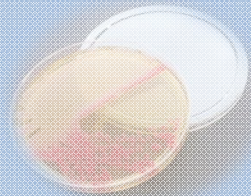# Neuartige Einsichten in die Phylogenomik von ESBL-*E. coli* im One Health Kontext

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Do we need a virulence gene scoring system for ESBL *E. coli* isolates?

Multidrug resistant
Gram-negative bacteria
with **disease potential**

❖ **600.000** Nosocomial infections
❖ **15.000** Fatal cases

Colonization | Clinical relevant infection

Scoring system

Study protocol based on the One Health approach

101 *E. coli* producing Extended spectrum β-lactamases (ESBLs)

Human (n = 52)

Animal (n = 49)

Subset of 40 isolates (randomly chosen)

Phylotyping
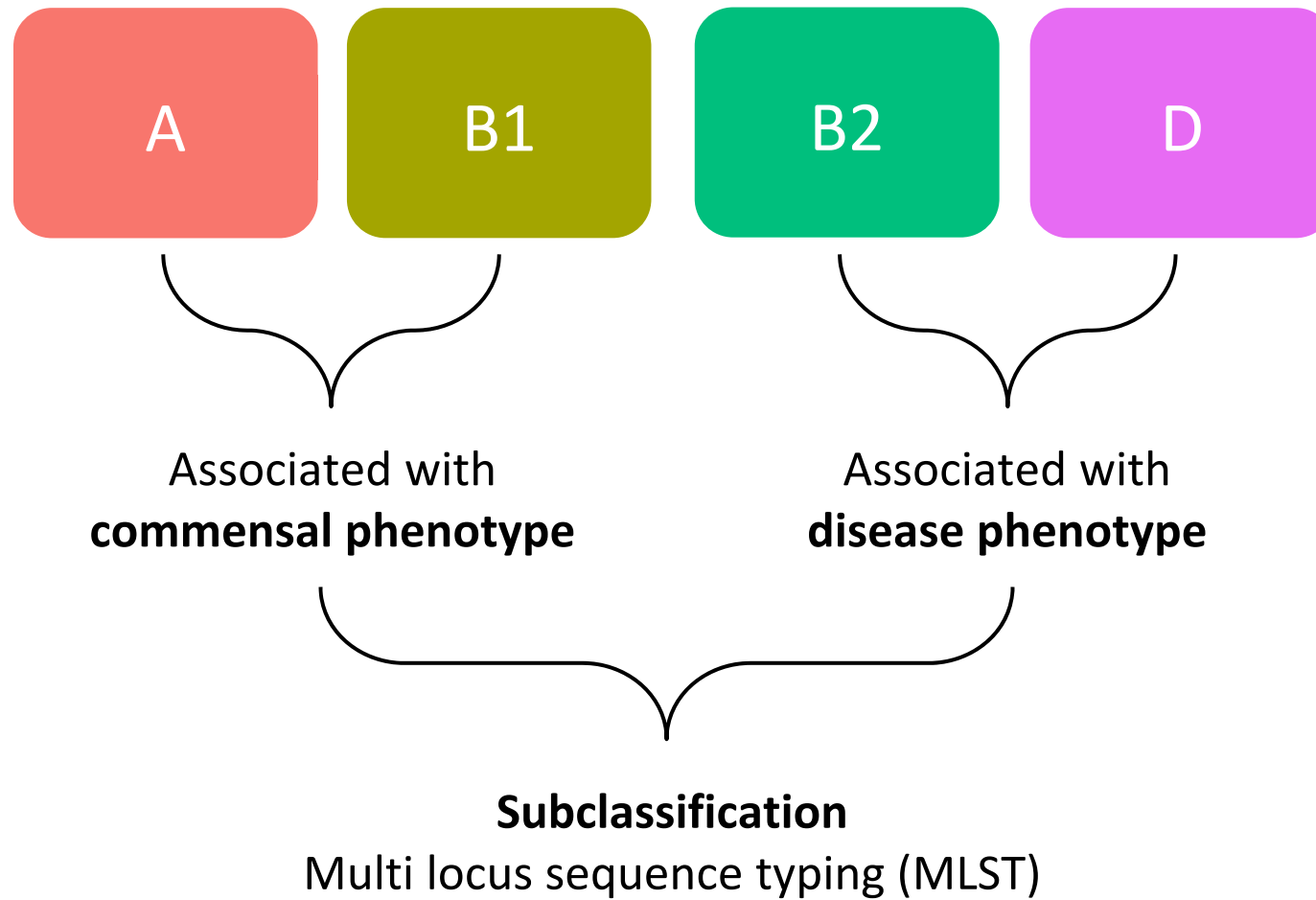Sequence typing
Virulence genes
Resistance genes

