Are all *L. monocytogenes* strains of health concern?

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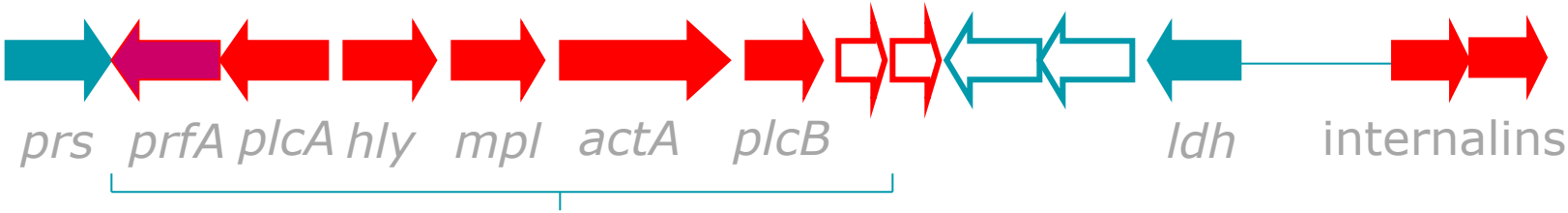
efsa
European Food Safety Authority

IMPORTANT MOLECULAR TRAITS FOR LISTERIA VIRULENCE

LIPI-1



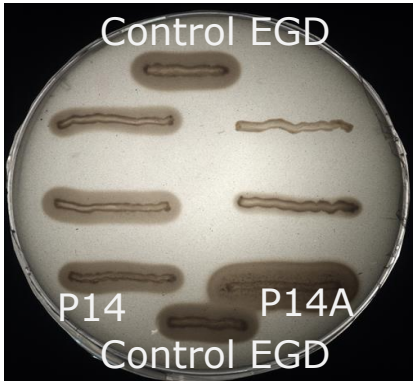
LIPI-2: in *Listeria ivanovii* (Dominguez-Bernal et al., 2006)

LIPI-3: streptolysin S (Molloy et al., 2011) clinical lineage 1 isolates

LIPI-4: a cellobiose-family phosphotransferase system (Maury et al., 2016)

More than 80% of virulence markers (n=115) were present in >95% of strains of lineage I and II

L. MONOCYTOGENES: VIRULENCE VARIABILITY



- Evidence: Only three (1/2a, 1/2b and 4b) out of 13 serovars cause disease regularly
- Virulence variability shown in different models (cell culture, chick embryos, gerbils…)
- Difficulty to close the gap between virulence (ability to spread a trait/bug in a population) and pathogenicity (ability to cause disease)
- Loss of virulence occurs naturally in ~ 0.1% of isolates mostly due to point mutations in gene regulators or genes (Maury et al., 2017)

