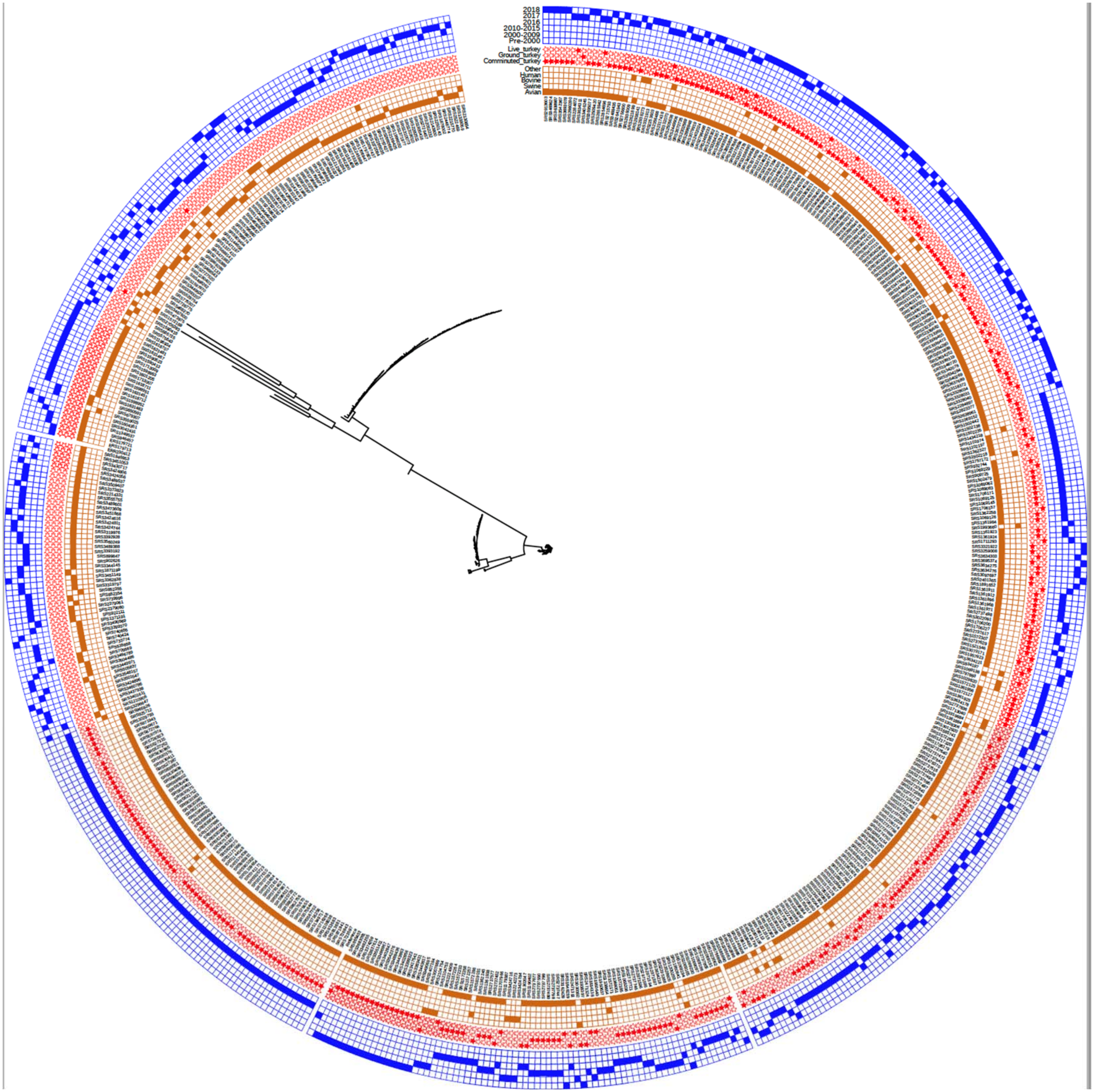


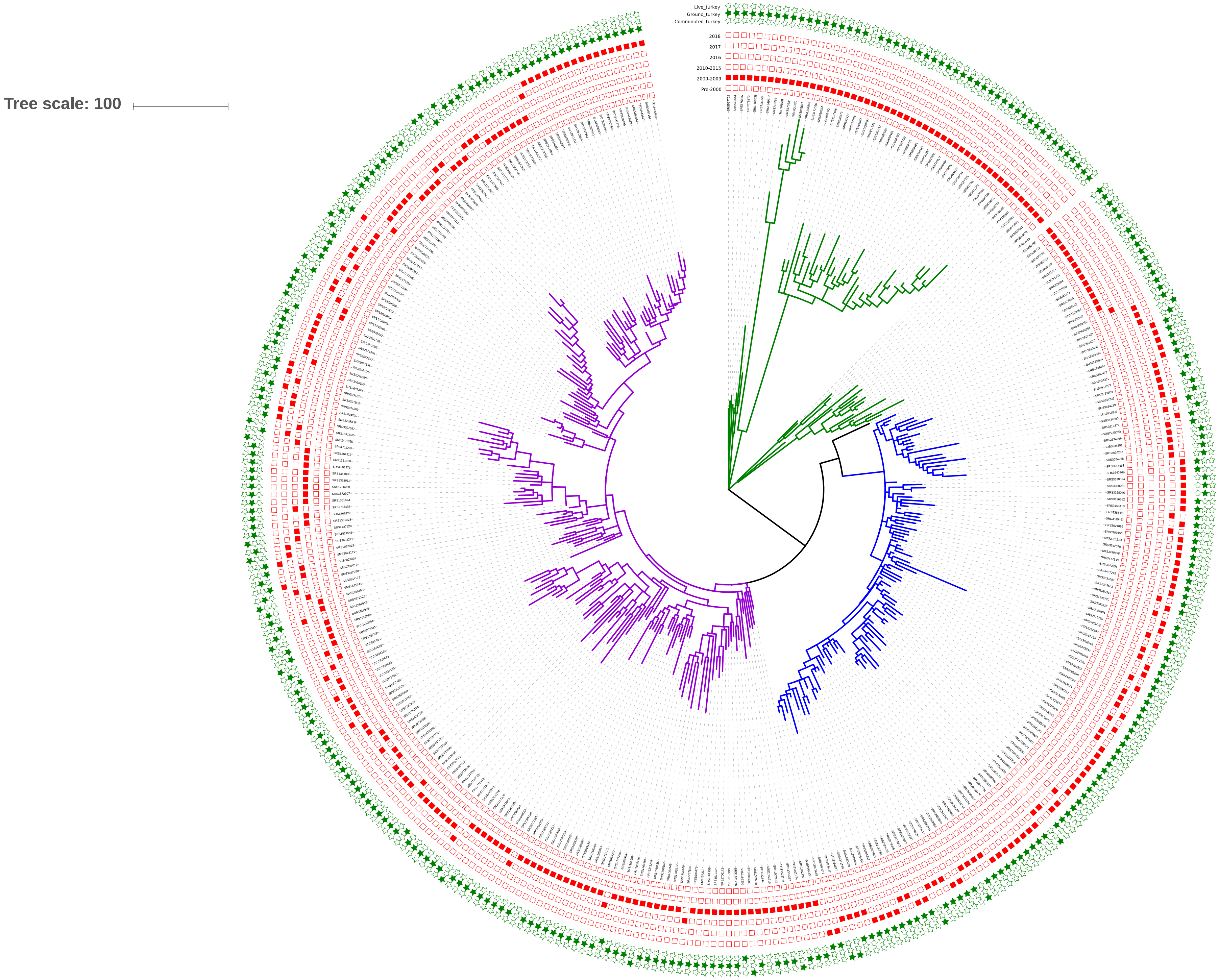
*n=90 for whom information was reported as of July 11, 2018. Some illness onset dates have been estimated from other reported information.

People infected with the outbreak strains of *Salmonella* Typhimurium, by date of illness onset*



*n=265 for whom information was reported as of April 4, 2018. Some illness onset dates have been estimated from other reported information.

