

Bestandsaufnahme und genetische Charakterisierung mobiler Colistin-Resistenzen in kommensalen *E. coli* aus Nutztieren und Lebensmitteln



Dr. Jens A. Hammerl

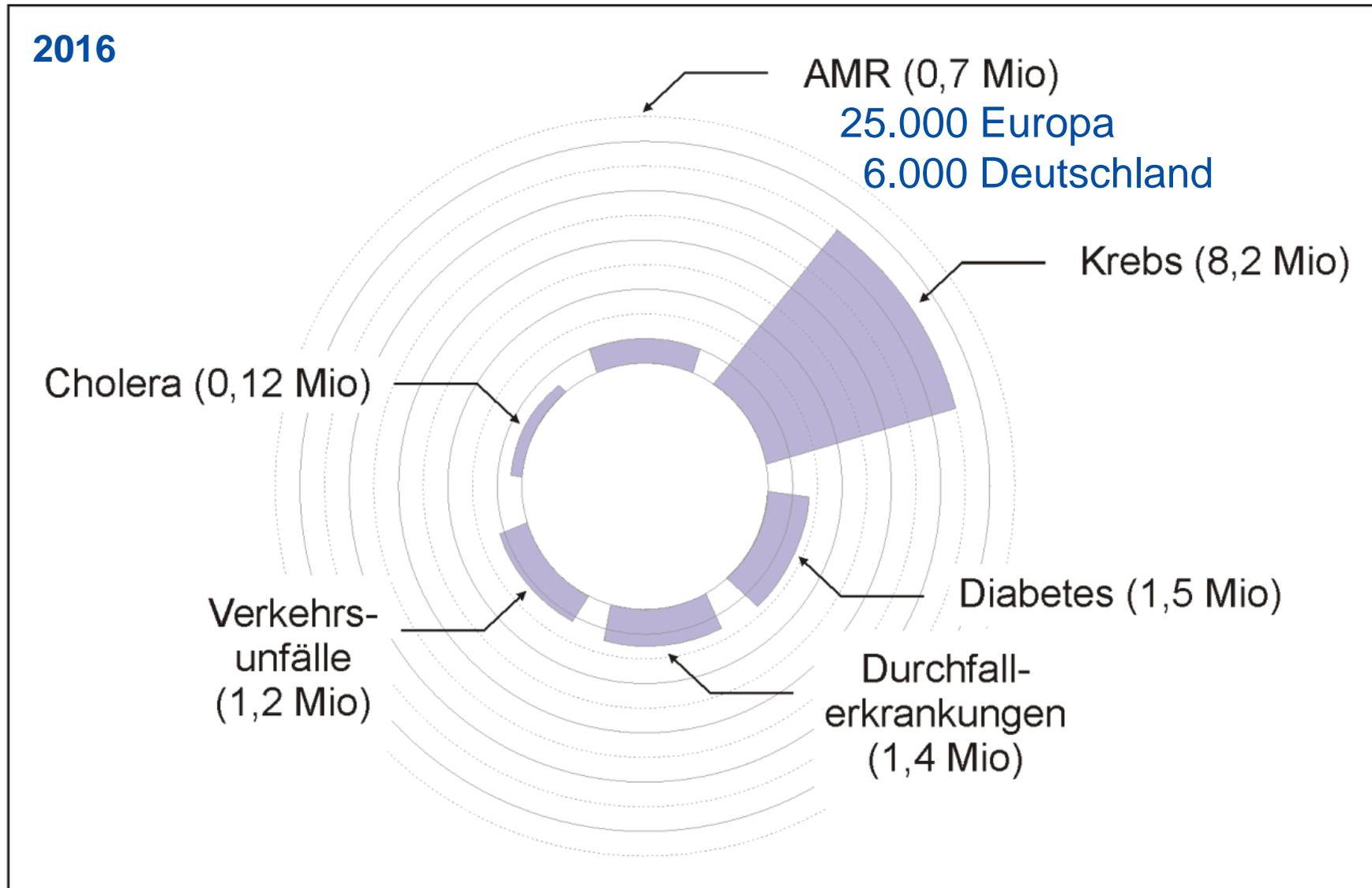
Nationales Referenzlabor für Antibiotikaresistenz (NRL-AR)

Fachgruppe Epidemiologie, Zoonosen und Antimikrobielle Resistenzen

Abteilung Biologische Sicherheit

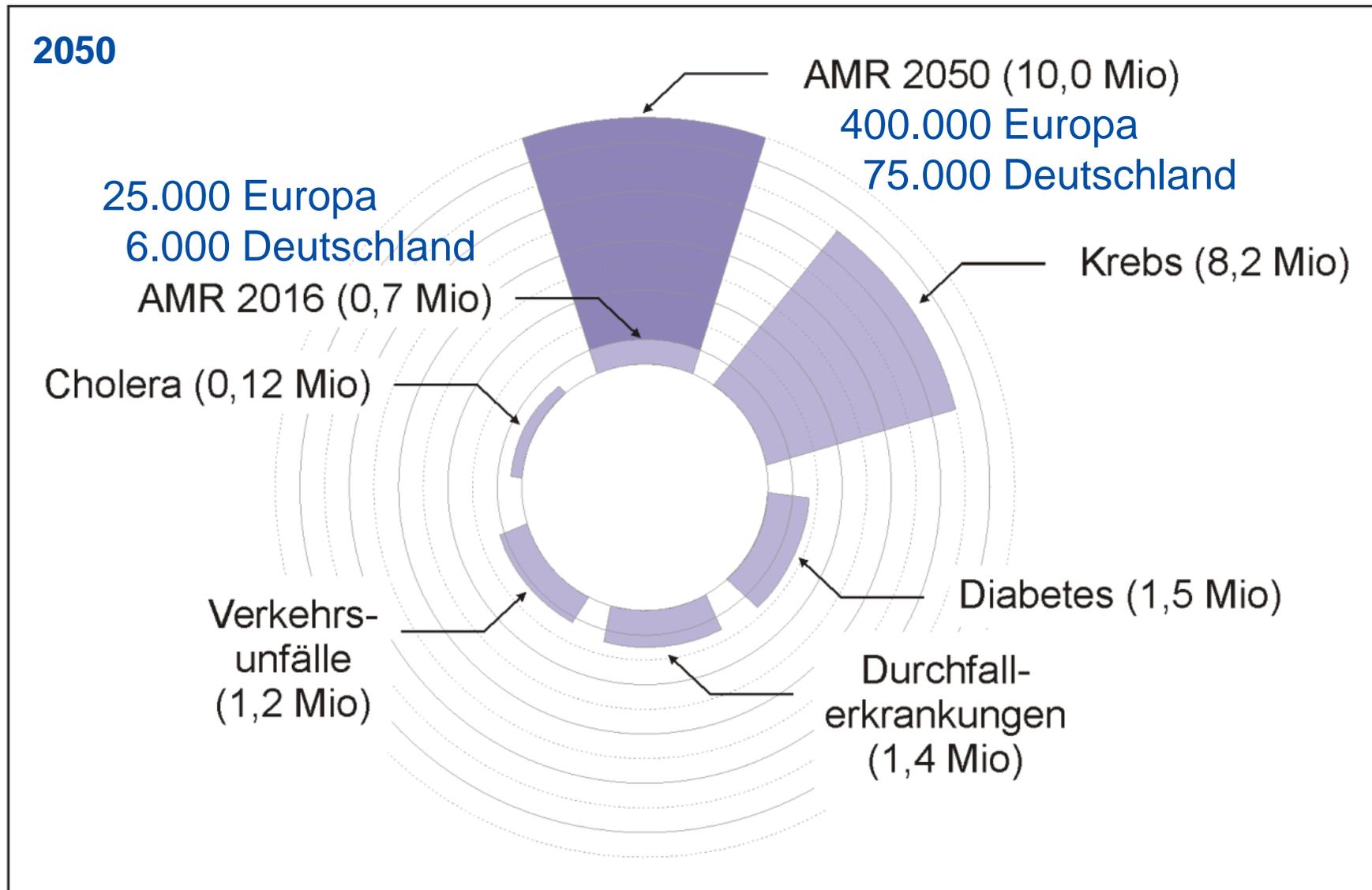
Bundesinstitut für Risikobewertung

Weltweite Bedeutung antimikrobieller Resistenzen



Modifiziert aus: Tackling Drug-Resistant Infections Globally: Final Report And Recommendations Review On Antimicrobial Resistance, 2016, <http://amr-review.org/>