Larvicidal activity
in the greater wax moth
(*Galleria mellonella*)

Kaplan-Maier
Cox regression
Multinominal
logistic regression

	Stepwise Logistic regression (LR) PG		Stepwise LR STC		Stepwise Cox Regression		Cox Regression	
	LR Chisq	Pr(>Chisq)	LR Chisq	Pr(>Chisq)	Chisq	Pr(>|Chi|)	Chisq	Pr(>|Chi|)
Number of operons	9.5	0.050	2.1	0.542	0.3	0.585	0.3	0.585
Toxins	26.5	<0.001	3.4	0.331	1.5	0.221	1.5	0.221
iss	16.3	0.003	1.0	0.798	118.8	<0.001	118.8	<0.001
ompT	18.1	0.001	7.3	0.063	10.5	0.001	10.5	0.001
traI			1.0	0.808	1.3	0.254	1.3	0.254
malX	16.5	0.002	2.8	0.430	3.9	0.049	3.9	0.049
usp			0.0	1.000	35.4	<0.001	35.4	<0.001
capsula	12.2	0.016	0.8	0.841	23.4	<0.001	23.4	<0.001
sitA			0.0	1.000	40.8	<0.001	40.8	<0.001
hlyF			0.0	1.000			1.2	0.269
origin [animal -0; human -1]	11.1	0.026	1.1	0.779			1.6	0.211
combination of siderophores			16.5	0.744	111.5	<0.001	108.8	<0.001

Classical *E. coli* phylotyping

| A | B1 | B2 | D |

Associated with **commensal phenotype**

Associated with **disease phenotype**

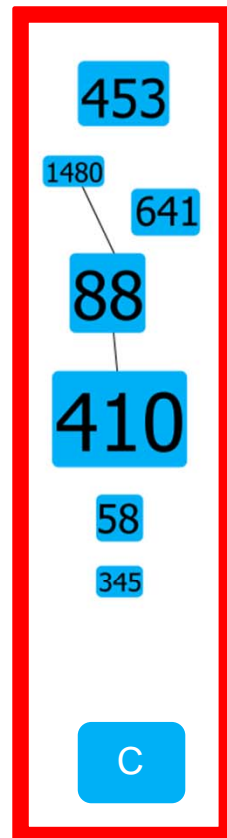**Subclassification**
Multi locus sequence typing (MLST)

