GenEpi Bio-Train Virtual training 23

Pathogenic *E. coli:* diagnostics, typing and when the infection is notifiable – an overview

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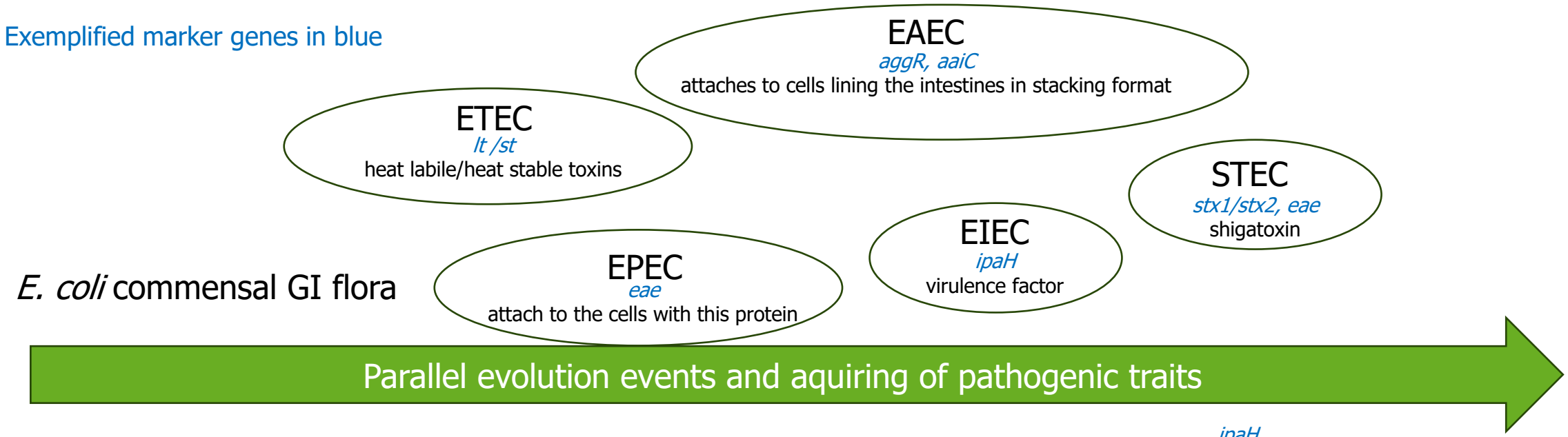
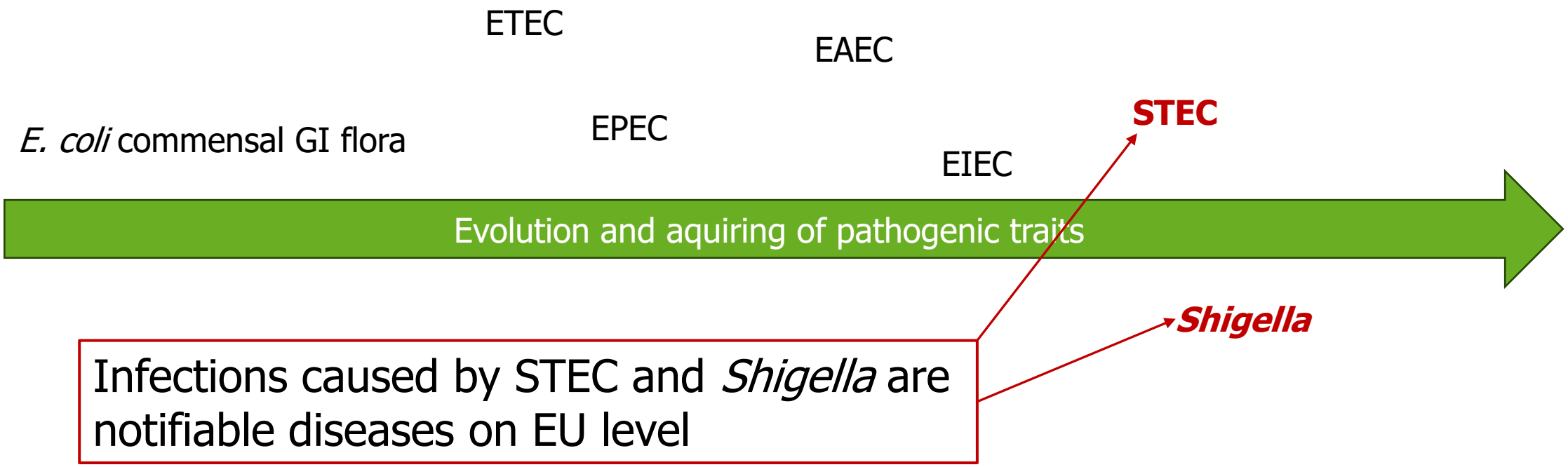
E. coli: the good, the bad, and the deadly*



- **ETEC**: (Enterotoxigenic *E. coli*) attaches to the intestines via fimbriae. Produces toxins. "Travelers' diarrhoea". Produces heat labile/heat stable toxins (*lt /st*)
- **EPEC**: (Enteropathogenic *E. coli*) attaches to cells in the intestines via the protein intimin (eae) and causes watery, sometimes bloody diarrhoea.
- **EAEC**: (Enteroaggregative *E. coli*) attaches to the cells lining the intestines in stacking format. Produce toxins. (*aggR, aaiC*)
- **EIEC**: (Enteroinvasive *E. coli*) invades and disrupt colon cells lining. (*ipaH*)
- **STEC**: (Shiga toxin-producing *E. coli*).Attach by intimin protein (*eae*), produce shigatoxins (stx1/stx2). Could progress to kidney failure and hemolytic uremic syndrome (HUS) which can be fatal.