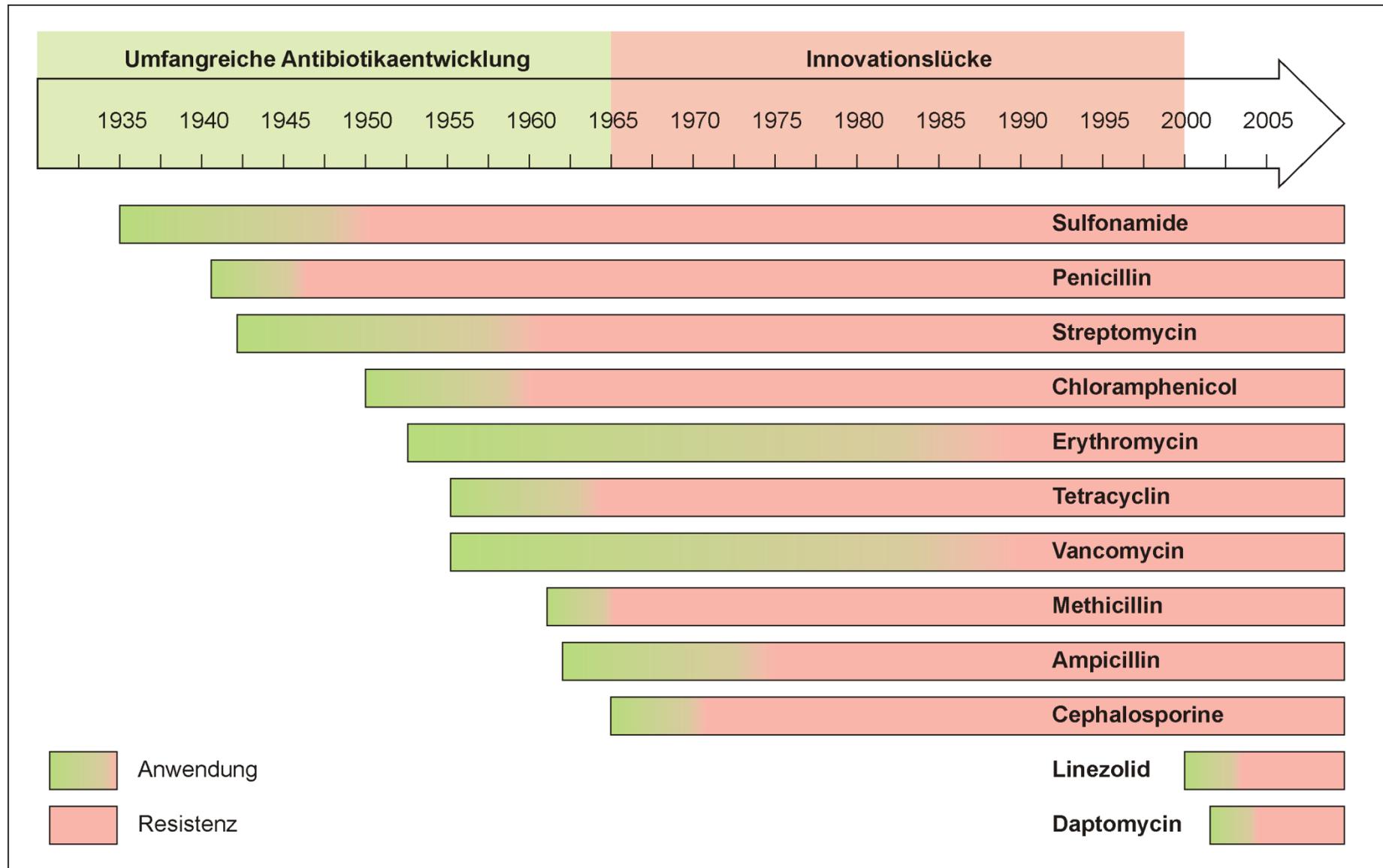
Weltweite Bedeutung antimikrobieller Resistenzen



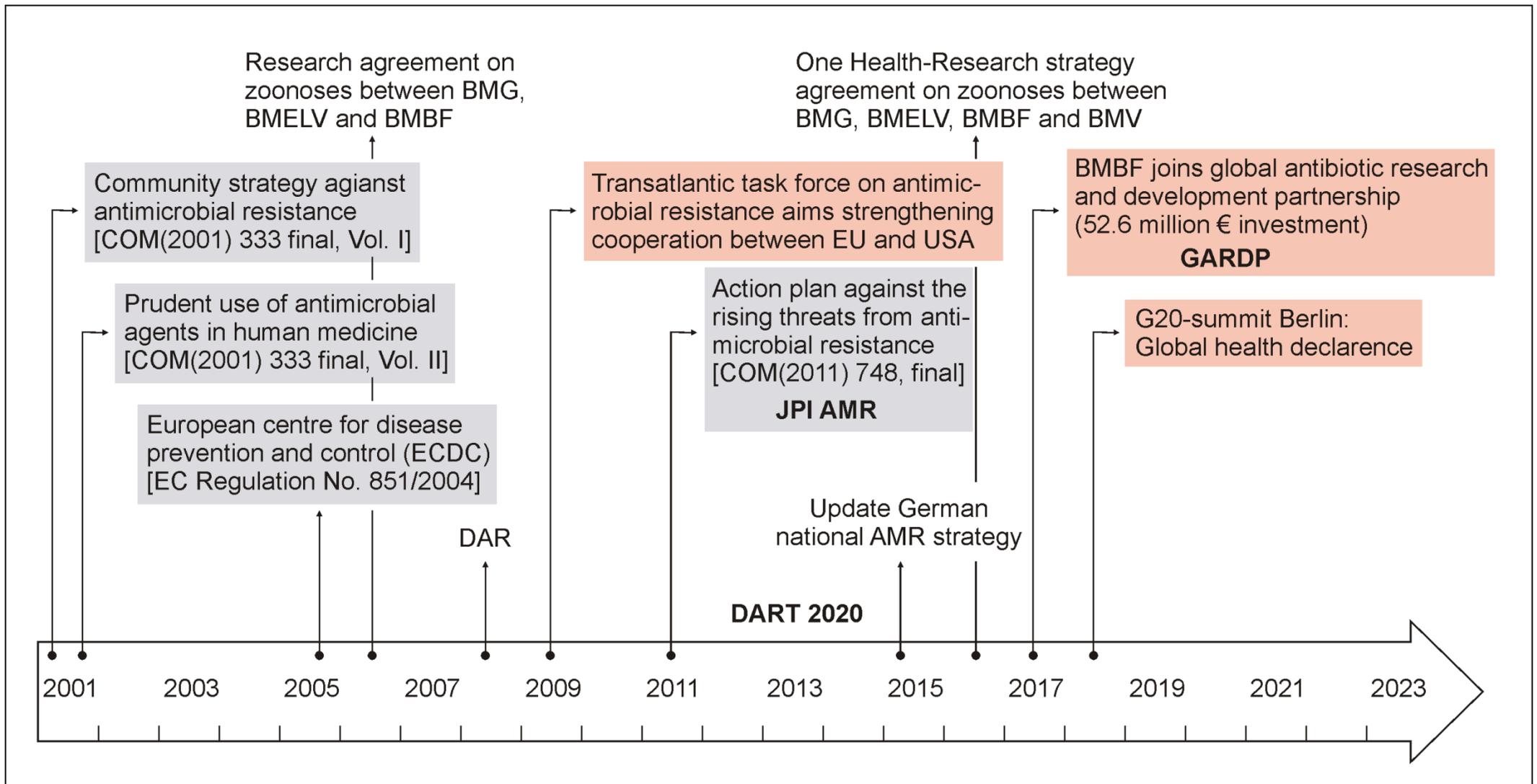
Modifiziert aus: Tackling Drug-Resistant Infections Globally: Final Report And Recommendations Review On Antimicrobial Resistance, 2016, <http://amr-review.org/>

Resistenzentwicklung: Ein Wettlauf gegen die Zeit

- Limitierung von Therapieoptionen bei bakteriellen Infektionen
- bedeutender ökonomischer Verluste und Ausfälle



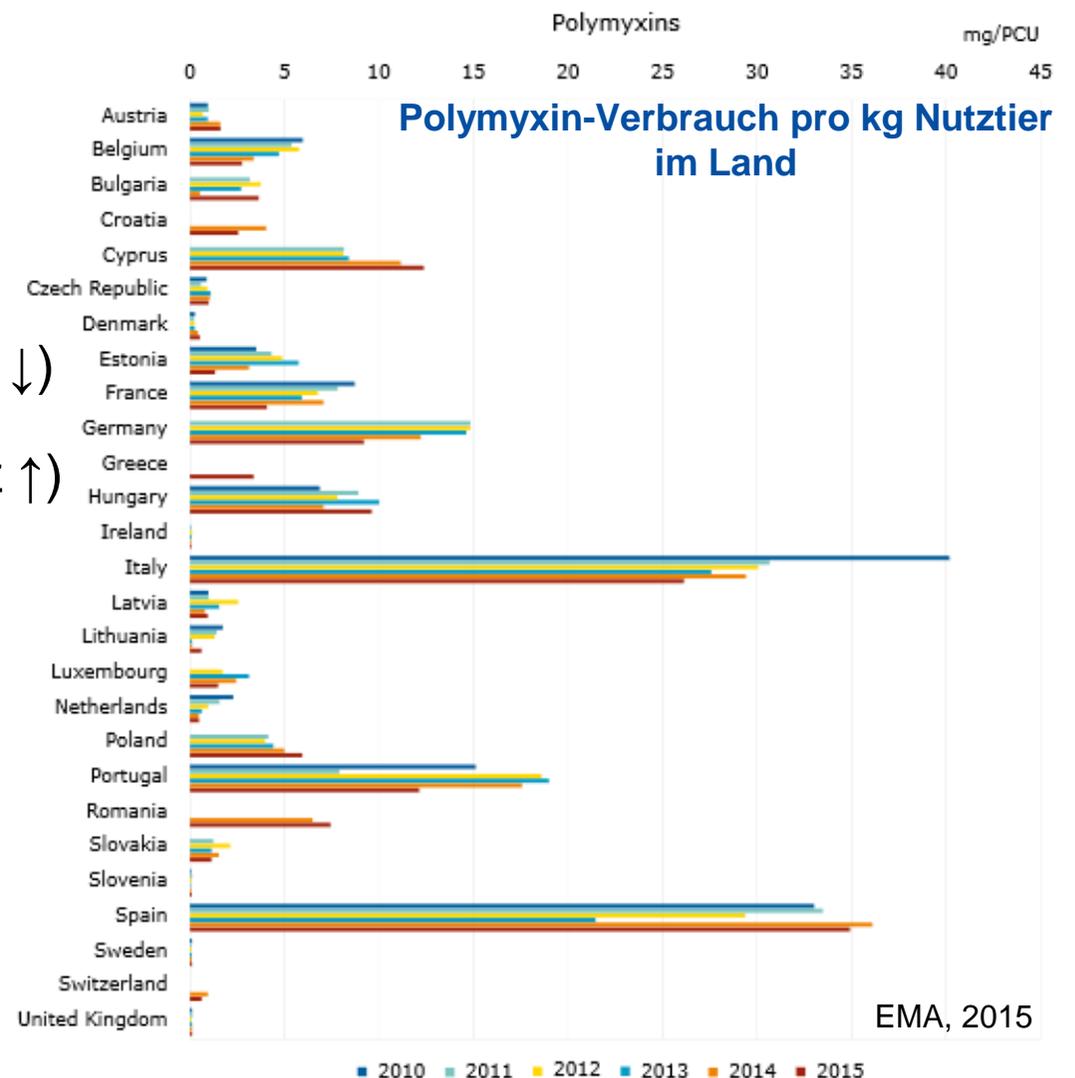
Forschungs-/politische Lösungsansätze zur Vermeidung ...