Turrientes *et al.* (2014)
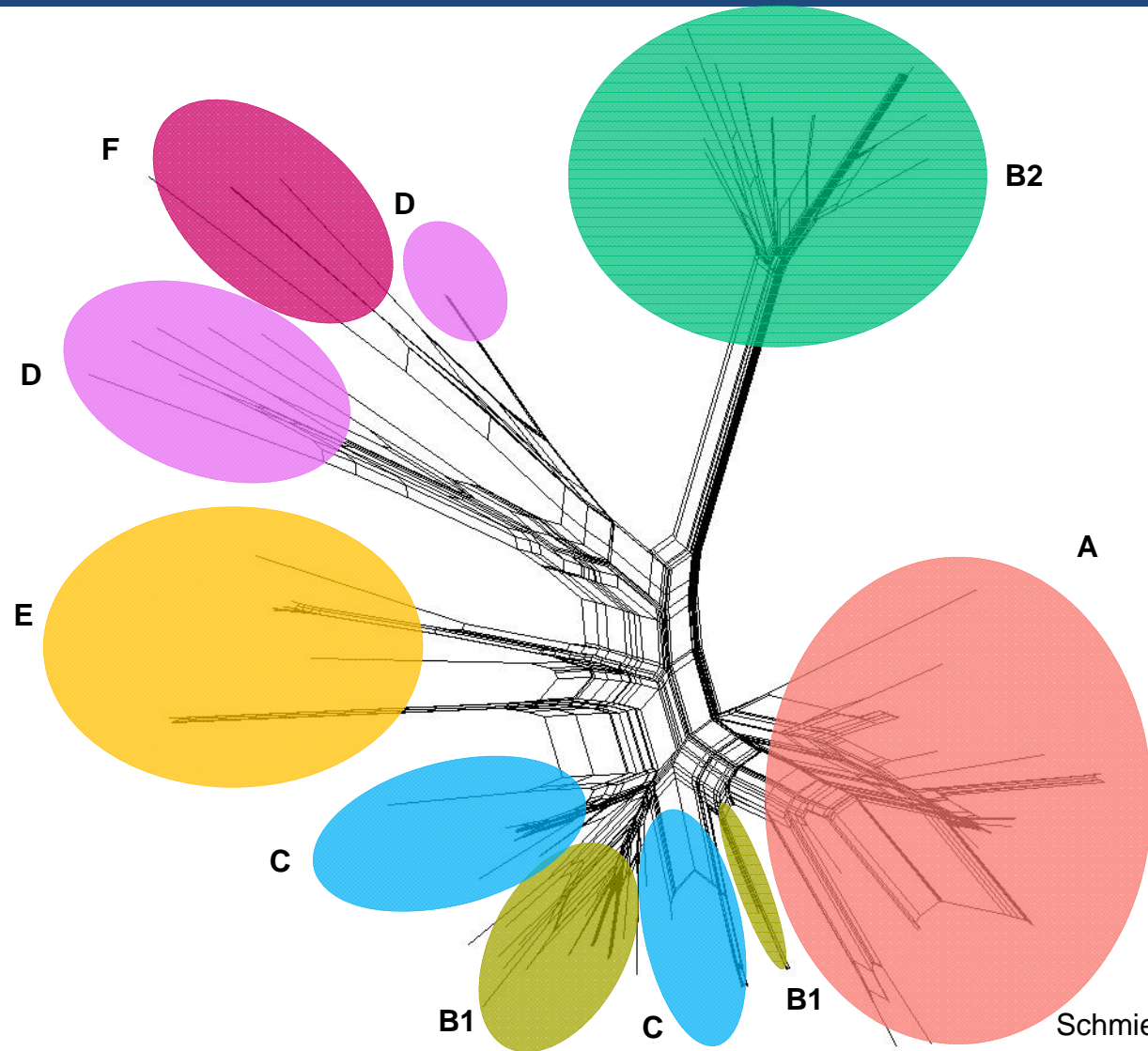
Schmiedel *et al.* Manuscript in preparation

