

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



Dr. Jens A. Hammerl

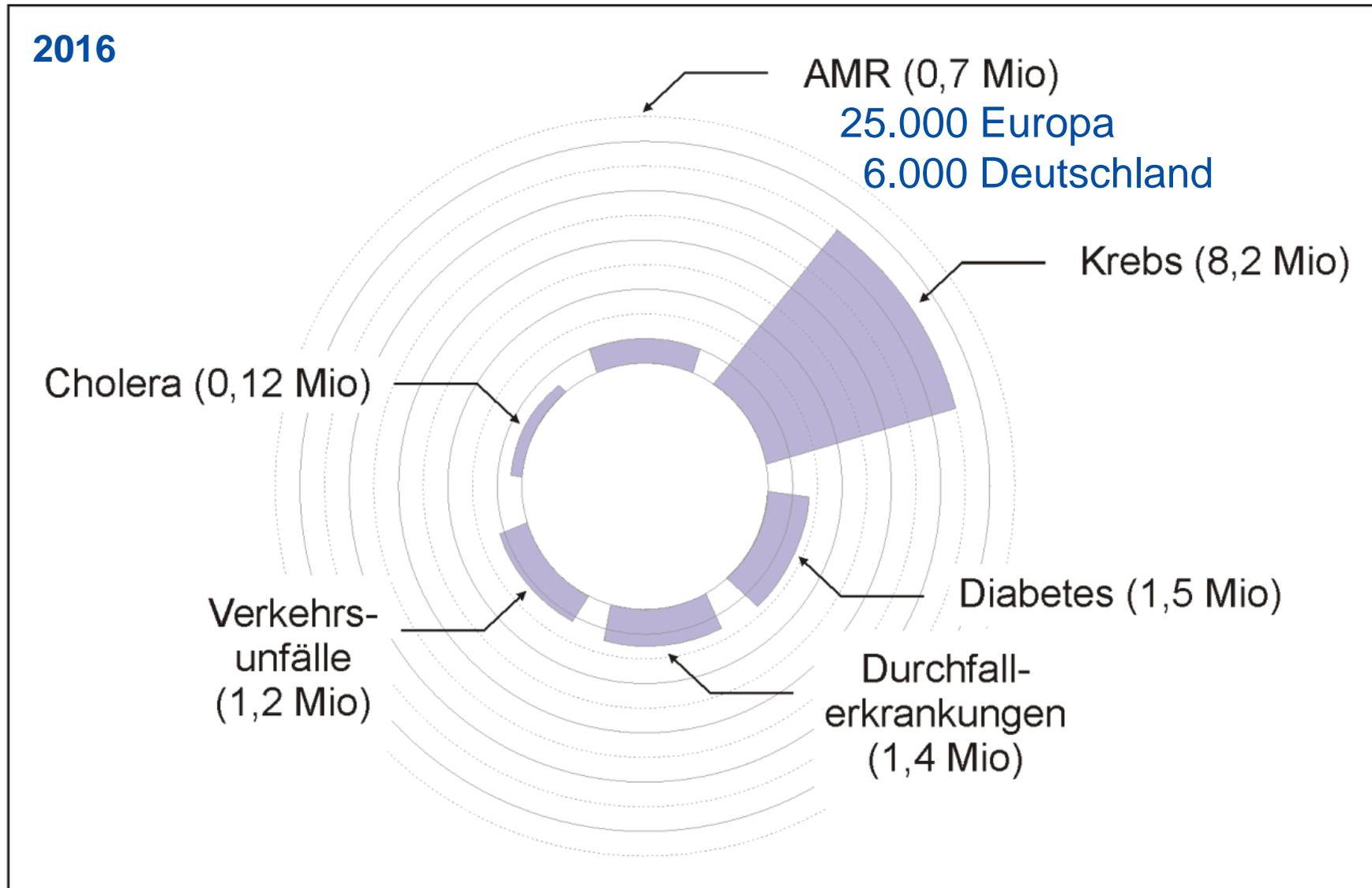
Nationales Referenzlabor für Antibiotikaresistenz (NRL-AR)