* Expression borrowed from FAQ: E. Coli: Good, Bad, and Deadly | ASM.org

E. coli: the good, the bad, and the deadly*



Infections caused by STEC and *Shigella* are notifiable diseases on EU level

EU case definitions on notifiable diseases within the context of pathogenic *E. coli*/ *Shigella*

Simplified versions for laboratory criteria for a confirmed case

- Shiga toxin-producing *E. coli* – STEC:
  - Isolation/cultivation of *E.coli* that produces shigatoxin or harbours *stx1* or *stx2* genes.
  - Direct detection of *stx1* or *stx2* gene(s) nucleic acid
- *Shigella*:
  - Confirmed case: Isolation of *Shigella* spp. from a clinical specimen
  - Probable case: Detection of *Shigella* spp. nucleic acid in a clinical specimen

EU case definitions: COMMISSION IMPLEMENTING DECISION (EU) 2018/ 945 - of 22 June 2018 - on the communicable diseases and related special health issues to be covered by epidemiological surveillance as well as relevant case definitions

Many microbiological laboratories in EU/EEA use PCR panels, i.e. syndromic panels as diagnostic procedure

GI PCR panel

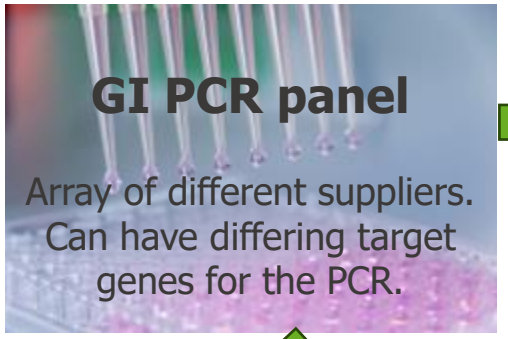
Array of different suppliers. Can have differing target genes for the PCR.

Notification only (no isolate)

- **To medical doctor/patient for possible treatment and follow up measures**
- **If notifiable disease, report to national authority -> ECDC**

TYPING

Many microbiological laboratories in EU/EEA use PCR panels, i.e. syndromic panels as diagnostic procedure



Notification only (no isolate)

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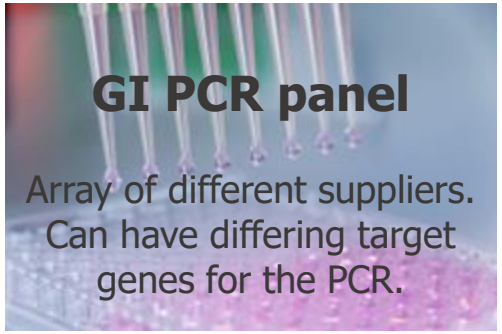
Benefits and drawbacks of using PCR-panels (a k a syndromic panels, culture-independent diagnostic tests)



Benefits - examples

- The ability to detect multiple pathogens in one test
- Higher sensitivity for difficult-to-culture bacteria
- Faster results enabling timely treatment and control measures