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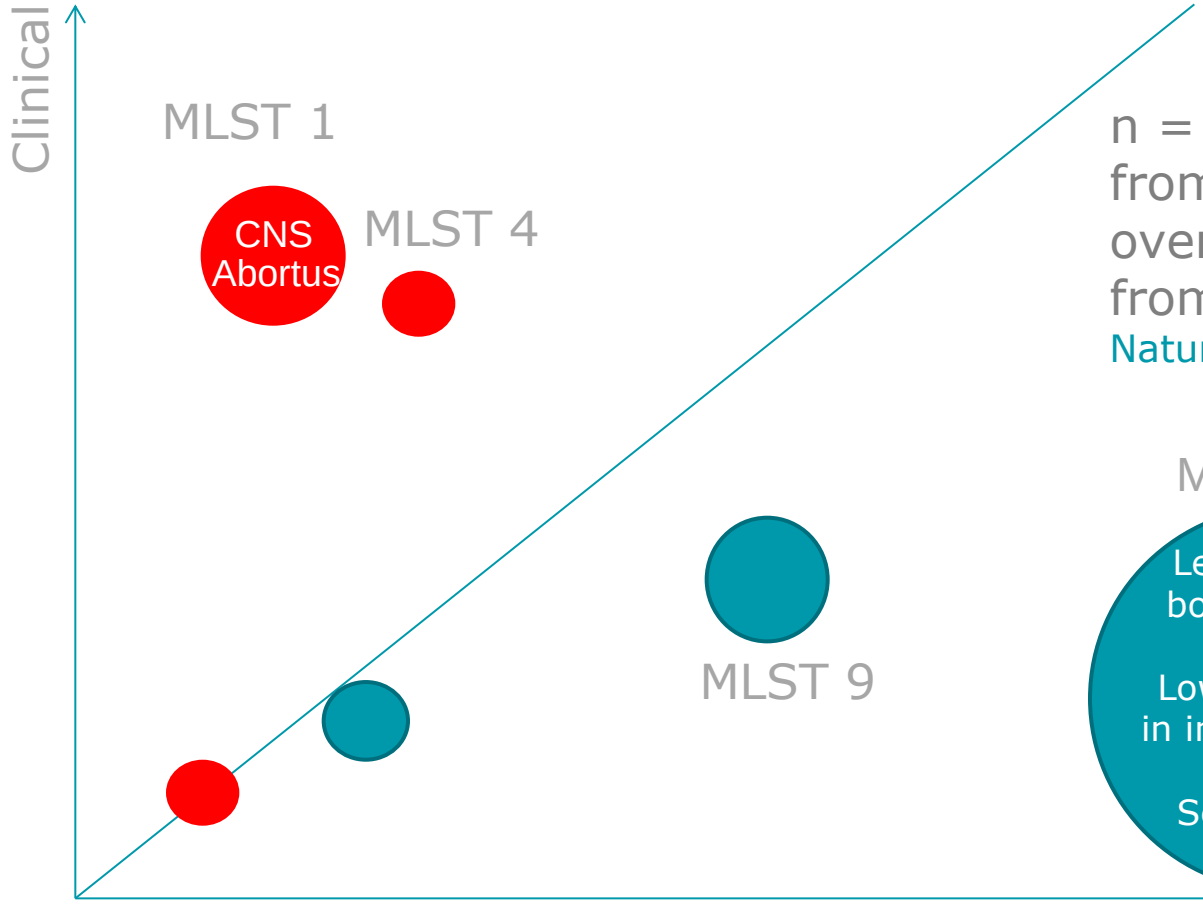


n = 6,600 isolates from France recovered over 7 years simplified from Maury et al. (2016) Nature Genetics

L. MONOCYTOGENES MLST 121: MOLECULAR FEATURES

- .. possess a transposon mediated tolerance mechanisms against QATS
- .. possess a stress survival islet-2 (lmo0464/lmo0465, acquired from *Listeria innocua*)
- .. other factors outcompeting *L. monocytogenes* non-MLST 121?
- .. are impaired with regard to virulence (*inlA*, *actA*?)