Fachgruppe Epidemiologie, Zoonosen und Antimikrobielle Resistenzen

Abteilung Biologische Sicherheit

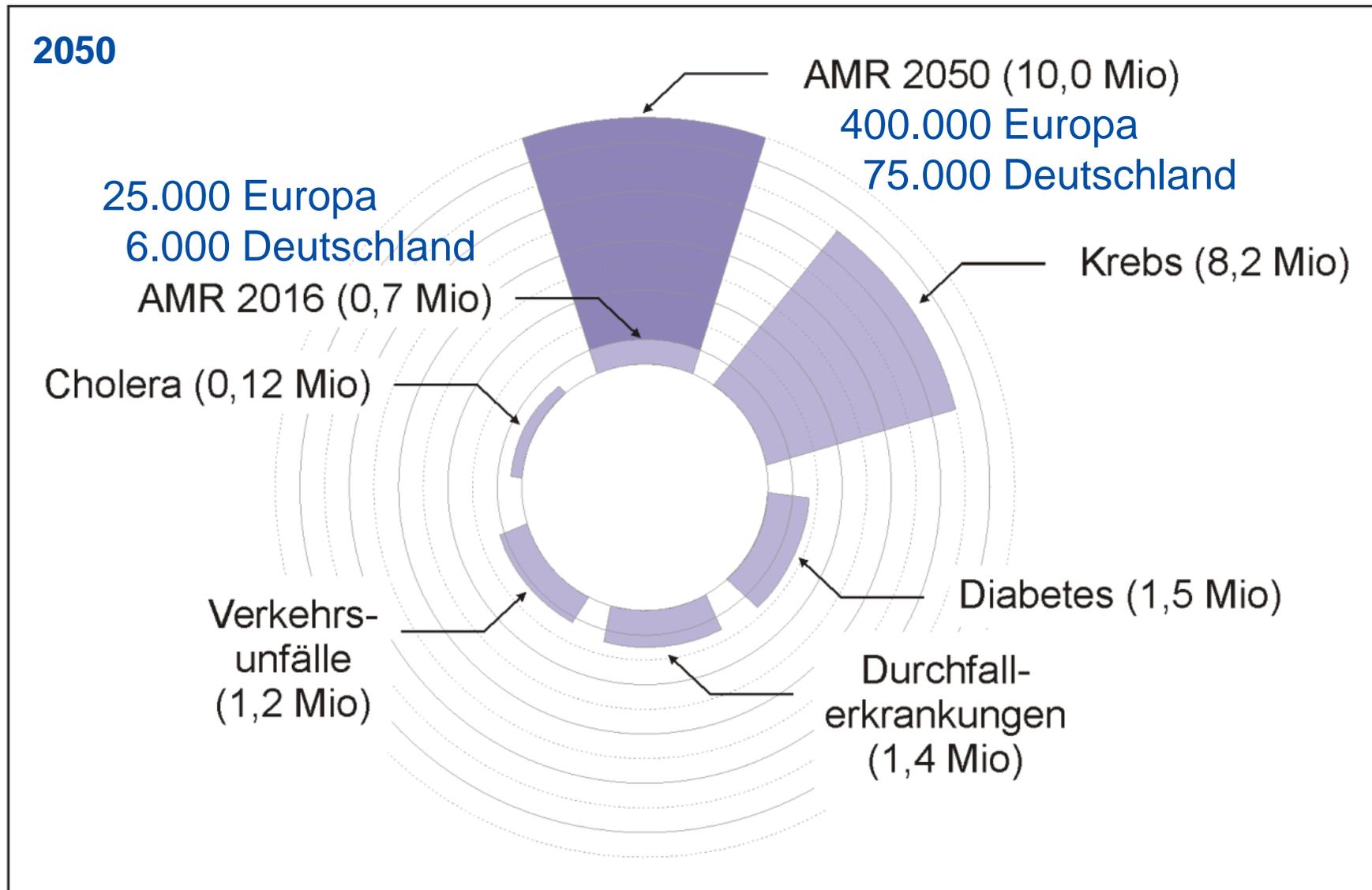
Bundesinstitut für Risikobewertung

Weltweite Bedeutung antimikrobieller Resistenzen



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

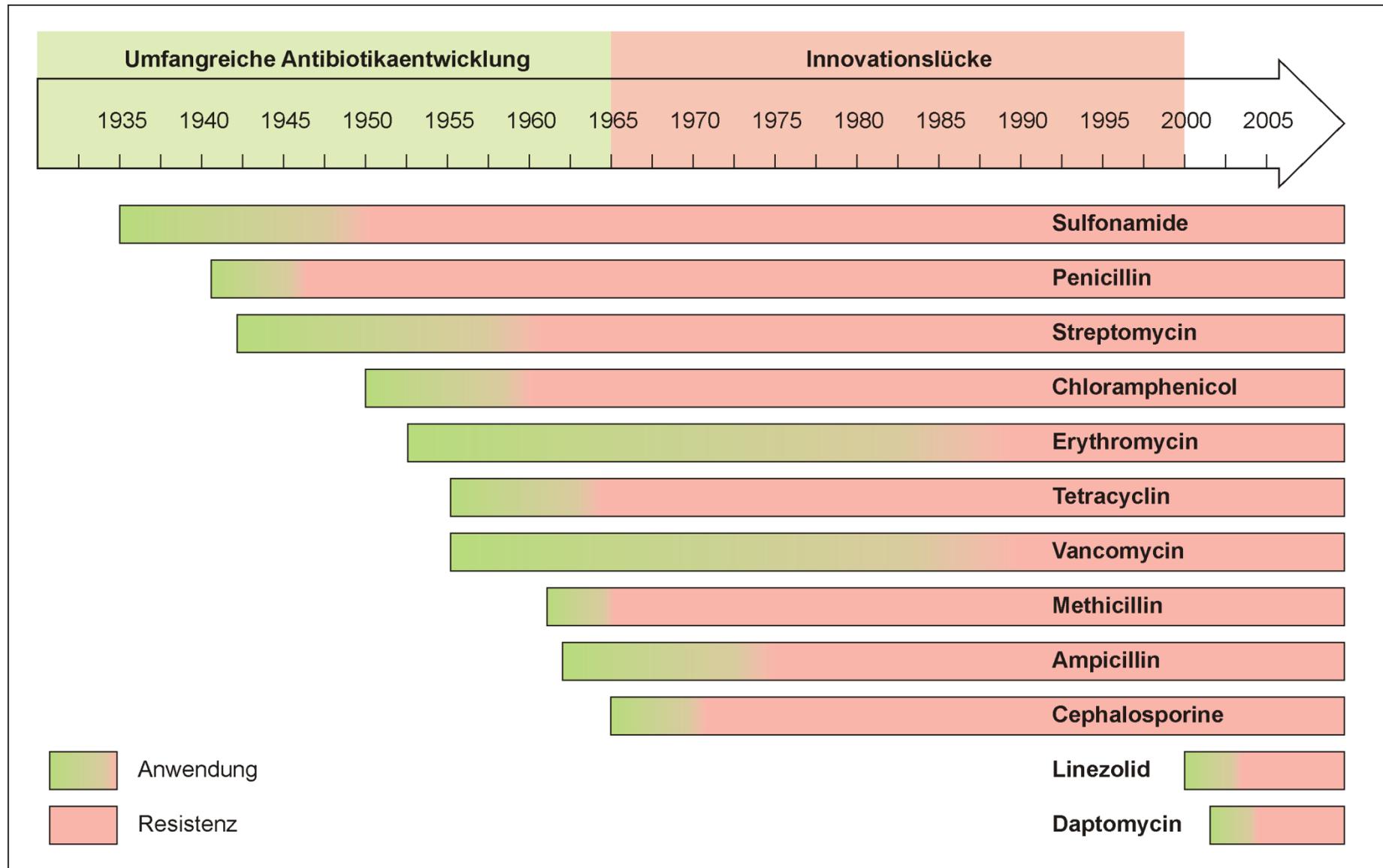
Weltweite Bedeutung antimikrobieller Resistenzen