- Sachgerechter/reduzierter Einsatz der Antibiotika
- Erforschung und Entwicklung neuer Antibiotika (einschl. Reserveantibiotika) und Alternativmethoden

Bedeutung des Reserveantibiotikum Colistin in der Veterinärmedizin

- große Bedeutung in Geflügel-, Schweine- und Kälbermast
- zweithäufigstes Antibiotika in der Putenmast (NRW)
- keine systemische Wirkung
(kurze Wartezeit)
- Deutschland (2014): 107 t (Tendenz ↓)
- weltweit (2014): 11.942 t (Tendenz ↑)



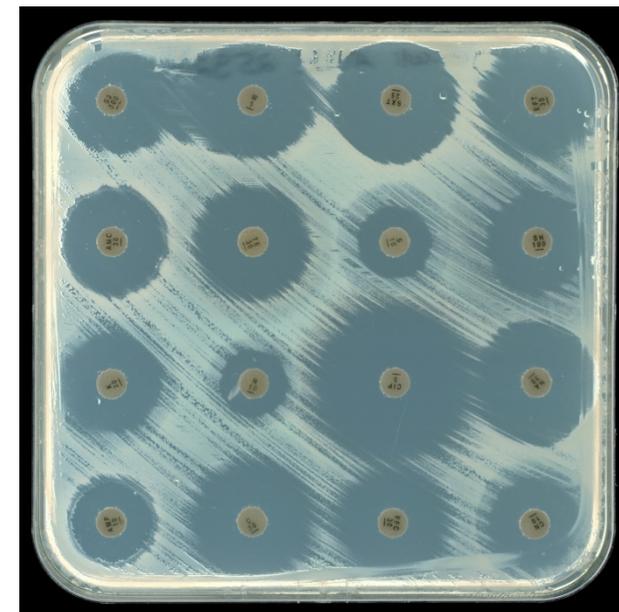
Colistin-Resistenz in Gram-negativen Bakterien

Intrinsische Resistenz

z.B. *Proteus* spp., *Burkholderia* spp.

Erworbene (extrinsische) Resistenz

- Effluxpumpen (z.B. Yersinien, Klebsiellen)
- Veränderung der Kapselzusammensetzung (Klebsiellen)
- Verlust des LPS (*A. baumannii*)
- **Modifikationen der äußeren Membran bzw. LPS (Deacylierung, Hydroxylierung, Anlagerung von Aminoarabinose oder Phosphoethanolamin)**



Colistin-Resistenzverbreitung: Ein Paradigmenwechsel...

- chromosomal-assoziierte Resistenz

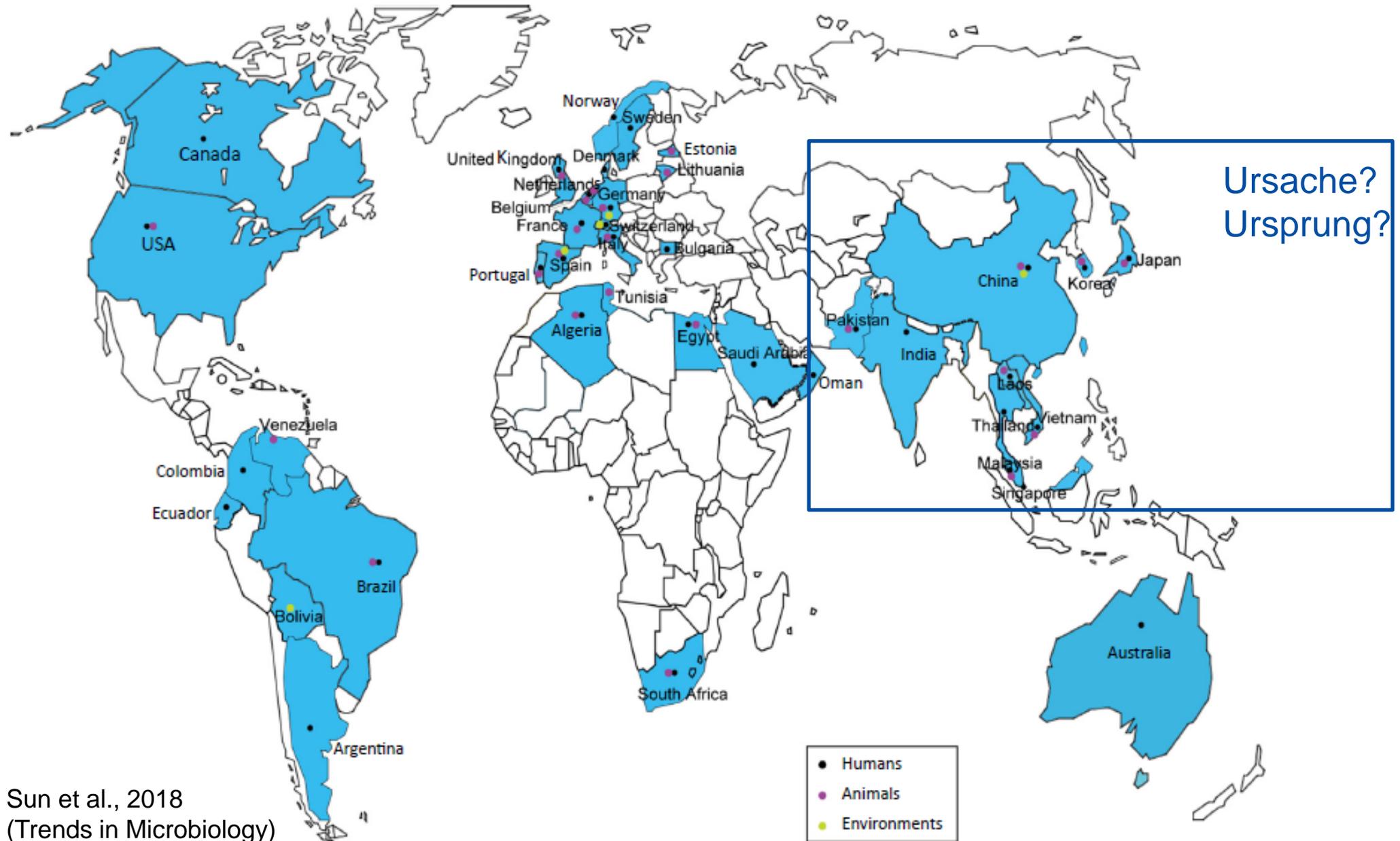
Vertikale Verbreitung



- spezifischer Colistin-Resistenzgenachweis (*mcr-1*)
- Resistenz ist übertragbar
(konjugatives bzw. mobilisierbares Plasmid)
- Resistenz ist mobil (Transposon)

Horizontale Verbreitung

MCR-1: Ein „neues“ globales Resistenzproblem?



Sun et al., 2018
(Trends in Microbiology)

Retrospektive Untersuchung des *mcr-1* Vorkommens in *E. coli* aus Nutztieren/Lebensmitteln Deutschlands

- MHK: >15.000 Isolate (~5% MIC >2 mg/l Colistin)
- ~80% *mcr-1* positiv (~4% aller Proben)
- große Unterschiede bezüglich Herkunft der Isolate

RESEARCH ARTICLE

Prevalence of *mcr-1* in *E. coli* from Livestock and Food in Germany, 2010–2015

Alexandra Irrgang^{1*}, Nicole Roschanski^{2*}, Bernd-Alois Tenhagen¹, Mirjam Grobbei¹, Tanja Skladnikiewicz-Ziemer¹, Katharina Thomas¹, Uwe Roesler², Annemarie Käbbohrer^{1*}

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Rind:

Kalb (Fleisch):

Schwein:

Huhn (Kot):

Hühnerfleisch:

Pute (Kot):

Putenfleisch:

COL-R

0-0,9%

0,8-14,5% (6,1%)

0,0-4,0%

5,1-8,9%

1,2-9,3%

11,8% (10-19,5%)

4,3-9,2%

mcr-1

n.n.