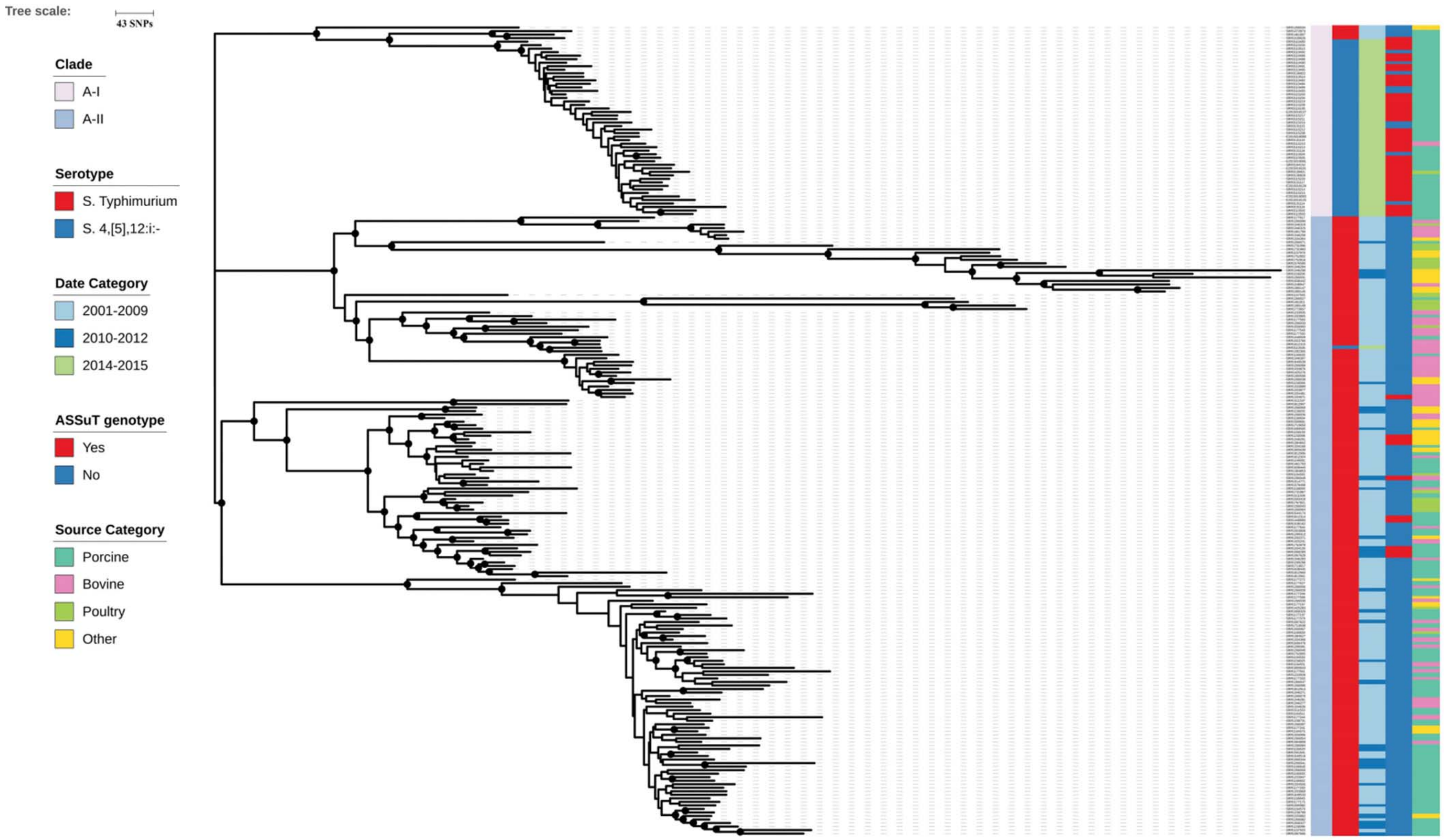

2018
2017
2016
2010-2015
2000-2009
Pre-2000
Live_turkey
Ground_turkey
Comminuted_turkey
Other
Human
Bovine
Swine
Avian


Tree scale: 100
Live_turkey
Ground_turkey
Comminuted_turkey
2018
2017
2016
2010-2015
2000-2009
Pre-2000