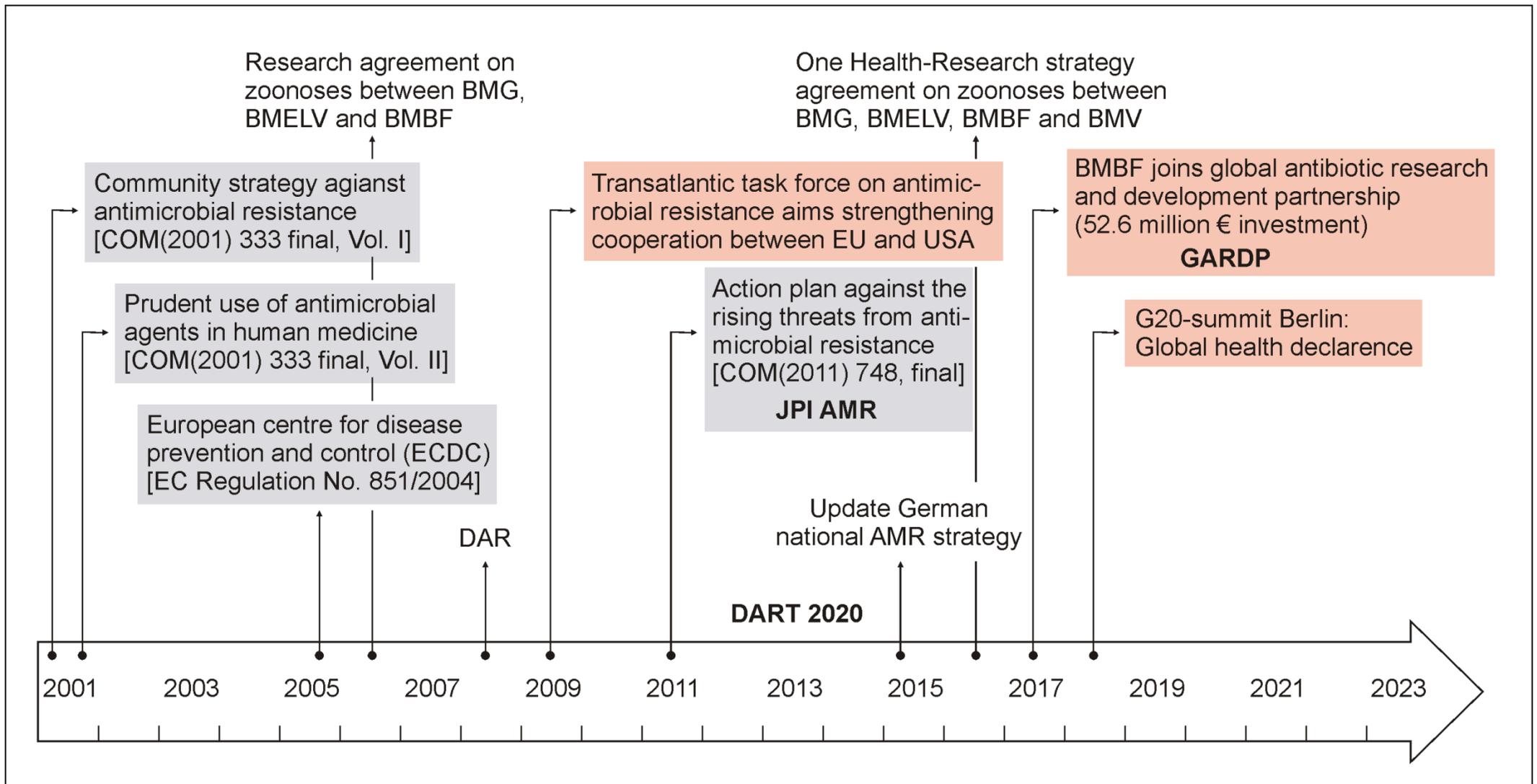
Modifiziert aus: Tackling Drug-Resistant Infections Globally: Final Report And Recommendations Review On Antimicrobial Resistance, 2016, <http://amr-review.org/>