70,1-100% (25%)

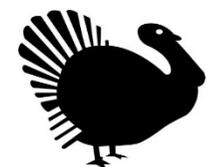
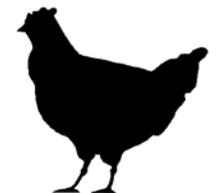
43-75,4%

85,2-100%

50-88,9%

81,1-93,9%

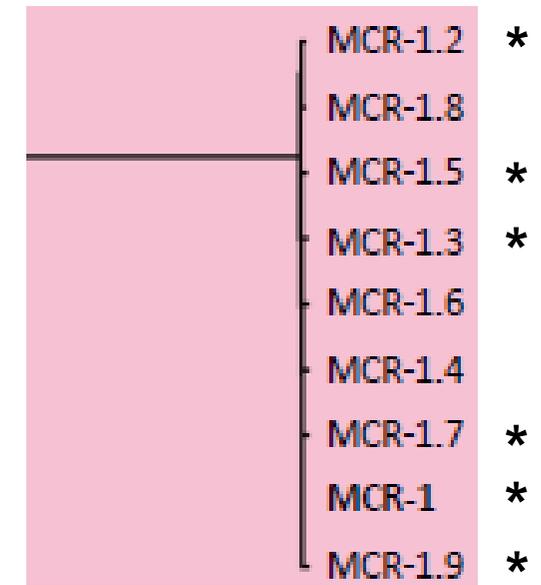
~90%



mcr-1 Variabilität in deutschen *E. coli*

- zahlreiche Varianten bekannt (*mcr-1.2* bis *mcr-1.XX*)
- ~800 *mcr-1* positive *E. coli* (2010-2018) untersucht
- sieben *mcr-1* Varianten mit Aminosäureaustauschen
- sporadisches Auftreten der Varianten
- keine erkennbarer Zusammenhang (Matrix, Isolationsjahr, Herkunft)

Sun et al., 2018
(Trends in Microbiology)

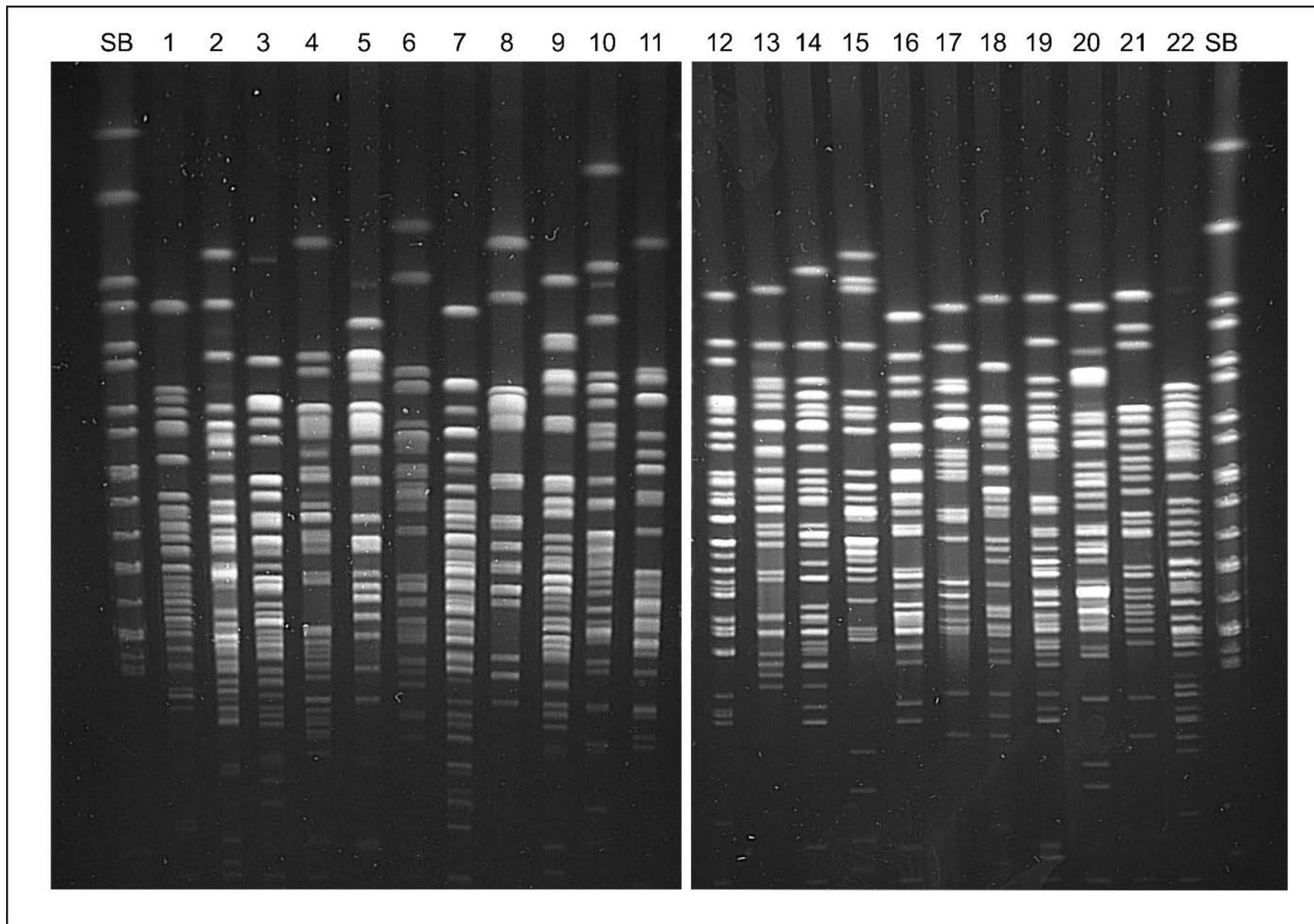


Bedeutung der Varianten unbekannt!

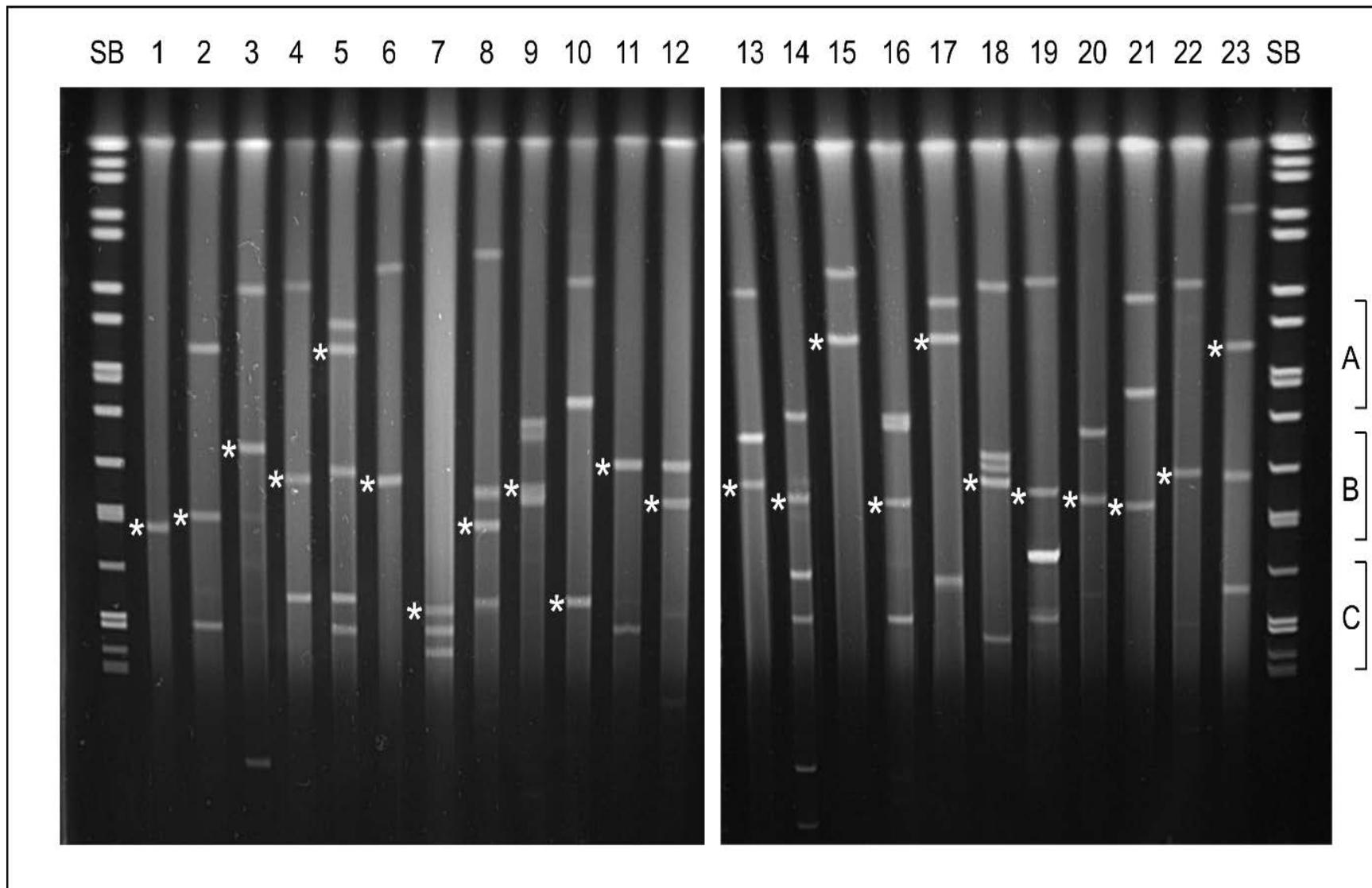
Untersuchungen zur Diversität *mcr-1* positiver *E. coli*

Isolat-ID	Herkunft	Resistenzprofil
2012		
12-AB00025	Truthahn, Kot	AMP, CHL, CIP, COL, NAL, SMX, TET, TMP
12-AB00501	Truthahn, Fleisch	AMP, CHL, CIP, COL, NAL, SMX, TET, TMP
12-AB00876	Truthahn, Fleisch	AMP, CIP, COL, NAL, TET
12-AB01842	Truthahn, Kot	AMP, CHL, CIP, COL, GEN, NAL, SMX, TET, TMP
12-AB01861	Truthahn, Blinddarminhalt	AMP, CHL, CIP, COL, NAL, SMX, TET, TMP
12-AB02079	Truthahn, Kot	AMP, CHL, CIP, COL, NAL, SMX, TET, TMP
2013		
13-AB00012	Huhn, Kot	COL
13-AB00742	Huhn, Fleisch	AMP, COL, FOT, TAZ
13-AB00885	Huhn, Blinddarminhalt	AMP, CHL, CIP, COL, GEN, NAL, SMX, TET, TMP
13-AB01479	Huhn, Blinddarminhalt	AMP, CHL, CIP, COL, GEN, NAL, SMX, TET, TMP
13-AB01693	Huhn, Fleisch	AMP, COL, FOT, SMX, TAZ
2014		
14-AB00001	Huhn, Kot	AMP, CHL, CIP, COL, NAL, SMX, TET, TMP
14-AB00714	Truthahn, Kot	AMP, CHL, CIP, COL, NAL, SMX, TET, TMP
14-AB00941	Truthahn, Blinddarminhalt	AMP, CHL, CIP, COL, GEN, SMX, TET, TMP
14-AB01030	Truthahn, Kot	AMP, CHL, CIP, COL, SMX, TMP
14-AB01041	Truthahn, Blinddarminhalt	AMP, CIP, COL, GEN, NAL, SMX, TET, TMP
14-AB01081	Truthahn, Fleisch	AMP, CIP, COL, GEN, NAL, TET
14-AB01513	Truthahn, Fleisch	AMP, CIP, COL, NAL, SMX, TET, TMP
2015		
15-AB00959	Schwein, Kot	AMP, CHL, COL, SMX, TET
15-AB01098	Schwein, Kot	AMP, CIP, COL, GEN, NAL, SMX, TET, TMP
15-AB01173	Schwein, Kot	CHL, COL, SMX, TET, TMP
15-AB01276	Schwein, Kot	AMP, CIP, COL, GEN, NAL, SMX, TET, TMP
15-AB01775	Schwein, Kot	AMP, COL, SMX, TET, TMP
15-AB02086	Schwein, Kot	AMP, CHL, CIP, COL, NAL, SMX, TET, TMP