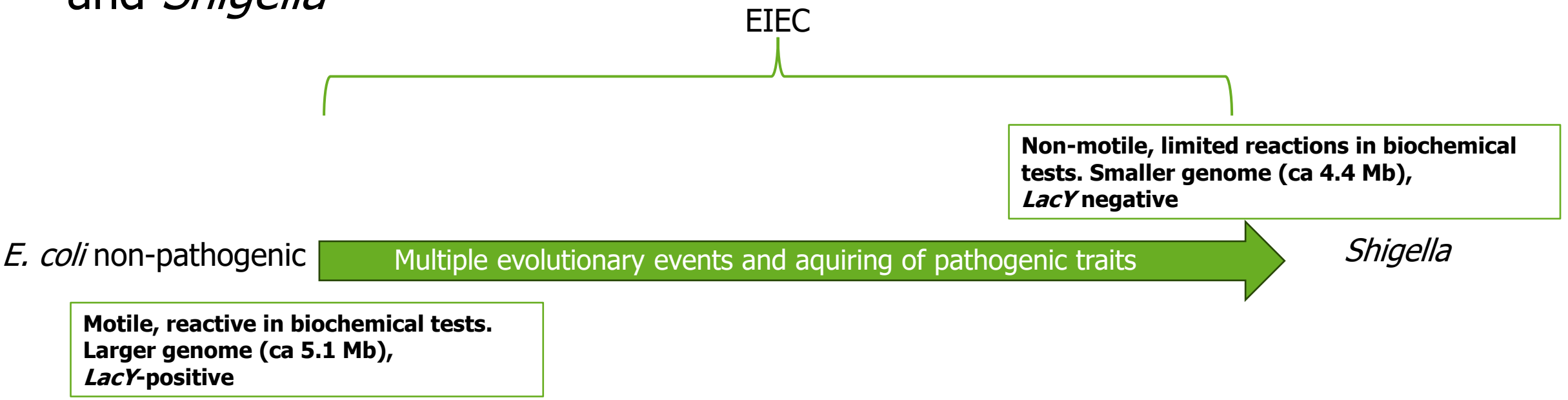
Challenges - examples

- Lack of cultured isolates critical for outbreak detection, antimicrobial resistance testing, and molecular surveillance.

- Inability to distinguish some closely related pathogens (e.g. *Shigella* vs EIEC) or gene variants (e.g., *stx1* vs *stx2* in STEC).

EIEC (Enteroinvasive *E. coli)* vs *Shigella*

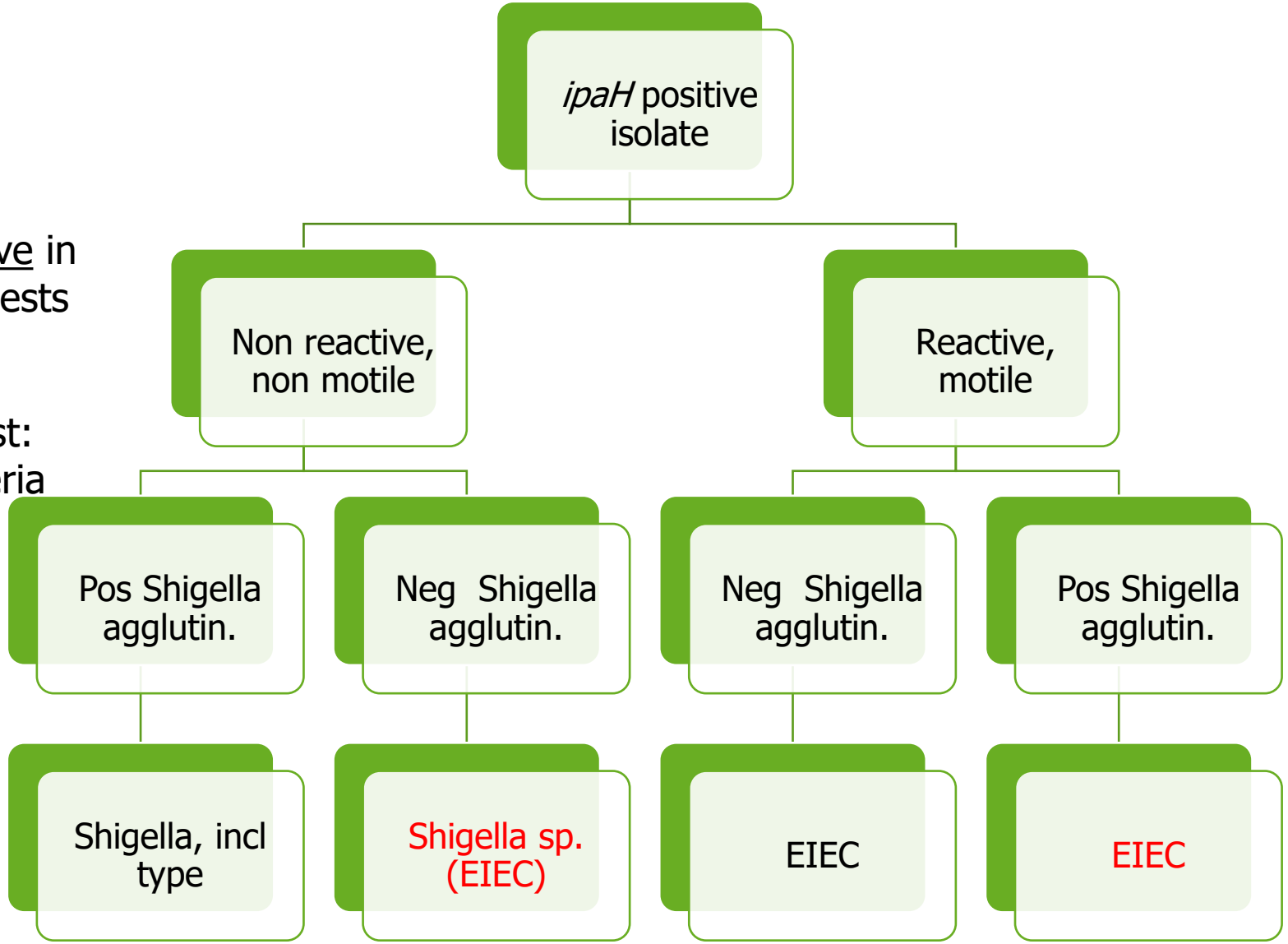
- EIEC can be found on a spectrum between *E.coli* like to *Shigella* like phenotypic properties.
- Marker gene for molecular detection, *ipa*H, is found both in EIEC and *Shigella*