Resistenzentwicklung: Ein Wettlauf gegen die Zeit

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



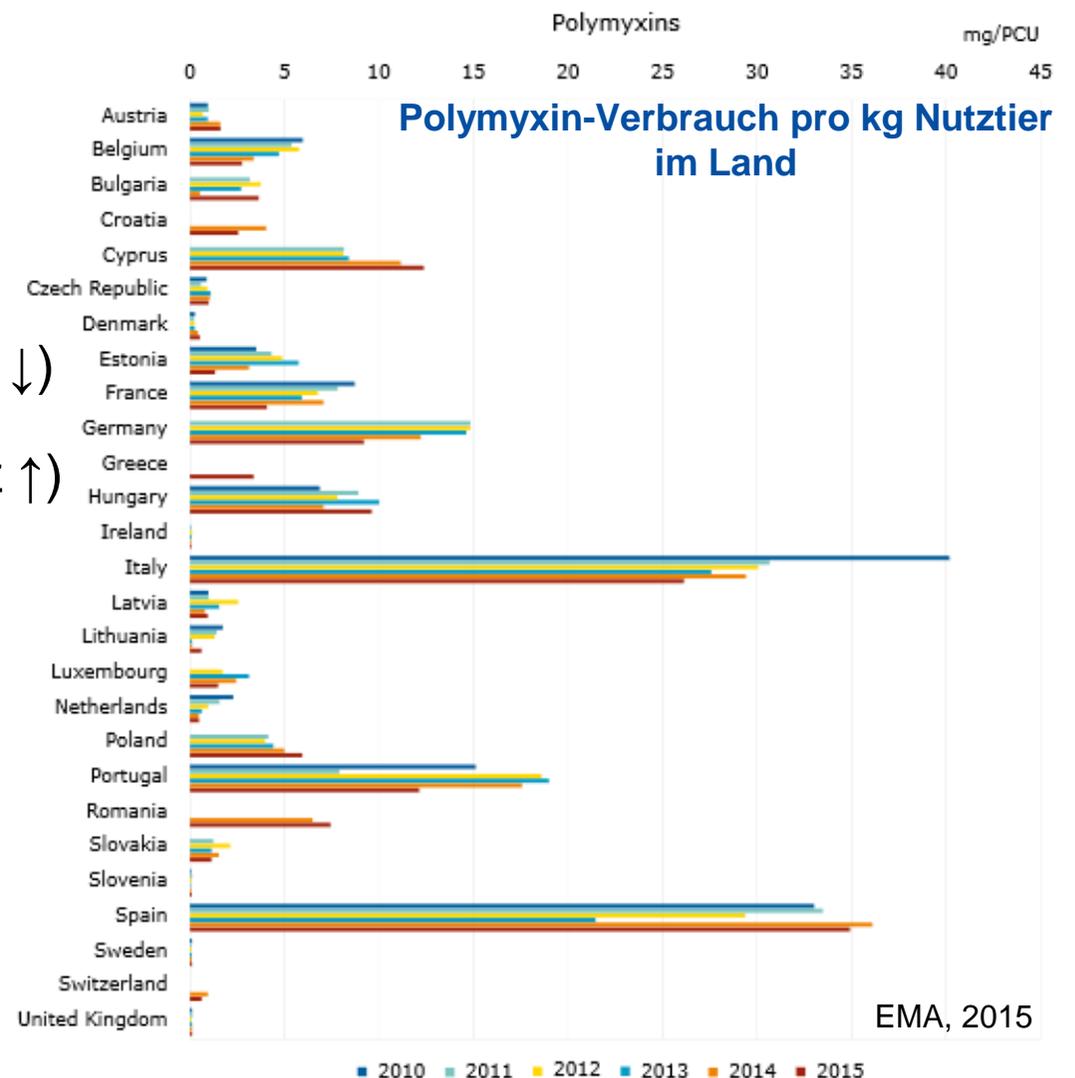
Forschungs-/politische Lösungsansätze zur Vermeidung ...



- 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 ↑)



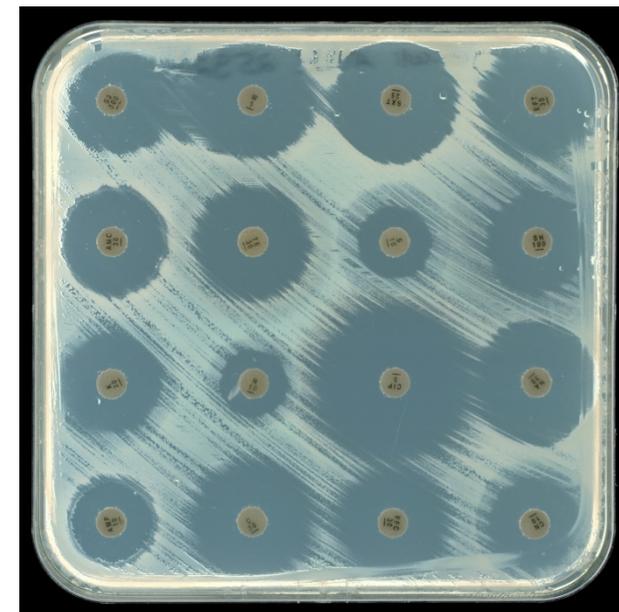
Colistin-Resistenz in Gram-negativen Bakterien

Intrinsische Resistenz

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

Erworbene (extrinsische) Resistenz

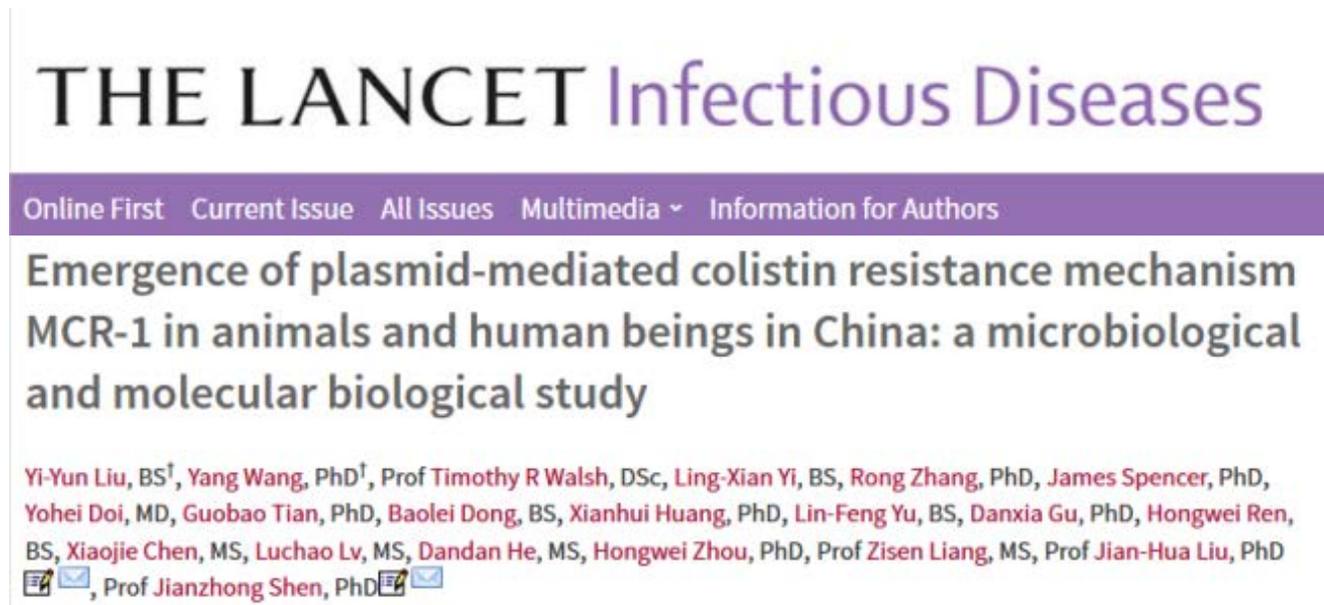
- Effluxpumpen (z.B. Yersinien, Klebsiellen)
- Veränderung der Kapselzusammensetzung (Klebsiellen)
- Verlust des LPS (*A. baumannii*)
- **Modifikationen der äußeren Membran bzw. LPS (Deacylierung, Hydroxylierung, Anlagerung von Aminoarabinose oder Phosphoethanolamin)**