Genetische Variabilität *mcr-1*-positiver *E. coli*

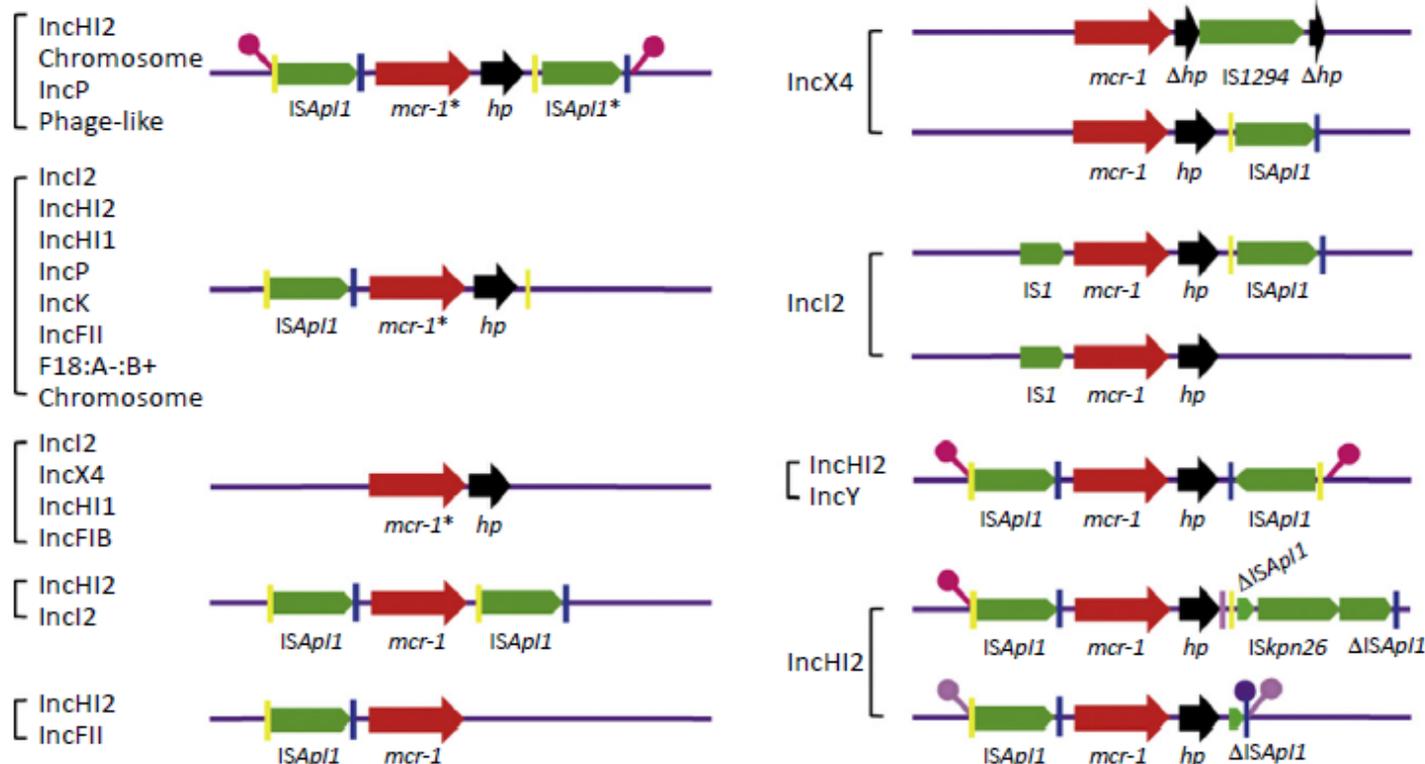


Genetische Variabilität *mcr-1*-positiver *E. coli*



Genetische Variabilität *mcr-1*-positiver *E. coli*

- WGS: Charakterisierung Colistin resistenter *E. coli* (n>100)
- Bioinformatische Auswertung: hohe Diversität
 - Serotypisierung, MLST- & cgMLST, etc.
 - Virulenzfaktoren
 - mobile genetische Elemente
 - Antibiotikaresistenzen



Plasmidtypen

Sun et al., 2018
(Trends in Microbiology)

J Antimicrob Chemother 2017; **72**: 3317–3324

doi:10.1093/jac/dkx327 Advance Access publication 18 September 2017

Identification of a novel transposon-associated phosphoethanolamine transferase gene, *mcr-5*, conferring colistin resistance in *d*-tartrate fermenting *Salmonella enterica* subsp. *enterica* serovar Paratyphi B

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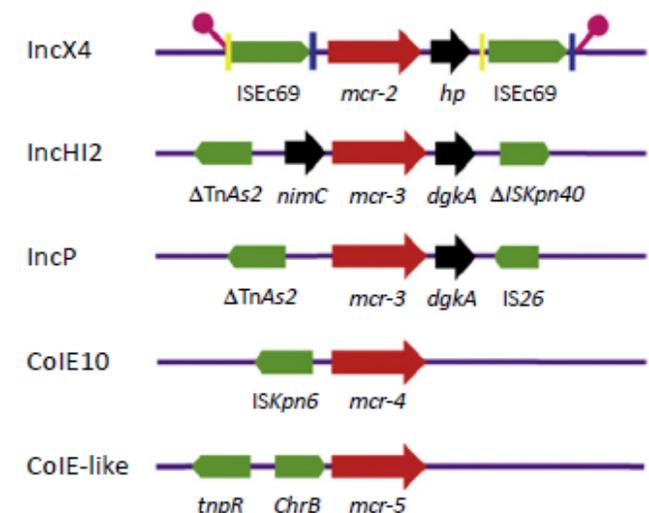
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Aktueller Überblick zu übertragbaren Colistin-Resistenzen

Resistenzgen	Vorkommen	Lokalisation	Literaturverweis
<i>mcr-1</i>	insb. Enterobacteriaceae: <i>E. coli</i> , <i>Salmonella</i> spp., <i>Klebsiella</i> spp., etc.	plasmidal (z.T. chromosomal)	Liu et al., 2015
<i>mcr-2</i>	Enterobacteriaceae: <i>E. coli</i> , <i>Salmonella</i> sp.	plasmidal	Xavier et al., 2016
<i>mcr-3</i>	Enterobacteriaceae: <i>E. coli</i> , <i>Salmonella</i> sp.	plasmidal	Yin et al., 2017
<i>mcr-4</i>	Enterobacteriaceae: <i>E. coli</i> , <i>Salmonella</i> sp.	plasmidal	Carattoli et al., 2017
<i>mcr-5</i>	Enterobacteriaceae: <i>E. coli</i> , <i>Salmonella</i> sp.	plasmidal	Borowiak et al., 2017

- *mcr* Gene überwiegend plasmidal lokalisiert
- Plasmide selbst-transferierbar oder mobilisierbar
- Plasmide unterschiedlicher Inkompatibilitätsgruppen tragen *mcr*



RESEARCH ARTICLE

Multiplex PCR for detection of plasmid-mediated colistin resistance determinants, *mcr-1*, *mcr-2*, *mcr-3*, *mcr-4* and *mcr-5* for surveillance purposes

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mcr-Genverbreitung in Colistin-resistenten Nutztier-/Lebensmittel-Isolaten (2010-2017)

PCR nach Rebelo et al. 2018

Target gene	Size (bp)
<i>mcr-1</i>	320
<i>mcr-2</i>	715
<i>mcr-3</i>	929
<i>mcr-4</i>	1116
<i>mcr-5</i>	1644

	<i>mcr-1</i>	<i>mcr-2</i>	<i>mcr-3</i>	<i>mcr-4</i>	<i>mcr-5</i>
Rind:	+	-	-	+	-
Kalb (Fleisch):	+	-	-	+	-
Schwein:	+	-	-	+	+
Huhn (Kot):	+	-	-	-	-
Hühnerfleisch:	+	-	-	-	-
Pute (Kot):	+	-	-	-	-
Putenfleisch:	+	-	-	-	-

Vorkommen von *mcr*-Genen in Colistin-sensiblen *E. coli*

- *mcr*-Multiplex PCR Screening von Colistin-sensiblen *E. coli*
- **MIC>2 mg/L (n>700):** ~80% *mcr-1*, <1% *mcr-4*, <1% *mcr-5*
- MIC=2 mg/L (n=60): vereinzelt *mcr-1* Nachweis
- MIC<2 mg/L (n=100): keine *mcr*-Gene nachweisbar
- Sanger-Sequenzierung intakte *mcr-1* Gene und Regulationssequenzen
- Transfer der *mcr-1* Plasmide in *E. coli* resultiert in stammabhängiger MIC Ausprägung

Genotyp des Stammes scheint entscheidend für die Ausprägung der Resistenz zu sein!