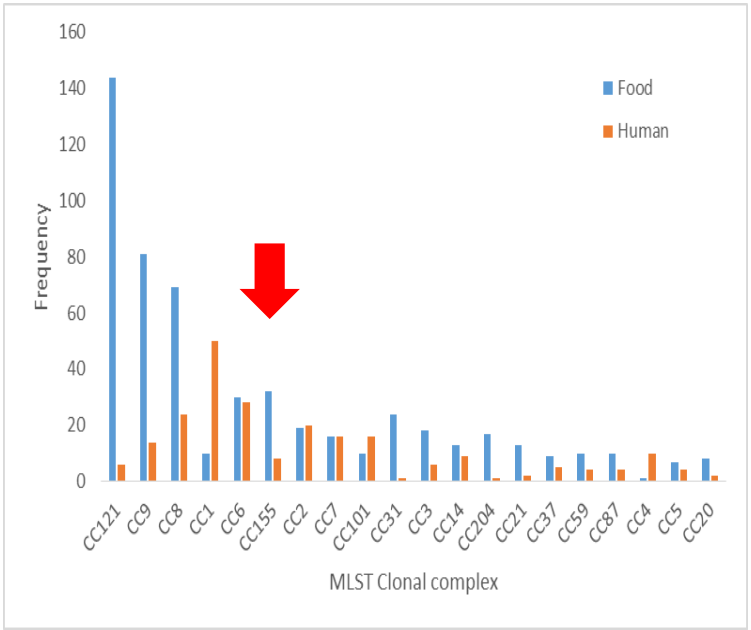
KNOWN MUTATIONS IN *L. MONOCYTOGENES*

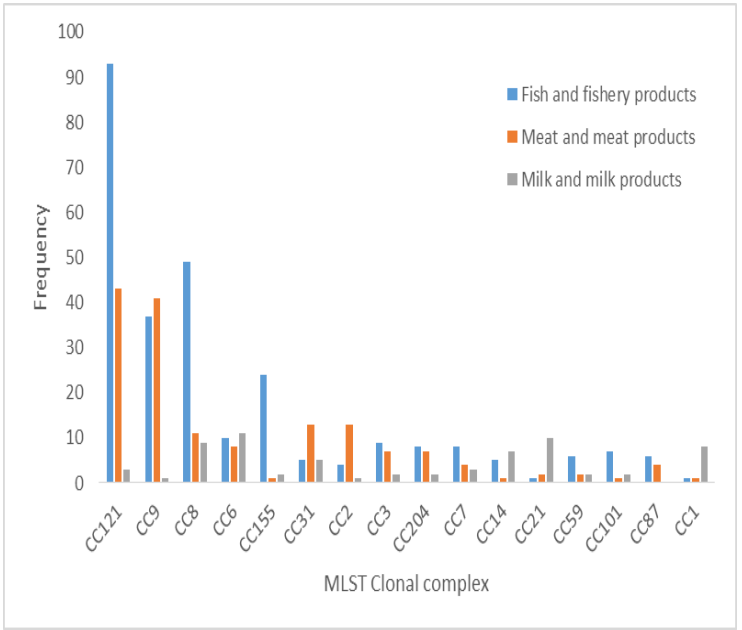
Source	Mutation-type	AA position	Genetic lineage/serotype
Human, Food	*inlA* PMSC (type 2)	656	I (1/2b)
Human	*inlA* PMSC (type 18)	404	I (4b)
n. s.	*inlA* PMSC (type 16, 17)	170, 253	I (1/2b)
Food	*inlA* PMSC (type 8, 10)	460, 677	II (1/2a)
Human, Food, FPE	*inlA* PMSC (type 5, 7)	189, 562	II (1/2a, 3a)
n. s.	*inlA* PMSC (type 15)	77	II (1/2a)
Food	*inlA* PMSC (type 9)	519	II (1/2c)
Human	*inlA* PMSC (type 14)	539	II (1/2c, 3c)
Human, Food, FPE	*inlA* PMSC (type 3)	700	II (1/2a, 3a; 3c)
Food, FPE	*inlA* PMSC (type 4)	9	II (1/2a, 3a; 1/2c, 3c)
Human, Food	*inlA* PMSC (type 1)	606	I (1/2b, 4b)+II (1/2a, 3a)
Human, Food	*inlA* PMSC (type 6)	492	I (1/2b, 4b)+II (1/2a, 3a)
Human, Food, FPE	*inlA* PMSC (type 12)	576	I (4b)+II (1/2c, 3c)
Food	*inlA* PMSC (type 11)	685	I (1/2b)+II (1/2c)
Seafood	*inlA* PMSC (type 13)	527	n. s.
Food (dairy products)	*inlB*-substitution (9bp)	LRR-region	II (1/2a)
Food (dairy products)	*plcA*-substitution (12bp)	17, 119, 262	II (1/2a)
Human	*brtA*-deletion (188bp)	79	II (1/2c)
Bovine placenta (abortion)	*prfA*-deletion	701	II (1/2a, 3a)
Pet food	*prfA*-deletion (1kb)	n.s.	II (1/2a)
Human, Food	*actA*-deletion (105bp)	n.s.	I (4a, 4b)