Colistin-Resistenzverbreitung: Ein Paradigmenwechsel...

- chromosomal-assoziierte Resistenz

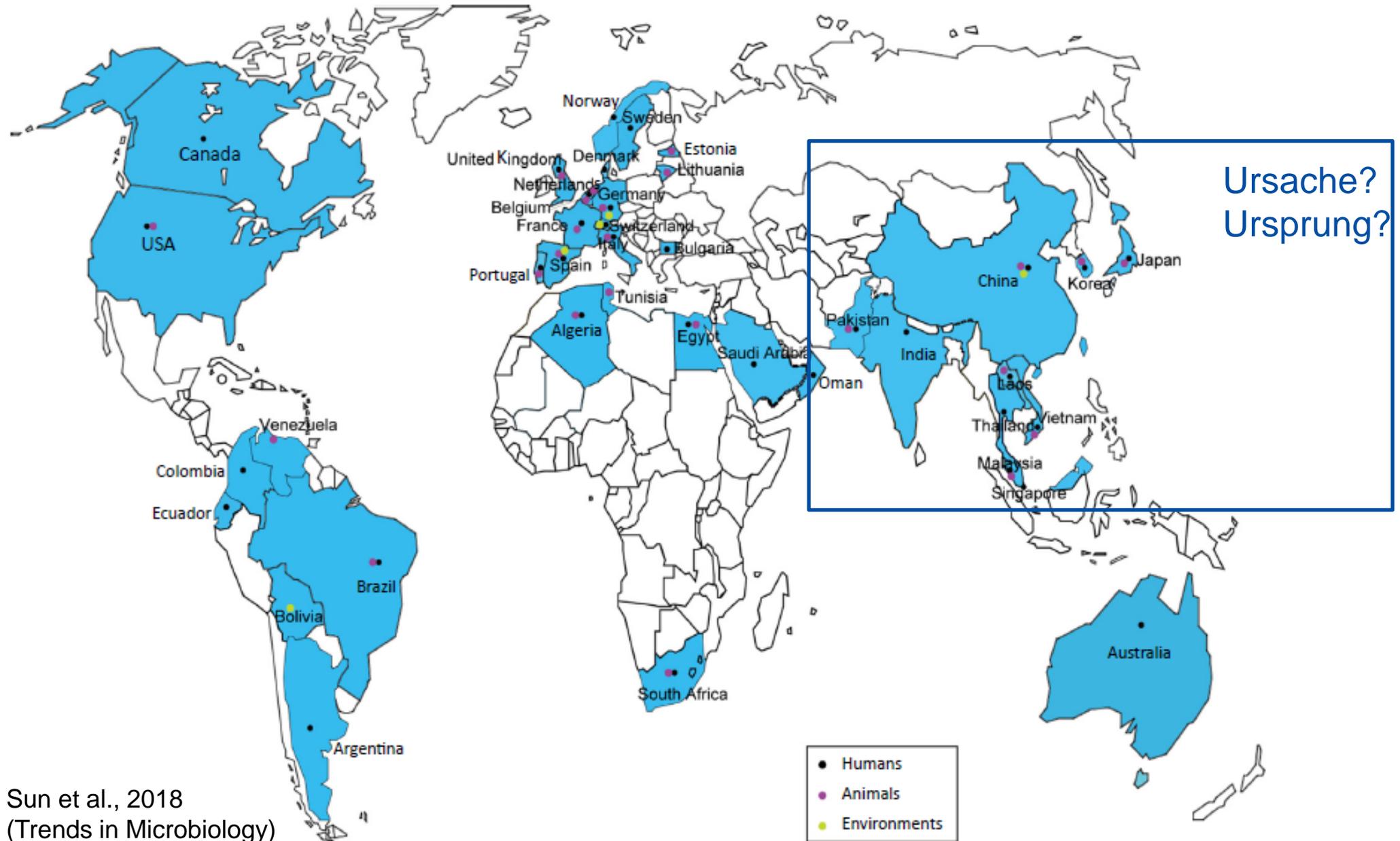
Vertikale Verbreitung



- 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*}

¹ Department Biological Safety, National Reference Laboratory for Antimicrobial Resistance, Federal Institute for Risk Assessment, Berlin, Germany, ² Institute for Animal Hygiene and Environmental Health, Freie Universität Berlin, Berlin, Germany

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%)