Recombination blurs *E. coli* phylogenetic groups

Concatenated Multi locus sequence typing (ConMLST)
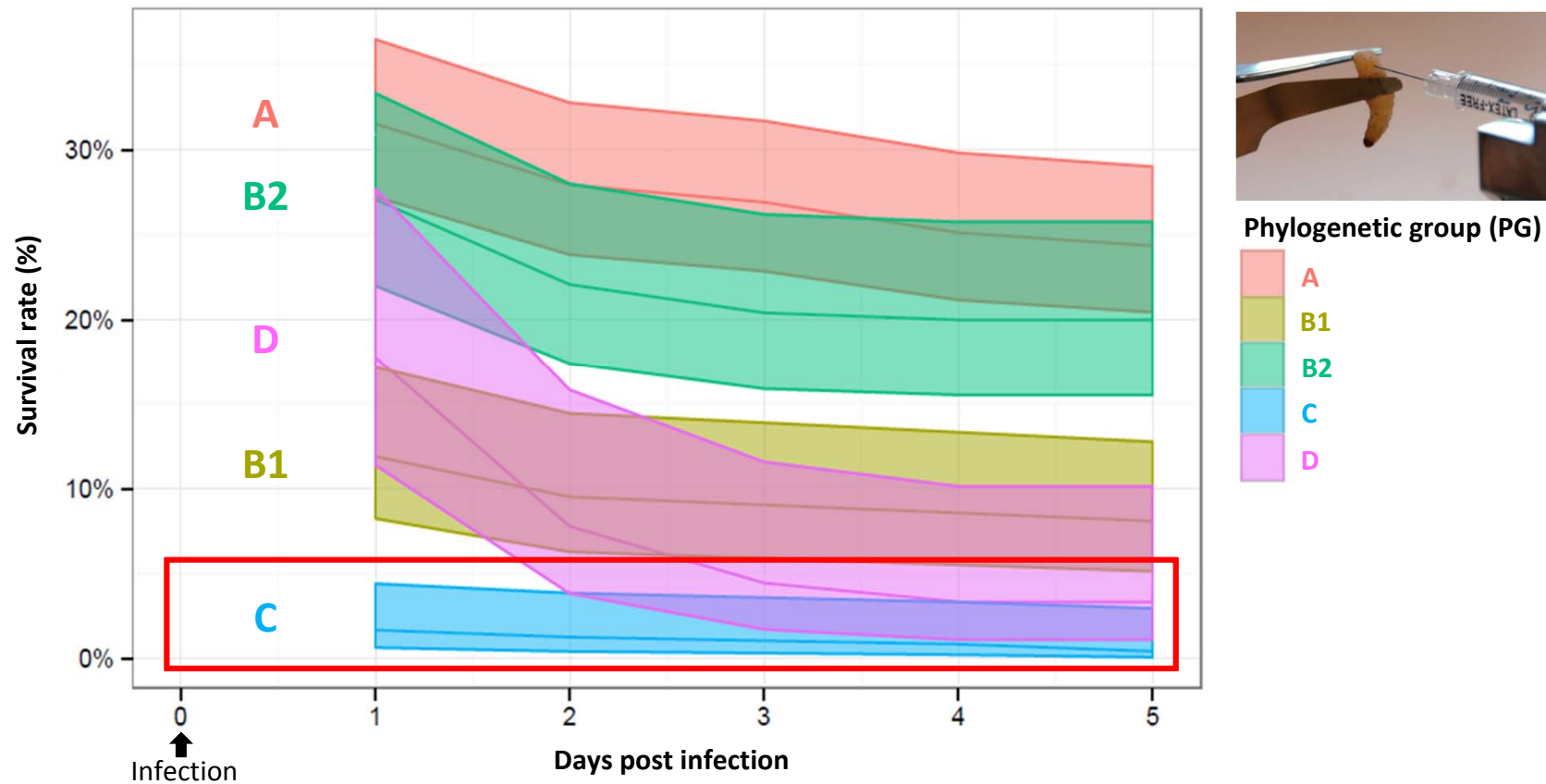