Classical phenotypic distinction between *Shigella* and EIEC isolates

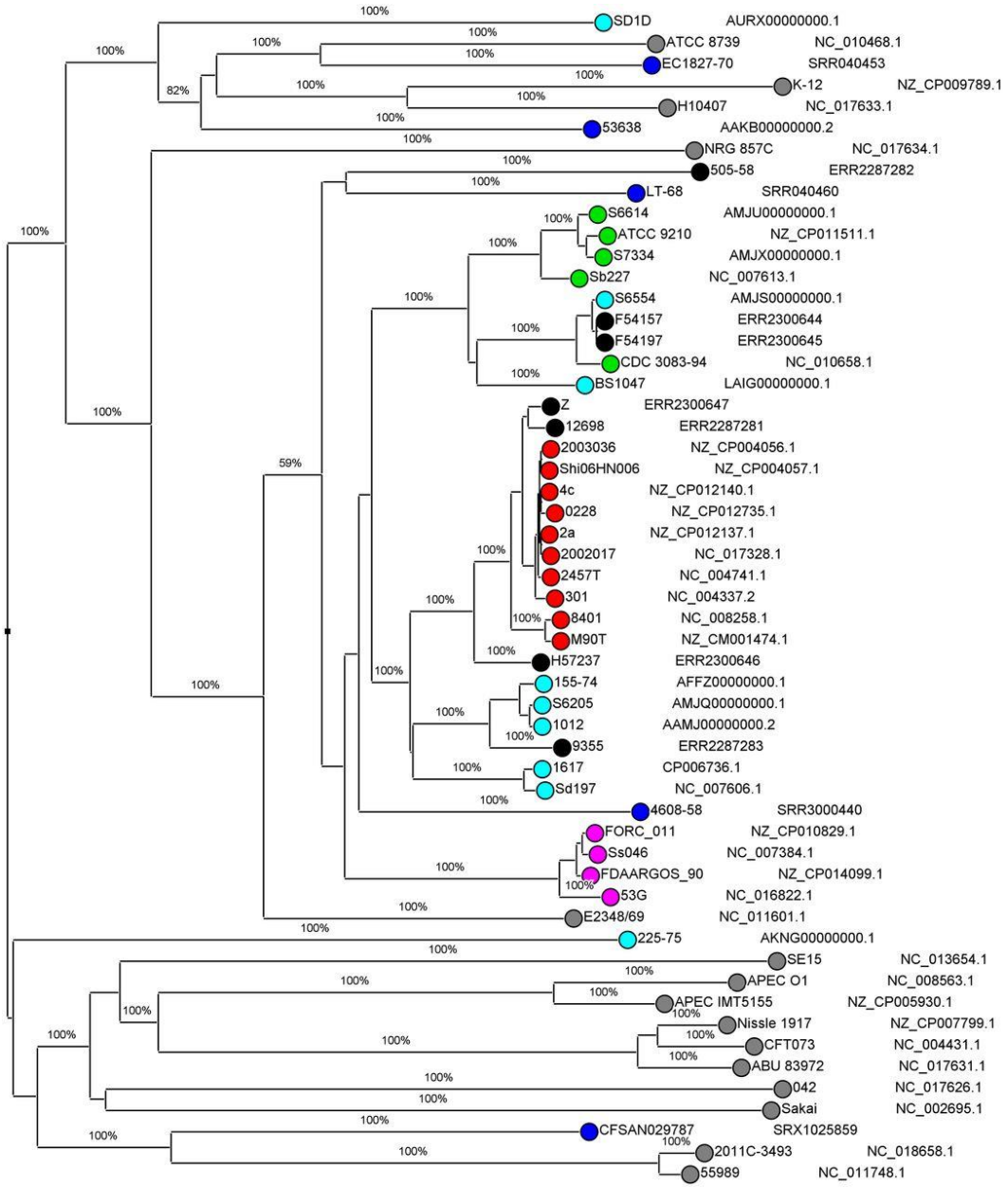
(Non-) reactive in biochemical tests

Agglutination test: serotyping bacteria (O and H)



Simplified schema

Clustering the four *Shigella* species, EIEC and additional *E. coli* pathotype in the phylogenetic tree same



Neighbor-joining tree for core-genome MLST, with distance based on *E. coli* cgMLST (EnteroBase).