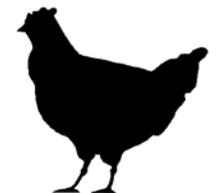
43-75,4%

85,2-100%

50-88,9%

81,1-93,9%

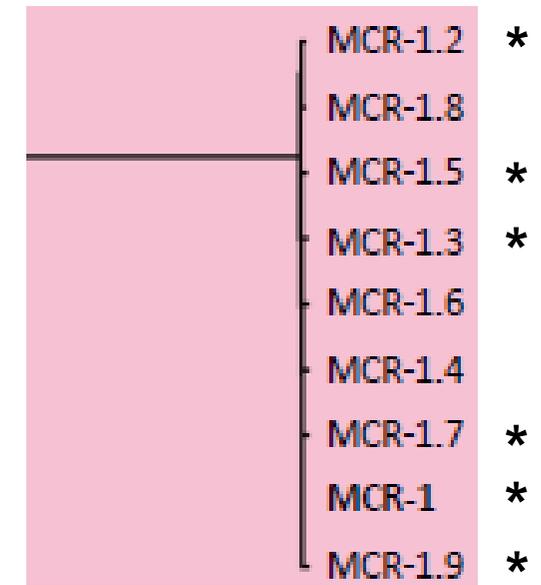
~90%



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)

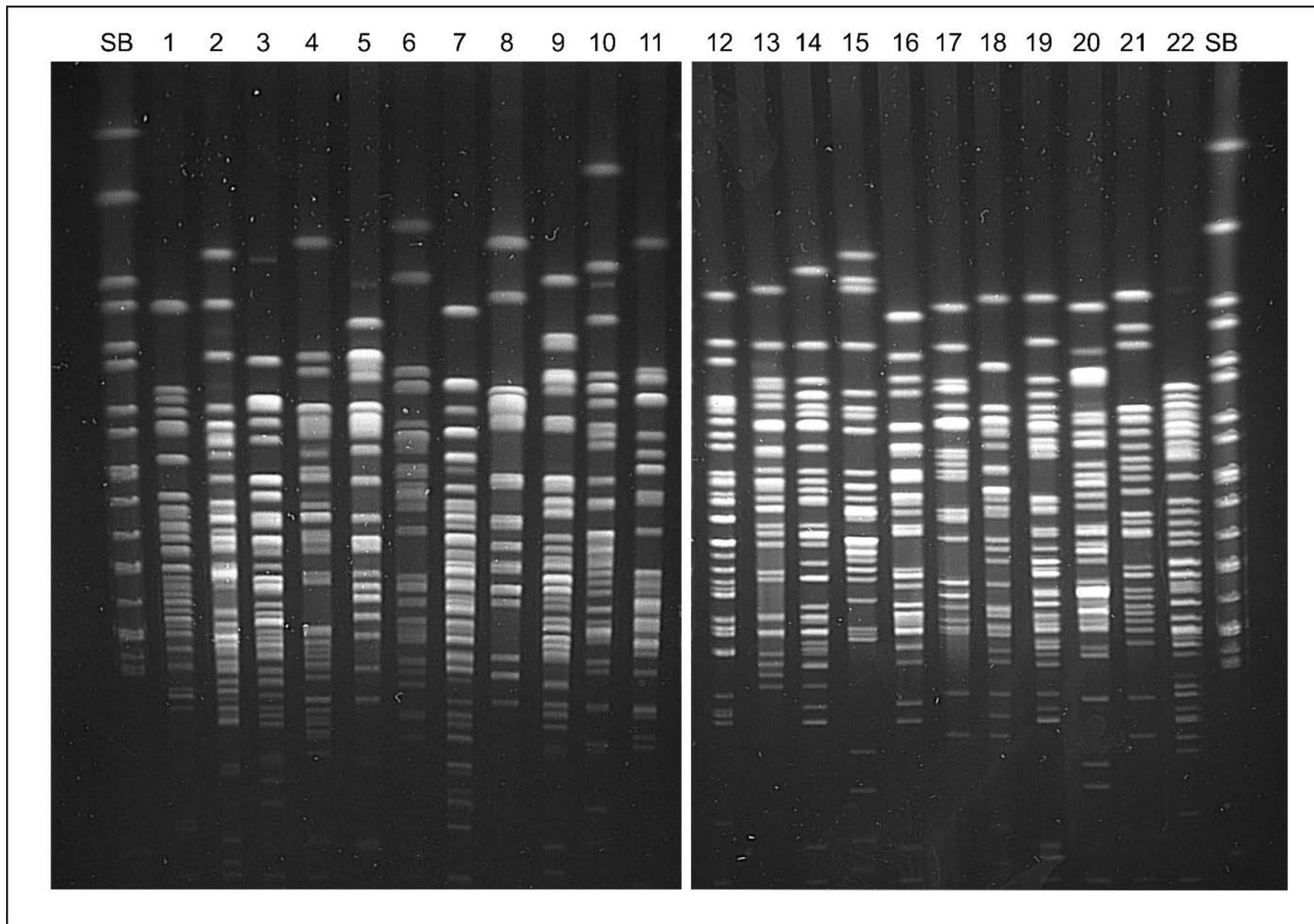


Bedeutung der Varianten unbekannt!