Phosphatidylinositol phospholipase C (PI-PLC); Amino acid (AA); Premature stop codon (PMSC); Leucine-rich repeat region (LRR); n.s. not specified; Source: Burall et al. (2014); Hain et al. (2012); Roche et al. (2005); Rupp et al. (2015); Schwartz et al. (2012); Temoin et al. (2008); Van Stelten and Nightingale (2008); Van Stelten et al. (2010)

L. MONOCYTOGENES: VIRULENCE VARIABILITY

n = 1,143 isolates; 2 years isolation time frame





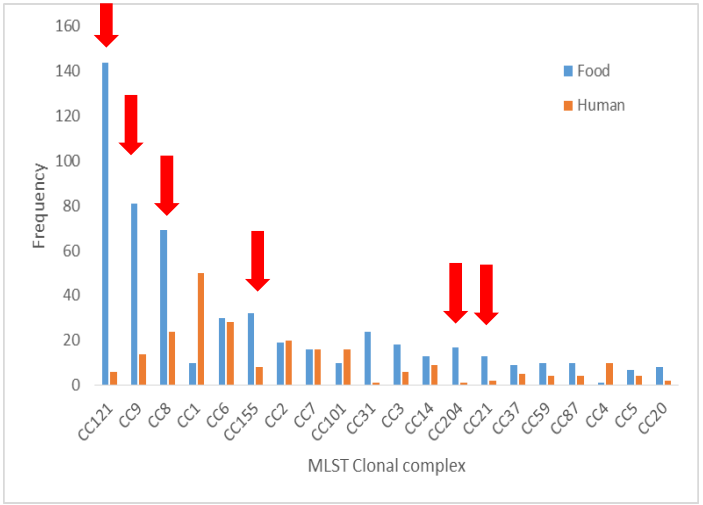
Activity 3: the comparison of isolates from different compartments along the food chain, and in humans using Whole Genome Sequencing

- OC/EFSA/BIOCONTAM/2014/01-CT1
- 7/10/2014-7/10/2016


EXTERNAL SCIENTIFIC REPORT

Closing gaps for performing a risk assessment on *Listeria monocytogenes* in ready-to-eat (RTE) foods: activity 3, the comparison of isolates from different compartments along the food chain, and from humans using whole genome sequencing (WGS) analysis

VIRULENCE AND POPULATION STRUCTURE



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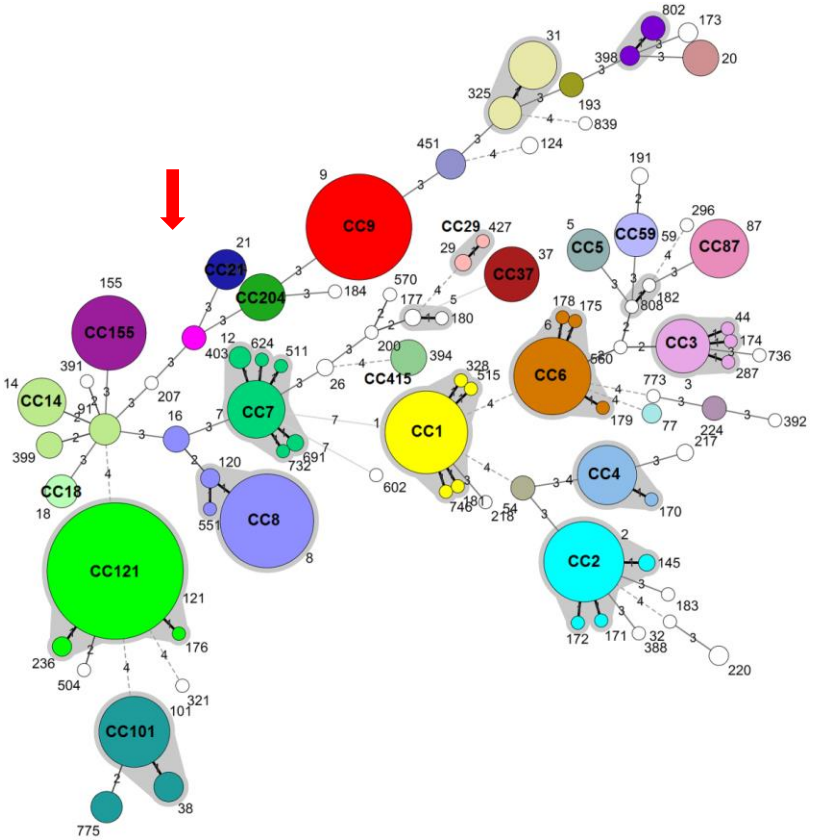
n=1,143 isolates recovered over 2 years