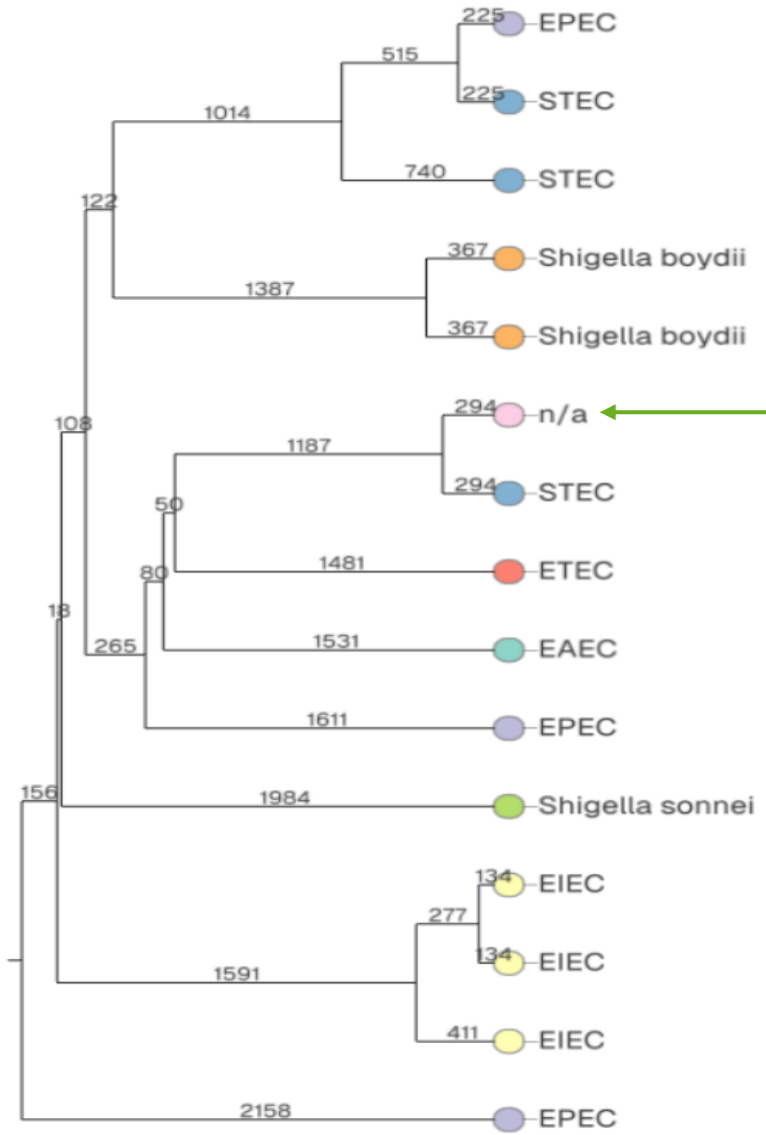
- *S. dysenteriae*
- *S. flexneri*
- *S. boydii*
- *S. sonnei*
- EIEC
- other pathotypes of *E. coli*

Courtesy Evaluation of a Culture-Dependent Algorithm and a Molecular Algorithm for Identification of Shigella spp., Escherichia coli, and Enteroinvasive E. coli | Journal of Clinical Microbiology

Molecular based typing of *E.coli* and Shigella, including whole genome sequencing

- Pathogenic marker genes providing the pathotype (*ipaH*, *stx*, *eae*.... etc)
- Serotype providing the O and H type (e.g. O157:H7)
- Sequence type (ST) based on the 7 gene MLST schema
- Cluster analysis