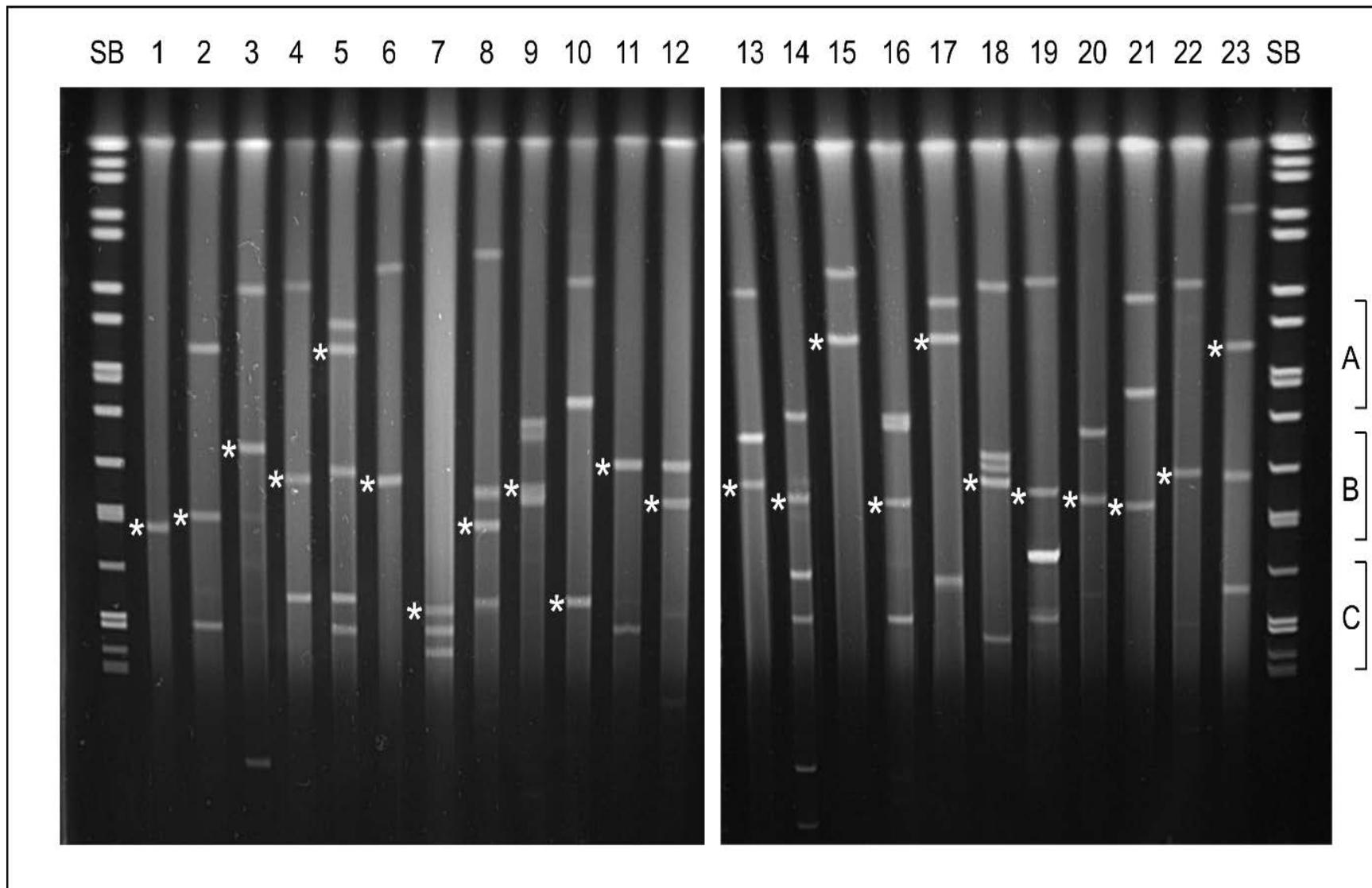
Untersuchungen zur Diversität *mcr-1* positiver *E. coli*