DETECTABILITY AND VIRULENCE

- Hypovirulent strains are underdetected (Gracieux et al., 2003; detection media e.g., antimicrobials added)
- Detection may be limited by the natural microbiota or by other *Listeria* spp. (Cornu et al., 2002; Zitz et al., 2011; Keys et al., 2013; Dailey et al., 2014)
- Strain competition within *L. monocytogenes* is one of the factors related to bias during enrichment (Gorski et al., 2006; Zilelidou et al., 2016b)

DETECTABILITY AND VIRULENCE

- Outcompetition could not be correlated with the serotype (Gorski et al., 2006; Zilelidou et al., 2016b)
- Lineage dependent detection of strains during enrichment (Bruhn et al., 2005) and a competitive advantage of serotype 1/2a strains over serotype 4b in biofilm formation were reported (Pan et al., 2009)

SOURCE ATTRIBUTION OF *L. MONOCYTOGENES*

based on 7 locus MLST

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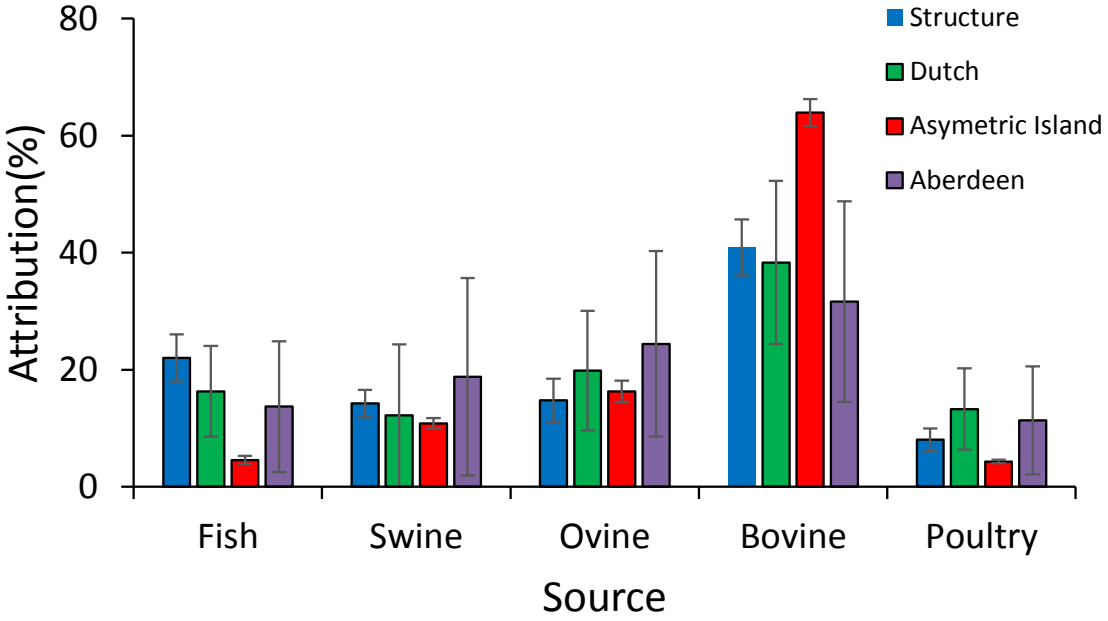

CONCLUSIONS

- In principal, all *L. monocytogenes* isolates are of health concern, but the impact to genotypes to the burden of diseases differs
- Sequencing of isolates has shown that most virulence markers are present in most strains-adaptation through genetic mobile elements
- In an increasingly vulnerable population, also the impact of low virulent clones on the burden of disease will increase (albeit not as massive as for high virulent clones)…
- Detectability of low-virulent clones is an actual problem