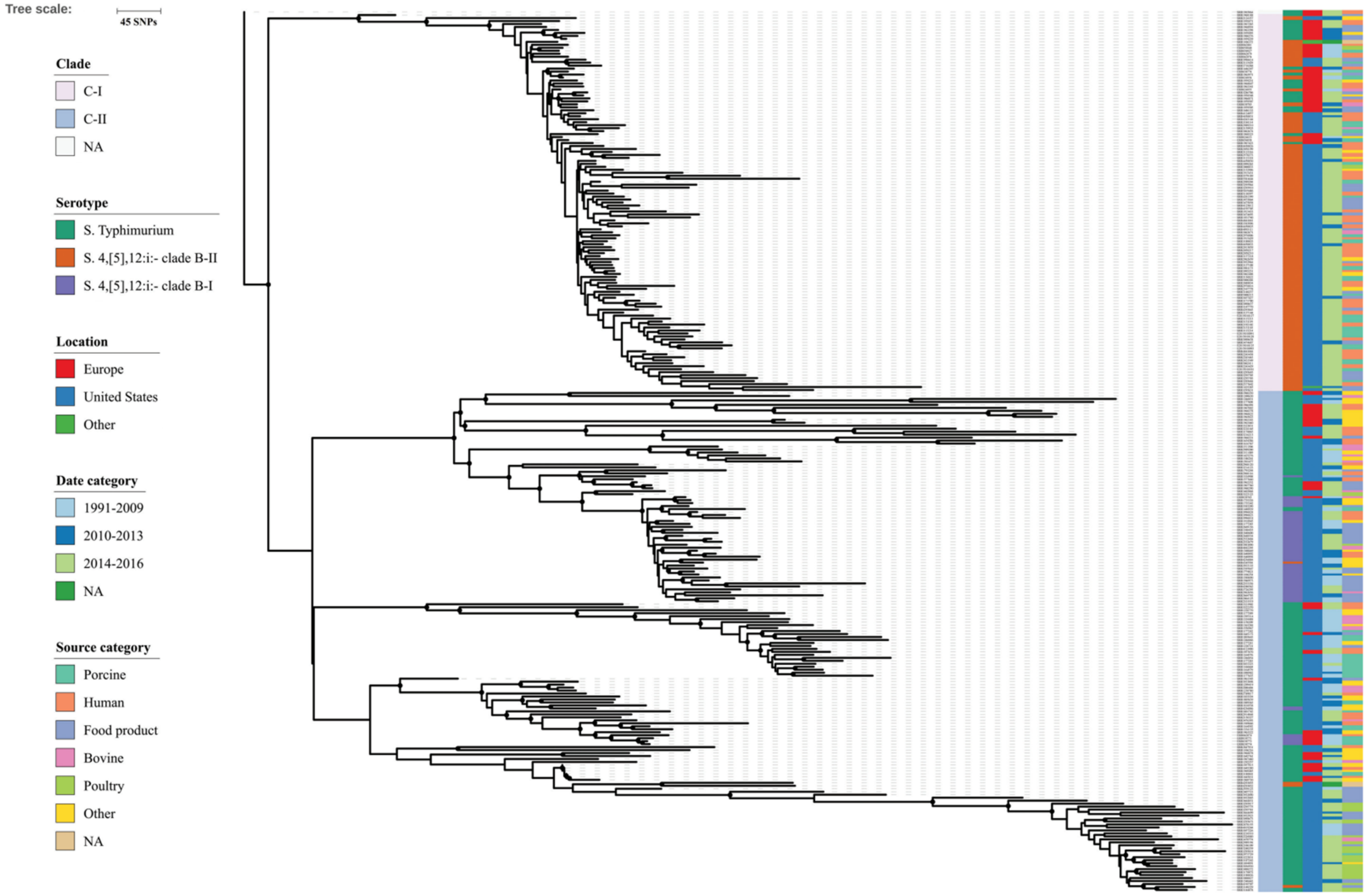
What I learned about the outbreak *Salmonella* Reading without any sampling of my own

- A new strain has emerged in the last two years
- The abundance of this strain is higher in turkey products than previous Reading strains
- It harbors a mobile DNA encoding drug resistance (ampicillin and tetracycline)
- Does not seem more virulent; however it has occupied a niche in turkeys

Salmonella 4,[5],12:i:- emergence in Europe and dissemination to USA



Salmonella 4,[5],12:i:- emergence in Europe and dissemination to USA



Take-home:

- *Salmonella* adapt and evolve to their surroundings
- Host adaptation versus host range are ongoing evolutionary forces
- Plasmids play a major role in adaptation
- Niche displacement occurs at both serovar and strain level