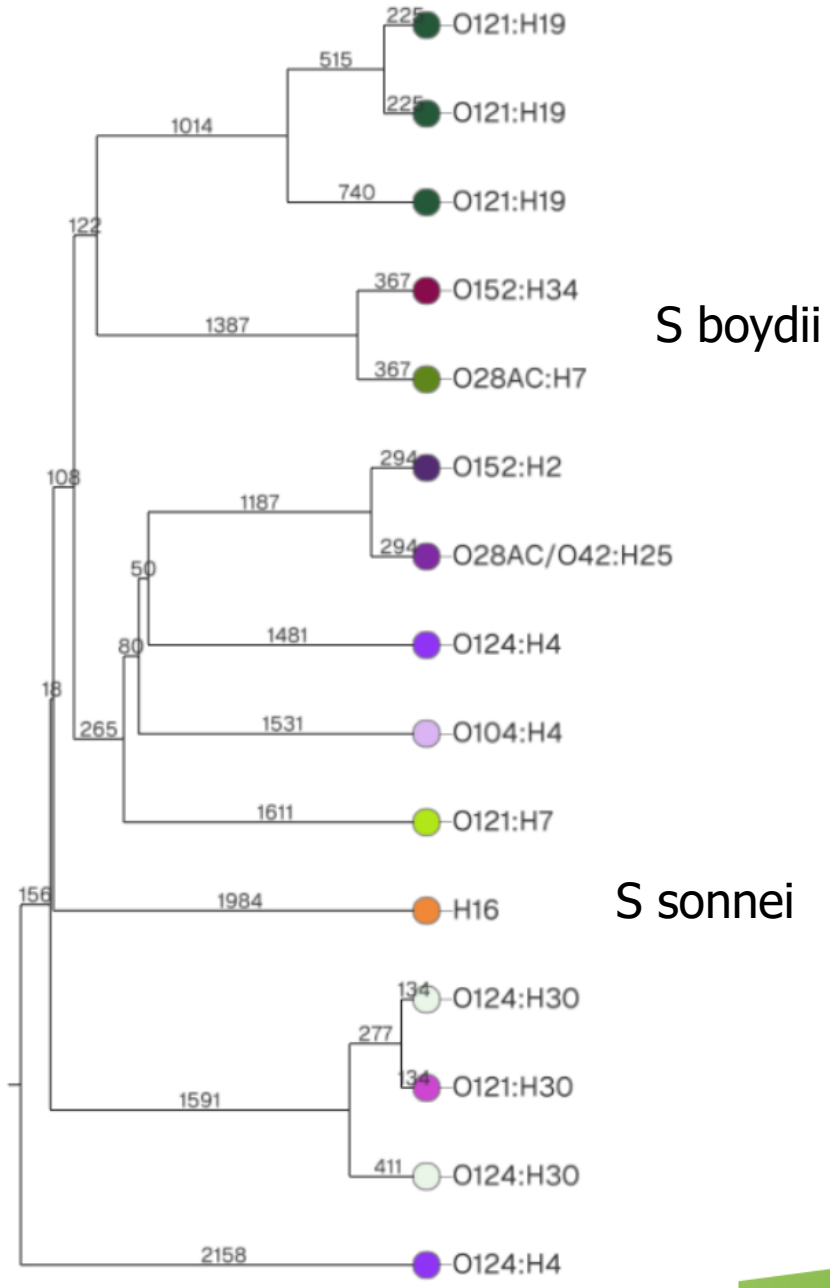
Pathotype/species



E. coli with no detected pathogenic marker genes

cgMLST, single linkage tree. From ECDC EpiPulse molecular typing tool with integrated Microreact

Serotype



S boydii

S sonnei

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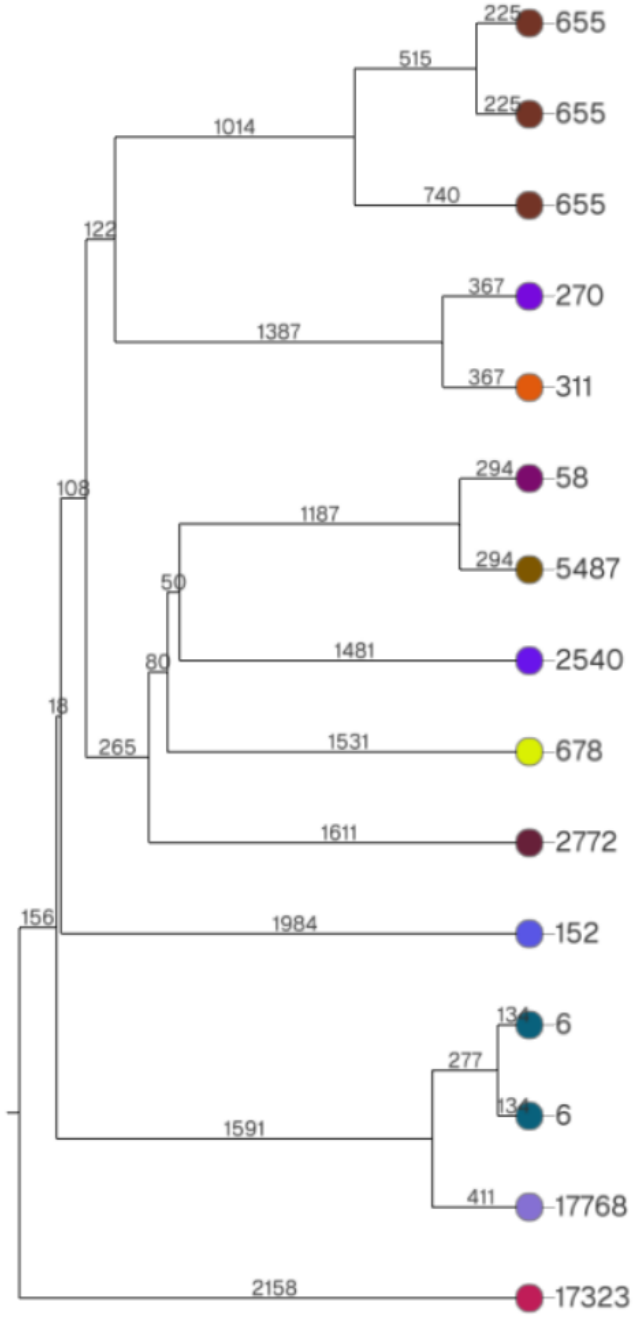
Sequence type (ST)