ConMLST PG C

❖ **Usually classified as PG A/B1**

162 **Sequence type (ST)**   B1 **ConMLST phylogenetic group (conMLST PG)**

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Larvicidal activity of *E. coli* ConMLST Phylogenetic groups in *G. mellonella*

- ❖ **Each ConMLST phylogenetic group** shows a different larvicidal effect
- ❖ **Most larvicidal:** **ConMLST PG C** (HR = 2.24, p < 0.001)

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Factors associated with larvicidal acitivity in *G. mellonella* (Cox regression)

Increase of larvicidal acitivity

Decrease of larvicidal acitivity

- ❖ *iss* (HR = 2.52, p < 0.001)
- ❖ *ompT* (HR = 2.29, p < 0.001)
- ❖ **Aerobactin** (HR = 1.89, p < 0.001)

- ❖ *usp* (HR = -8.84 , p < 0.001)
- ❖ *sitA* (HR = -3.18, p < 0.001)
- ❖ *kpsMT II* (HR = -2.79, p < 0.001)

Enabling **serum resistance** and **iron aquisition**

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Growth in human serum

ConMLST PGs

Legend: A, B1, B2, C, D

Optical density at 600 nm

Log2 (time + 1) − 20 hours

Clonal clusters

Legend: Other clusters, 10, 131, 23

Optical density at 600 nm
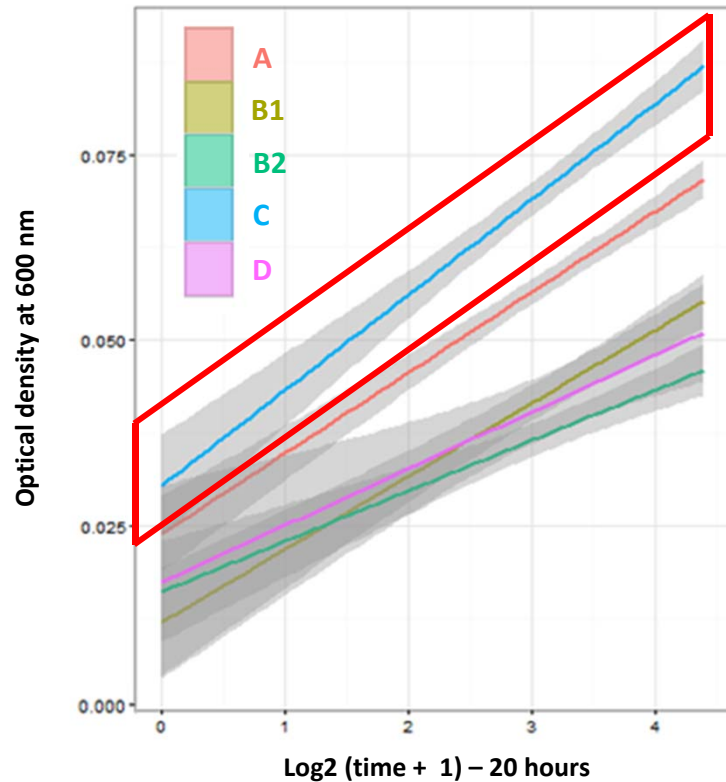
Log2 (time + 1) − 20 hours
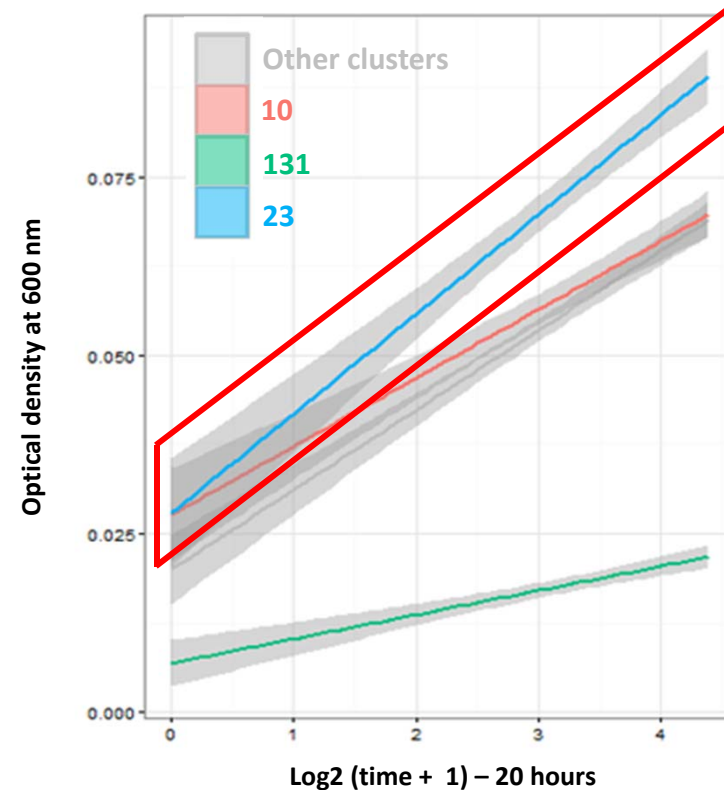
❖ **Best growth in human serum: ConMLST PG C / CC 23**

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Summary

❖ Definition of a **novel disease associated *E. coli* subgroup** (ConMLST PG C) with properties that enable survival in the **blood stream**

❖ Our results are supported by evidence from the literature (**outbreaks** with ConMLST PG C strains)

❖ Testing and further development of the model, specifically for strains **with higher risk for patients** ($\rightarrow$ blood culture isolates)

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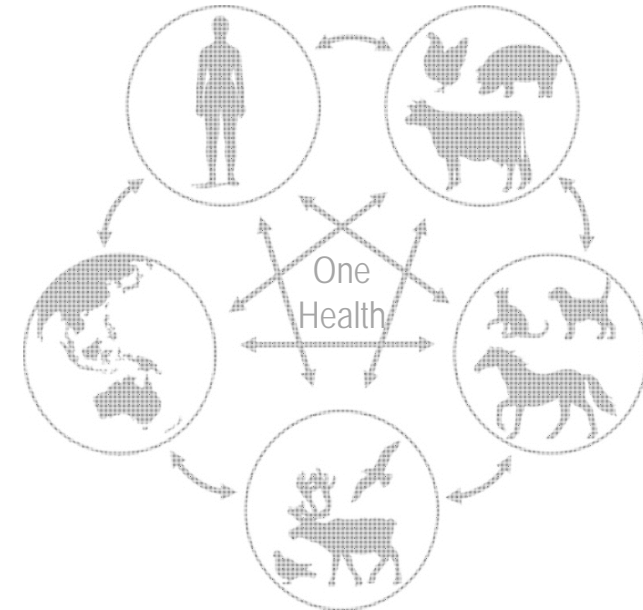- David Dippel
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