Charakterisierung von *mcr-4* positiven *E. coli*

RAPID COMMUNICATIONS

Novel plasmid-mediated colistin resistance *mcr-4* gene in *Salmonella* and *Escherichia coli*, Italy 2013, Spain and Belgium, 2015 to 2016

A Carattoli ¹, L Villa ¹, C Feudi ^{1,2}, L Curcio ³, S Orsini ³, A Luppi ⁴, G Pezzotti ³, CF Magistrali ³

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Citation style for this article:

Carattoli A, Villa L, Feudi C, Curcio L, Orsini S, Luppi A, Pezzotti G, Magistrali CF. Novel plasmid-mediated colistin resistance *mcr-4* gene in *Salmonella* and *Escherichia coli*, Italy 2013, Spain and Belgium, 2015 to 2016. *Euro Surveill.* 2017;22(31):pii=30589. DOI: <http://dx.doi.org/10.2807/1560-7917.ES.2017.22.31.30584>

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Charakterisierung von *mcr-4* positiven *E. coli*

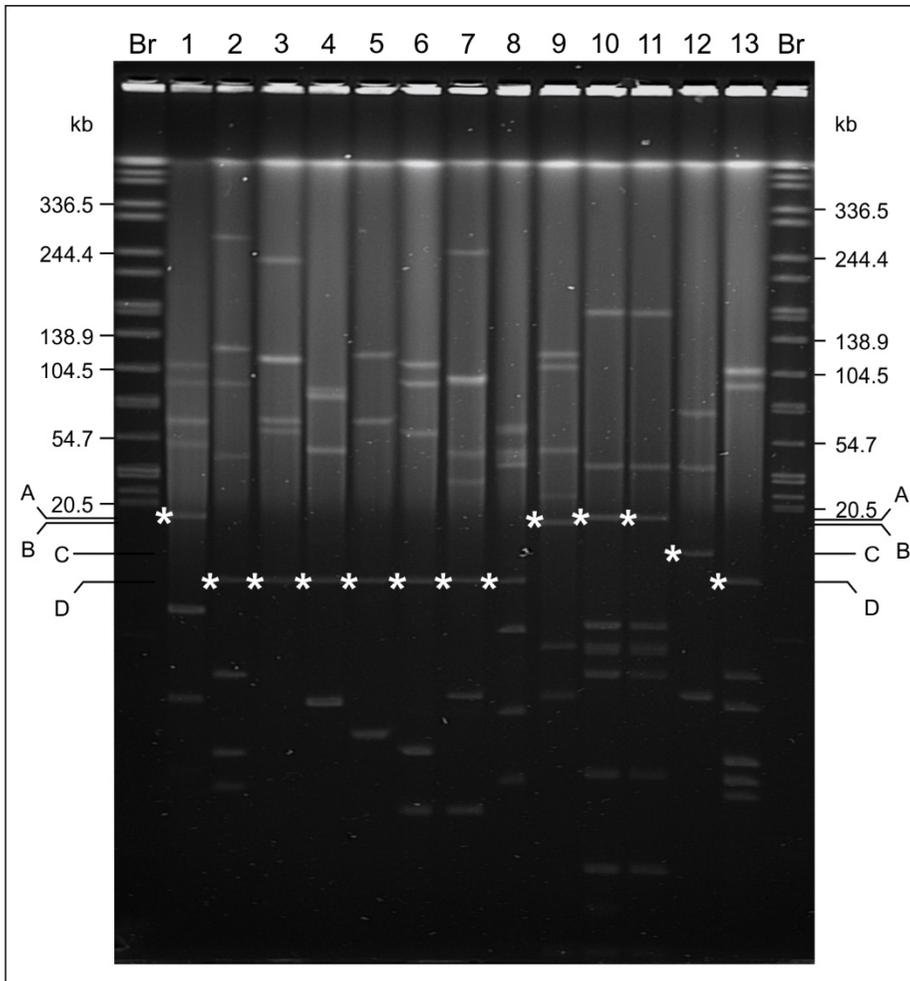
ID	Isolationsjahr	Herkunft	Bundesland	<i>mcr-4</i> -Variante
0761	2010	Kalb, Kot	Niedersachsen	<i>mcr-4.3</i> (Gln331→Arg)
1699	2011	Mastschwein, Kot	Nordrhein Westfalen	<i>mcr-4.2</i> (Val236→Phe)
1740	2011	Mastschwein, Kot	Niedersachsen	<i>mcr-4.2</i> (Val236→Phe)
2249	2011	Mastschwein, Kot	Nordrhein Westfalen	<i>mcr-4.3</i> (Gln331→Arg)
2281	2011	Mastschwein, Kot	Nordrhein Westfalen	<i>mcr-4.3</i> (Gln331→Arg)
3025	2011	Mastschwein, Kot	Nordrhein Westfalen	<i>mcr-4.3</i> (Gln331→Arg)
3068	2011	Mastschwein, Kot	Nordrhein Westfalen	<i>mcr-4.3</i> (Gln331→Arg)
3963	2011	Mastschwein, Kot	Nordrhein Westfalen	<i>mcr-4.3</i> (Gln331→Arg)
1656	2012	Kalb, Fleisch	Sachsen Anhalt	<i>mcr-4.3</i> (Gln331→Arg)
1299	2015	Mastschwein, Kot	Niedersachsen	<i>mcr-4.2</i> (Val236→Phe)
1940	2015	Ferkel, Kot	Sachsen	<i>mcr-4.2</i> (Val236→Phe)
2770	2017	Kalb, Blinddarminhalt	Nordrhein Westfalen	<i>mcr-4.3</i> (Gln331→Arg)
2773	2017	Kalb, Blinddarminhalt	Nordrhein Westfalen	<i>mcr-4.3</i> (Gln331→Arg)

Resistenzausprägung von *mcr-4*-positiven *E. coli*

Isolate	AMP	AZI	CHL	CIP	COL	FOT	GEN	MERO	NAL	SMX	TAZ	TET	TGC	TMP
0716	>64	8	>128	>8	8	1	32	≤0.03	>128	>1024	>8	>64	≤0.25	>32
1699	>64	8	≤8	≤0.015	4	≤0.25	≤0.5	≤0.03	≤4	>1024	≤0.5	>64	≤0.25	>32
1740	>64	16	32	≤0.015	4	≤0.25	2	≤0.03	≤4	>1024	≤0.5	>64	≤0.25	>32
2249	>64	4	≤8	0.03	4	≤0.25	≤0.5	≤0.03	≤4	>1024	≤0.5	>64	≤0.25	≤0.25
2281	>64	8	≤8	0.03	4	≤0.25	≤0.5	≤0.03	≤4	>1024	≤0.5	64	≤0.25	>32
3025	>64	8	≤8	0.03	4	≤0.25	≤0.5	≤0.03	≤4	>1024	≤0.5	>64	0.5	>32
3068	>64	8	128	≤0.015	4	≤0.25	32	≤0.03	≤4	>1024	≤0.5	>64	≤0.25	>32
3963	>64	8	≤8	≤0.015	4	≤0.25	≤0.5	≤0.03	≤4	>1024	≤0.5	64	≤0.25	>32
1656	>64	16	≤8	0.5	4	≤0.25	≤0.5	≤0.03	128	>1024	≤0.5	>64	≤0.25	>32
1299	>64	8	>128	>8	4	>4	8	≤0.03	>128	>1024	8	>64	0.5	>32
1940	>64	≤2	>128	0.25	4	≤0.25	≤0.5	≤0.03	64	>1024	≤0.5	64	0.25	>32
2770	>64	32	16	0.25	4	≤0.25	≤0.5	≤0.03	32	>1024	≤0.5	>64	0.5	>32
2773	>64	32	16	0.12	4	≤0.25	≤0.5	≤0.03	32	>1024	≤0.5	>64	≤0.25	>32

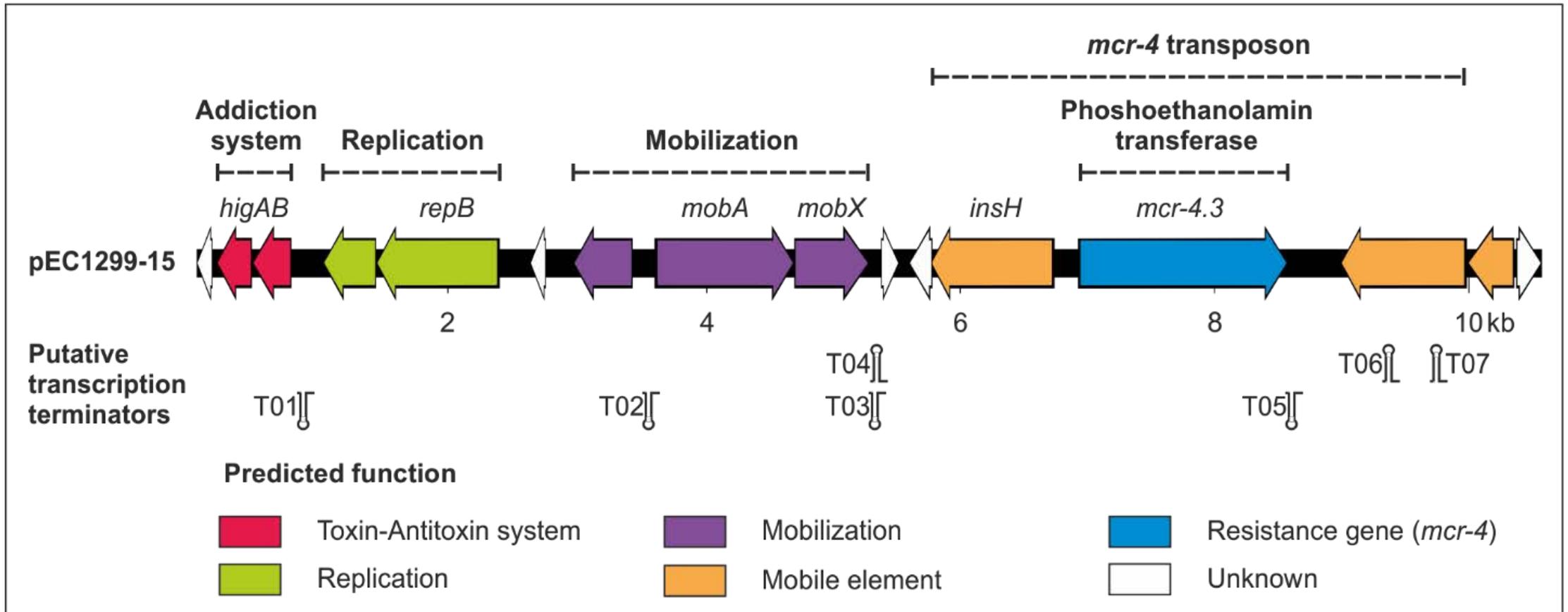
[mg/L]