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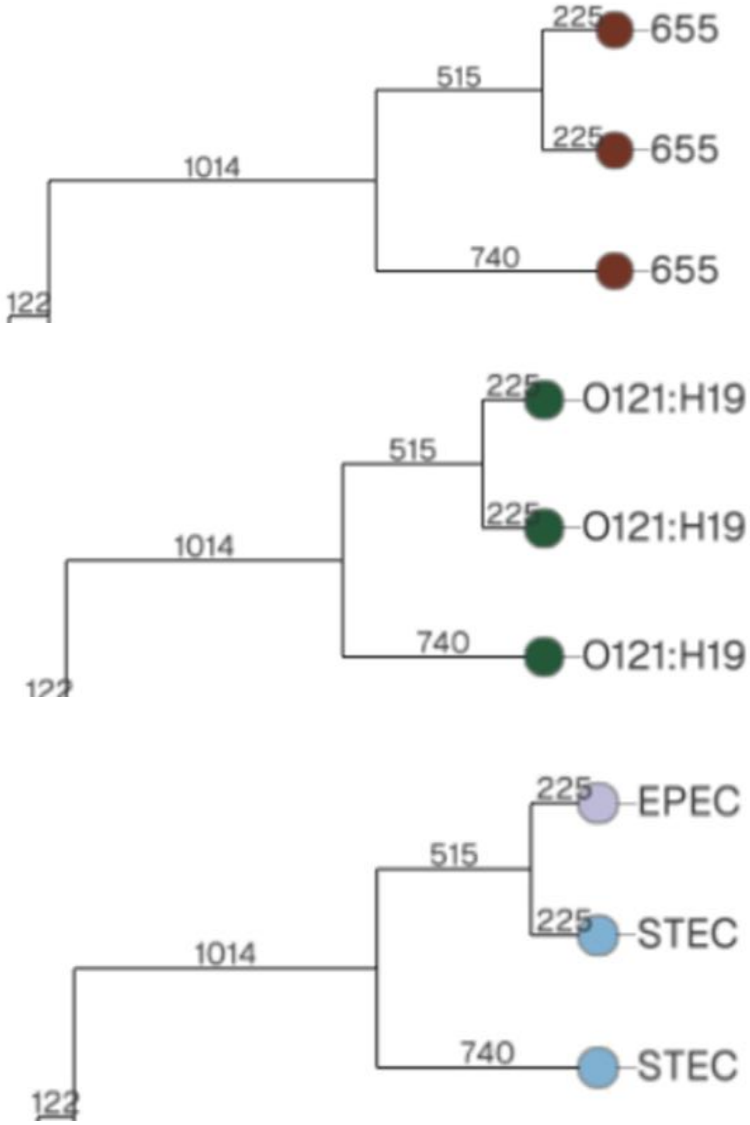


only *eae* positive

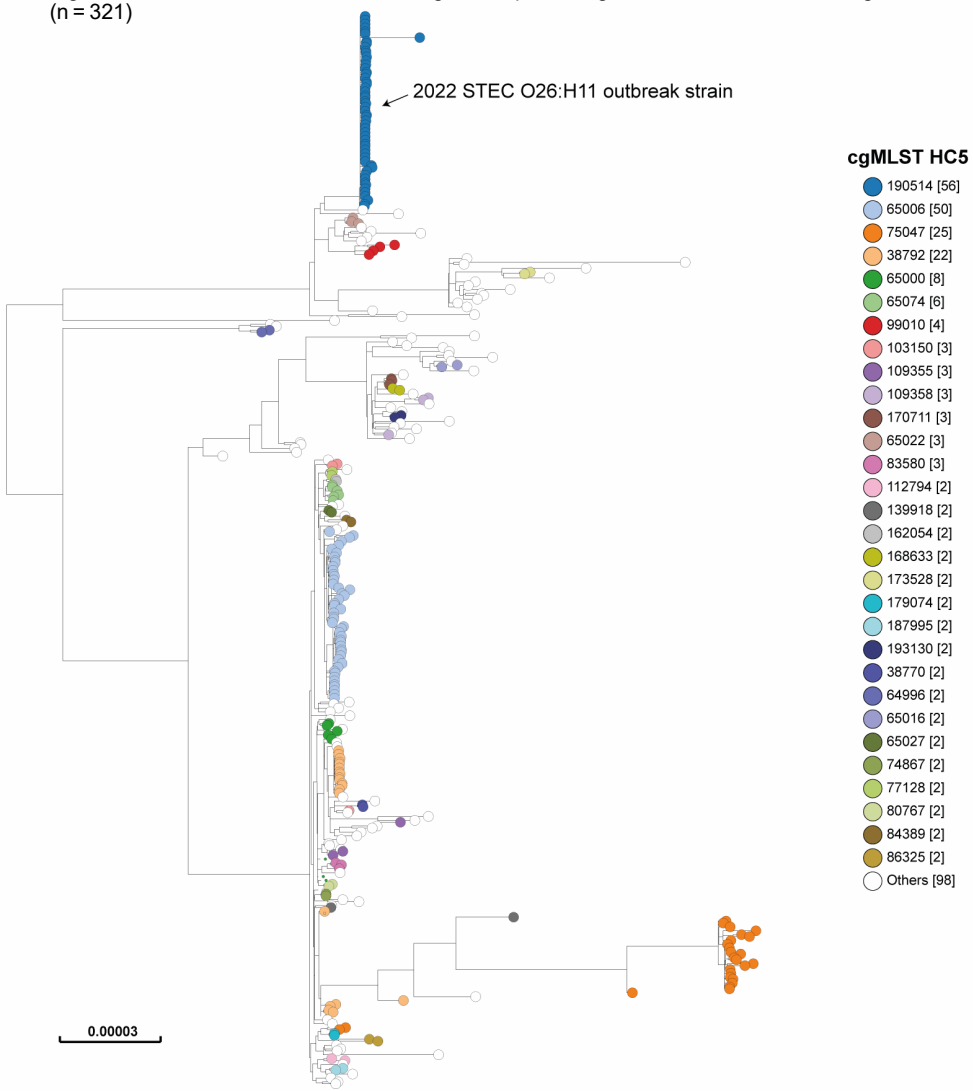
stx (and *eae*) positive

Nationwide outbreak of Shiga toxin-producing *Escherichia coli* infections associated with frozen pizzas, France, 2022