Plasmide in *mcr-4*-positiven *E. coli*



Plasmid ID	Stamm ID	Prototype Plasmid	Größe (bp)	Inc Gruppe	MIC in DH5α
p0716-10	0716	A	11599	ColE10	2 mg/L
p1699-11	1699	D	7807	ColE10	2 mg/L
p1740-11	1740	D	7807	ColE10	2 mg/L
p2249-11	2249	D	7803	ColE10	2 mg/L
p2281-11	2281	D	7803	ColE10	2 mg/L
p3025-11	3025	D	7807	ColE10	2 mg/L
p3068-11	3068	D	7807	ColE10	2 mg/L
p3963-11	3963	D	7807	ColE10	2 mg/L
p1656-12	1656	B	10705	ColE10	2 mg/L
p2770-17	2770	A	11599	ColE10	2 mg/L
p2773-17	2773	A	11599	ColE10	2 mg/L
p1299-15	1299	C	8645	ColE10	2 mg/L
p1940-15	1940	D	7807	ColE10	2 mg/L

Das *mcr-4* Prototyp-Plasmid



Zusammenfassung zu *mcr-4*-positiven *E. coli*

WGS (MiSeq) & bioinformatische Auswertung:

- hohe genetische Diversität *mcr-4* (n=14) positiver Isolate (PFGE, MLST, Serotyp, Virulenzfaktoren, antimikrobielle Resistenz)
- Nachweis der *mcr-4.2* & *mcr-4.3* Varianten
- ein Plasmidtyp (unterschiedliche Größen), bisher nicht konjugativ transferierbar

J Antimicrob Chemother 2017; **72**: 3317–3324

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Identification of a novel transposon-associated phosphoethanolamine transferase gene, *mcr-5*, conferring colistin resistance in *d*-tartrate fermenting *Salmonella enterica* subsp. *enterica* serovar Paratyphi B

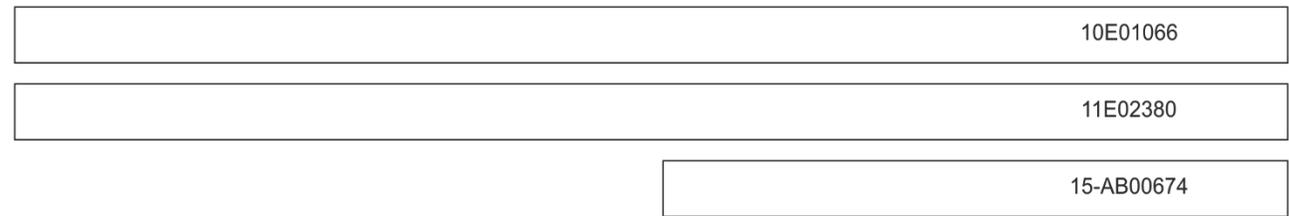
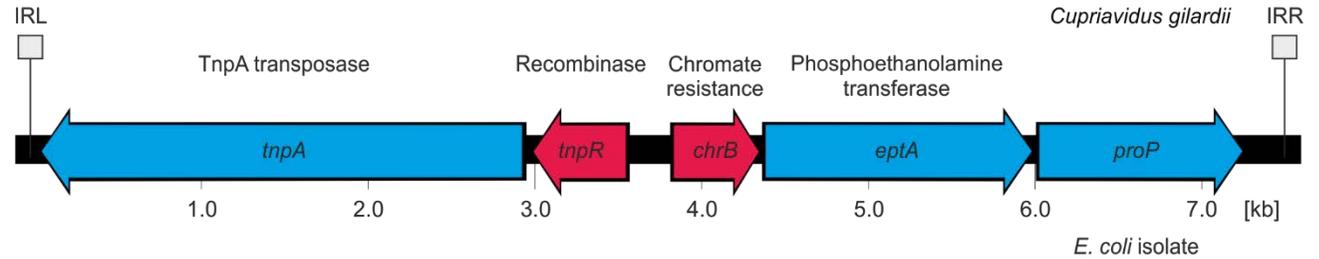
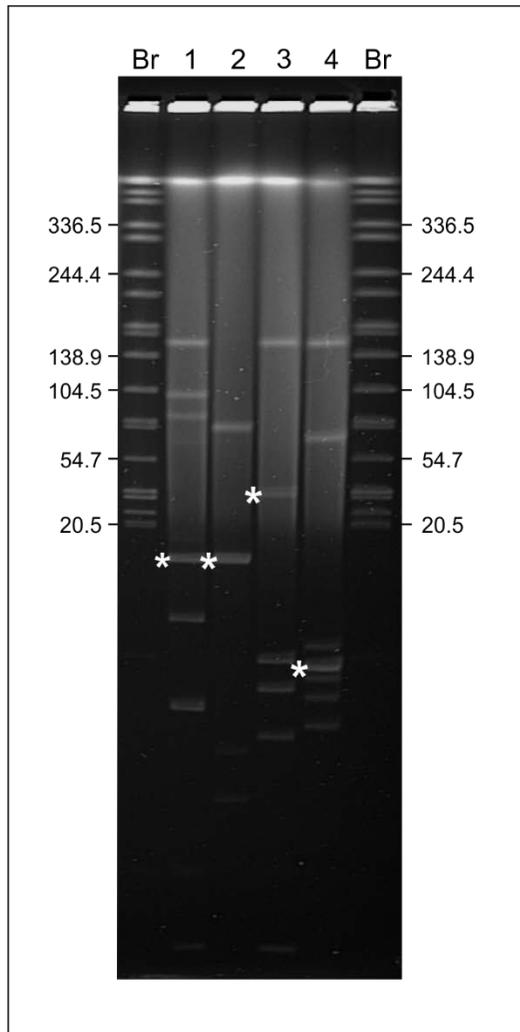
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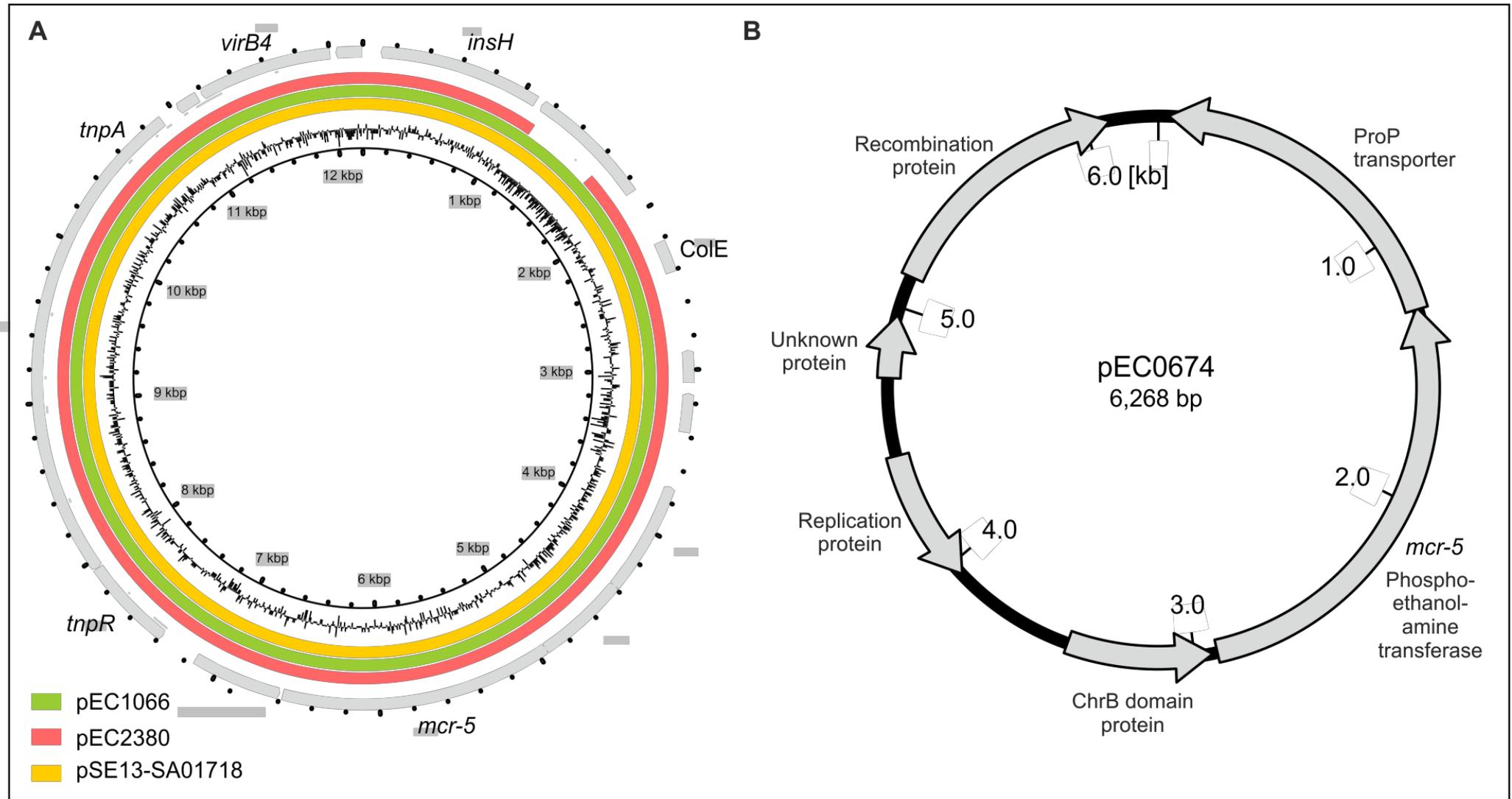
Received 23 June 2017; returned 17 July 2017; revised 4 August 2017; accepted 4 August 2017

Plasmide in *mcr-5*-positiven *E. coli*



1066	MRLSAFITFLKMRPQVRTEFLTLFISLVFTLLCNGVFWNALLIAGRDSLTSGTWMLLLCTG	60
2380	MRLSAFITFLKMRPQVRTEFLTLFISLVFTLLCNGVFWNALLIAGRDSLTSGTWMLLLCTG	60
1066	LLITGLQWLLLLLVATRWSVKPLLI LLAVMTPAAVYFMRNYGVYLDKAMLRNLMETDVRE	120
2380	LLITGLQWLLLLLVATRWSVKPLLI LLAVMTPAAVYFMRNYGVYLDKAMLRNLMETDVRE	120
1066	ASELLQWRMLPYLLVAAVSVWWIARVRVLRGTGWKQAVMMRSACLAGALAMI SMGLWPVMD	180
2380	ASELLQWRMLPYLLVAAVSVWWIARVRVLRGTGWKQAVMMRSACLAGALAMI SMGLWPVMD	180
1066	VLIPTLRENKPLRYLITPANYVISGIRVLTEQASSSADEAREVVAADAHRGPOE*QGRRPR	240
2380	VLIPTLRENKPLRYLITPANYVISGIRVLTEQASSSADEAREVVAADAHRGPO-QGRRPR	239
1066	ALVLVVG ET VRAANWGLSGYERQTTPELAARDVINFSDVTSCGTD T ATSLPCMFSINGR	300
2380	ALVLVVG ET VRAANWGLSGYERQTTPELAARDVINFSDVTSCGTD T ATSLPCMFSINGR	299
1066	DYDERQIRRRESVLHVLNRSVDN IL WRDNQSGCKGVCDGLPFENLSSAGHPTLCHGERCL	360
2380	DYDERQIRRRESVLHVLNRSVDN IL WRDNQSGCKGVCDGLPFENLSSAGHPTLCHGERCL	359
1066	DEILLEG LA EKI TT SRSDMLIVLHMLGN H GPAYFQRYPAS Y RRWSPTCD TT DLASC S HEA	420
2380	DEILLEG LA EKI TT SRSDMLIVLHMLGN H GPAYFQRYPAS Y RRWSPTCD TT DLASC S HEA	419
1066	LVNTYD NA VLYTDHVLARTIDLLSGIRSHDTALLYVSD H GESLGEKGLYLHGIPYVIAPD	480
2380	LVNTYD NA VLYTDHVLARTIDLLSGIRSHDTALLYVSD H GESLGEKGLYLHGIPYVIAPD	479
1066	EQIKVPMI W QSSQVYADQACMQTHASRAPVSHDHLFHTLLGMF D VKTAAYTPEL DL LAT	540
2380	EQIKVPMI W QSSQVYADQACMQTHASRAPVSHDHLFHTLLGMF D VKTAAYTPEL DL LAT	539
1066	CRKGQPQ	547
2380	CRKGQPQ	546

Plasmidtypen *mcr-5*-positiver *E. coli*



Zusammenfassung zu *mcr-5*-positiven *E. coli*

WGS (MiSeq) & bioinformatische Auswertung:

- hohe genetische Diversität *mcr-5* (n=4) positiver Isolate (PFGE, MLST, Serotyp, Virulenzfaktoren, antimikrobielle Resistenz)
- Nachweis der *mcr-5* & *mcr-5.2* Varianten
- zwei Plasmidtypen (unterschiedliche Größen), bisher nicht konjugativ transferierbar

Neue Colistin-Resistenzgene: Nach dem Screening ist vor dem Screening

NCBI Resources How To

Nucleotide Nucleotide Advanced

GenBank

Moraxella sp. MSG47-C17 mcr-6 gene for phosphoethanolamine-transferase MCR-6.1, complete CDS

NCBI Reference Sequence: NG_055781.1

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LOCUS NG_055781 1617 bp DNA linear CON 25-JAN-2018
 DEFINITION Moraxella sp. MSG47-C17 mcr-6 gene for phosphoethanolamine--lipid A transferase MCR-6.1, complete CDS.
 ACCESSION NG_055781
 VERSION NG_055781.1
 DBLINK BioProject: [FRJNA313047](#)
 KEYWORDS RefSeq.
 SOURCE Moraxella sp. MSG47-C17
 ORGANISM [Moraxella sp. MSG47-C17](#)
 Bacteria; Proteobacteria; Gammaproteobacteria; Pseudomonadales; Moraxellaceae; Moraxella.
 REFERENCE 1 (bases 1 to 1617)
 AUTHORS AbuOun,M., Stubberfield,E., Duggett,N., Kirchner,M., Dorma,L., Nunez-Garcia,J., Randall,L., Lemma,F., Crook,D., Teale,C., Smith,R.P. and Anjum,M.F.
 TITLE mcr-1 and mcr-2 variant genes identified in Moraxella species isolated from pigs
 JOURNAL Unpublished
 REFERENCE 2 (bases 1 to 1617)
 CONSRIM NCBI Refseq Project
 TITLE Direct Submission
 JOURNAL Submitted (25-JAN-2018) National Center for Biotechnology Information, NIH, Bethesda, MD 20894, USA
 COMMENT REVIEWED [REFSEQ](#): This record has been curated by NCBI staff. The reference sequence was derived from [MF176240.1](#). This record has been chosen as a reference for antimicrobial resistance. For more general information: <http://www.ncbi.nlm.nih.gov/pathogens/>
 COMPLETENESS: not full length.
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GenBank

Klebsiella pneumoniae strain SC20141012 plasmid pSC20141012, sequence

GenBank: MG267386.1

[FASTA](#) [Graphics](#)

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LOCUS MG267386 65631 bp DNA circular BCT 21-FEB-2018
 DEFINITION Klebsiella pneumoniae strain SC20141012 plasmid pSC20141012, complete sequence.
 ACCESSION MG267386
 VERSION MG267386.1
 KEYWORDS .
 SOURCE Klebsiella pneumoniae
 ORGANISM [Klebsiella pneumoniae](#)
 Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales; Enterobacteriaceae; Klebsiella.
 REFERENCE 1 (bases 1 to 65631)
 AUTHORS Yang,Y. and Wang,H.
 TITLE Novel plasmid-mediated colistin resistance gene mcr-7.1 in Klebsiella pneumoniae
 JOURNAL Unpublished
 REFERENCE 2 (bases 1 to 65631)
 AUTHORS Yang,Y. and Wang,H.
 TITLE Direct Submission
 JOURNAL Submitted (25-OCT-2017) College of Life Science, Sichuan University, No. 29 Wangjiang Rd, Chengdu, Sichuan 610064, China
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Nucleotide Nucleotide Advanced

[Learn more](#) about upcoming changes to the Nucleotide, EST, and GSS databases.

GenBank

Send to:

Klebsiella pneumoniae KP91 pKP91 mcr-8 gene for phosphoethanolamine--lipid A transferase MCR-8.1, complete CDS

NCBI Reference Sequence: NG_061399.1

[FASTA](#) [Graphics](#)

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LOCUS NG_061399 1898 bp DNA linear CON 01-AUG-2018
 DEFINITION Klebsiella pneumoniae KP91 pKP91 mcr-8 gene for phosphoethanolamine--lipid A transferase MCR-8.1, complete CDS.
 ACCESSION NG_061399
 VERSION NG_061399.1
 DBLINK BioProject: [FRJNA313047](#)
 KEYWORDS RefSeq.
 SOURCE Klebsiella pneumoniae
 ORGANISM [Klebsiella pneumoniae](#)
 Bacteria; Proteobacteria; Gammaproteobacteria; Enterobacteriales; Enterobacteriaceae; Klebsiella.
 REFERENCE 1 (bases 1 to 1898)
 AUTHORS Wang,X., Wang,Y. and Shen,Z.
 TITLE Identified a colistin-resistance gene mcr-8.1 in klebsiella pneumoniae
 JOURNAL Emerg Microbes Infect (2018) In press
 REFERENCE 2 (bases 1 to 1898)
 CONSRIM NCBI Refseq Project
 TITLE Direct Submission
 JOURNAL Submitted (01-AUG-2018) National Center for Biotechnology Information, NIH, Bethesda, MD 20894, USA
 COMMENT REVIEWED [REFSEQ](#): This record has been curated by NCBI staff. The reference sequence was derived from [MG736312.1](#). This record has been chosen as a reference for antimicrobial resistance. For more general information: <http://www.ncbi.nlm.nih.gov/pathogens/>
 COMPLETENESS: not full length.
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Zusammenfassung

- Diversität der Isolate hoch (keine prädominanten MLST-/PFGE-Typen)
- *mcr*-Plasmide mit verschiedenen Replikons, meist mit mob-Regionen
- Plasmide mosaikartig, aus funktionellen Modulen zusammengesetzt
- ca. 82% der Colistin-resistenten *E. coli* weisen *mcr*-Gene auf
- Bedeutung einzelner *mcr*-Gene für die Resistenzverbreitung unklar

- **Anpassung molekularer Typisierungsverfahren nötig**
- **Untersuchung der Biologie und Genetik einzelner Gene essentiell**
- **Bewertung: Wenige Daten zur *mcr*-Prävalenz in humanen Proben**

**Vielen Dank an alle
Mitarbeiter des NRL-AR
für die Unterstützung!**



Danke für Ihre Aufmerksamkeit

Jens A. Hammerl

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