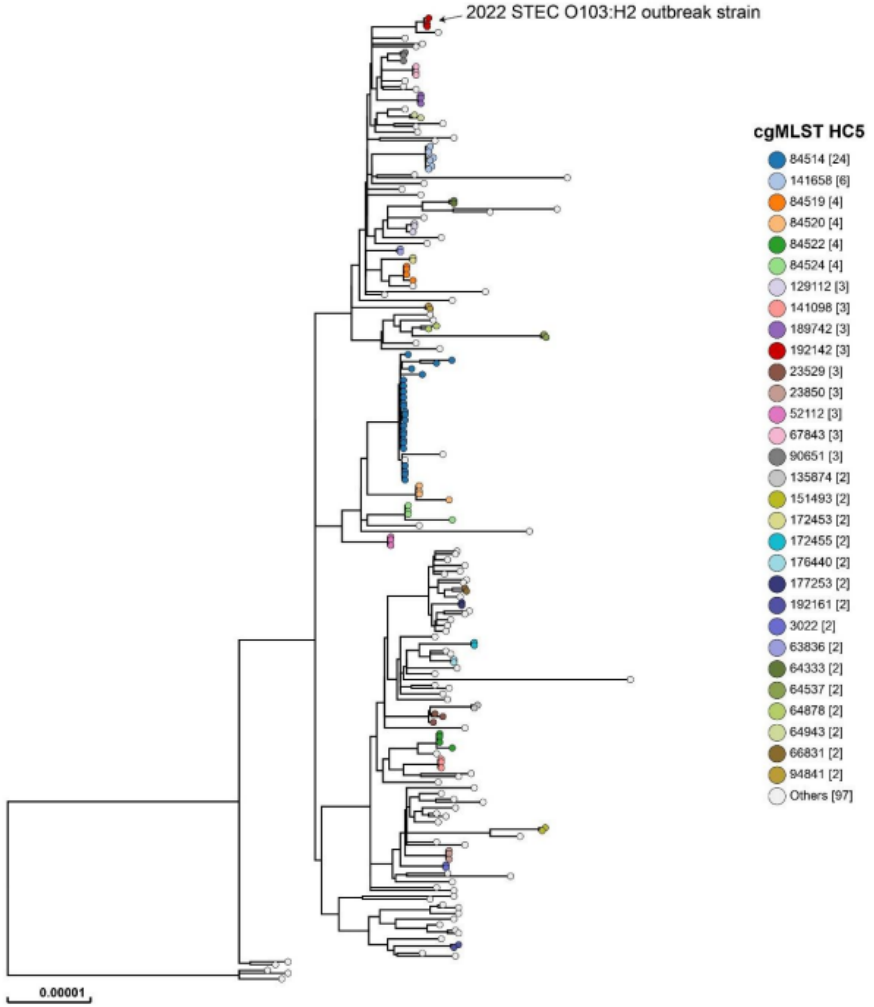
Catarina Krug[1,2], Nathalie Jourdan-Da Silva[1], Mathieu Tourdjman[1], Patricia Mariani-Kurkdjian[3], Aurélie Cointe[3], Sophie Lefèvre[4], Sophie Bélichon[5], Claire Postic[5], Marie Françon[6], Hubert Herber[6], Delphine Sergentet[7], Sarah Ganet[7], Alicia Faure-Bondat[7], Marion Debin[8], Charly Kengne-Kuetche[8], Henriette de Valk[1], Stéphane Bonacorsi[3], François-Xavier Weill[4] ORCID icon, Gabrielle Jones[1], on behalf of the Outbreak Investigation Team[9]

- Largest documented STEC outbreak in France
- High severity – 50 cases of HUS (haemolytic uraemic syndrome), two deaths
- Two different strains/serotypes with different *stx* gene variants
- Frozen pizza, specifically the dough, was the cause of the outbreak

Figure 2. Maximum-likelihood tree of Shiga toxin-producing Escherichia coli O26:H11 genomic sequences, France, 2015–2022 (n = 321)



Supplementary Figure 1 : Maximum-likelihood tree of Shiga toxin-producing *Escherichia coli* O103:H2 genomic sequences, 2001–2022 (n = 200)



Eurosurveillance | Nationwide outbreak of Shiga toxin-producing Escherichia coli infections associated with frozen pizzas, France, 2022

Thank you!