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*

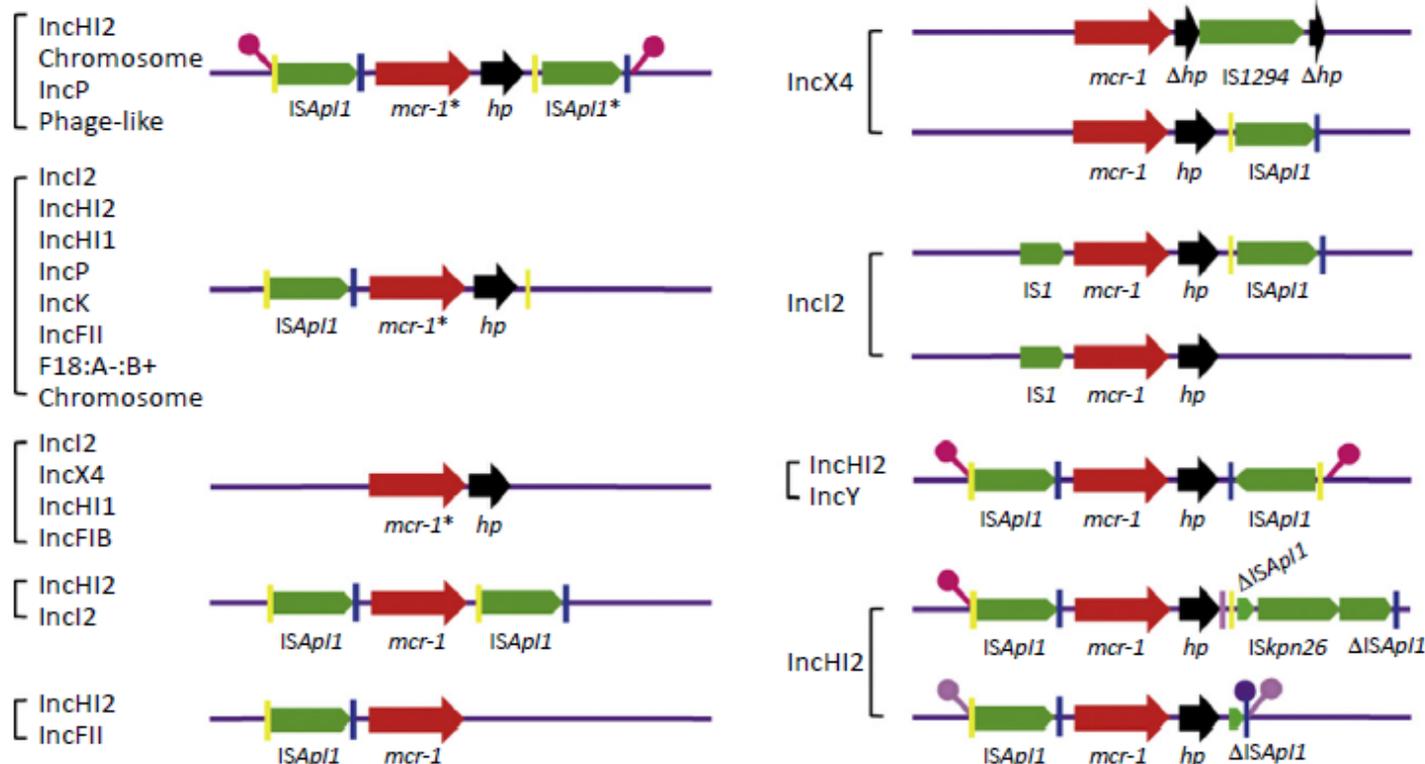


Genetische Variabilität *mcr-1*-positiver *E. coli*



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

Maria Borowiak¹, Jennie Fischer¹, Jens A. Hammerl¹, Rene S. Hendriksen², Istvan Szabo¹ and Burkhard Malorny^{1*}

¹German Federal Institute for Risk Assessment, BfR, Department for Biological Safety, Berlin, Germany; ²National Food Institute, Technical University of Denmark, WHO Collaborating Center for Antimicrobial Resistance in Foodborne Pathogens and European Union Reference Laboratory for Antimicrobial Resistance, Kgs Lyngby, Denmark

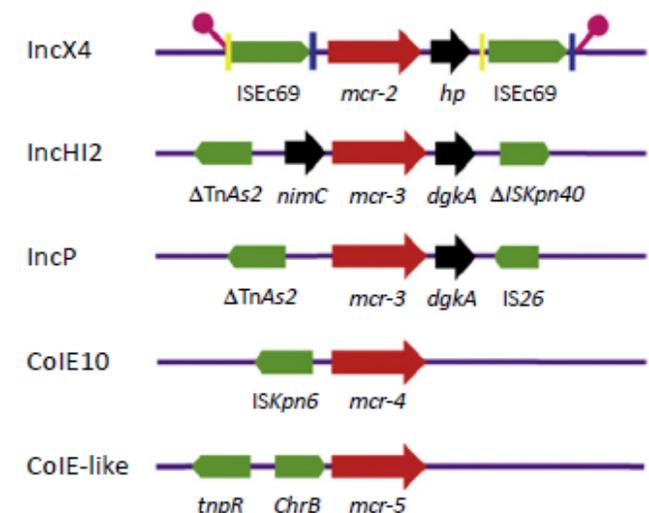
*Corresponding author. Tel: +49-30-18412-2237; E-mail: Burkhard.Malorny@bfr.bund.de

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

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

Ana Rita Rebelo¹, Valeria Bortolaia¹, Jette S Kjeldgaard¹, Susanne K Pedersen¹, Pimlapas Leekitcharoenphon¹, Inge M Hansen¹, Beatriz Guerra², Burkhard Malorny³, Marla Borowiak³, Jens Andre Hammerl³, Antonio Battisti⁴, Alessia Franco⁴, Patricia Alba⁴, Agnes Perrin-Guyomard⁵, Sophie A Granier⁶, Cristina De Frutos Escobar^{7*}, Surbhi Malhotra-Kumar⁸, Laura Villa⁹, Alessandra Carattoli⁹, Rene S Hendriksen¹

1. National Food Institute, Technical University of Denmark, WHO Collaborating Center for Antimicrobial Resistance in Food borne Pathogens and European Union Reference Laboratory for Antimicrobial Resistance, Kongens Lyngby, Denmark
2. European Food Safety Authority, Parma, Italy
3. German Federal Institute for Risk Assessment, Berlin, Germany
4. National Reference Laboratory for antimicrobial resistance, Istituto Zooprofilattico Sperimentale del Lazio e della Toscana, Rome, Italy
5. Anses, Fougères Laboratory, Fougères, France
6. Université Paris-Est, Anses, Laboratory for Food Safety, Maisons-Alfort, France
7. Laboratorio Central de Veterinaria, (LCV Algete), Madrid, Spain
8. Laboratory of Medical Microbiology, Vaccine & Infectious Disease Institute, University of Antwerp, Wilrijk, Belgium
9. Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy

Correspondence: Rene S. Hendriksen (rshe@food.dtu.dk)

Citation style for this article:

Rebelo Ana Rita, Bortolaia Valeria, Kjeldgaard Jette S, Pedersen Susanne K, Leekitcharoenphon Pimlapas, Hansen Inge M, Guerra Beatriz, Malorny Burkhard, Borowiak Maria, Hammerl Jens Andre, Battisti Antonio, Franco Alessia, Alba Patricia, Perrin-Guyomard Agnes, Granier Sophie A, De Frutos Escobar Cristina, Malhotra-Kumar Surbhi, Villa Laura, Carattoli Alessandra, Hendriksen Rene S. Multiplex PCR for detection of plasmid-mediated colistin resistance determinants, *mcr-1*, *mcr-2*, *mcr-3*, *mcr-4* and *mcr-5* for surveillance purposes. Euro Surveill. 2018;23(6):pii=17-00672. <https://doi.org/10.2807/1560-7917.ES.2018.23.6.17-00672>

Article submitted on 04 Oct 2017 / accepted on 13 Nov 2017 / published on 08 Feb 2018

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

1. Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy

2. Institute of Microbiology and Epizootics, Centre for Infection Medicine, Department of Veterinary Medicine, Freie Universität Berlin, Berlin, Germany

3. Istituto Zooprofilattico Sperimentale dell'Umbria e delle Marche, Perugia, Italy

4. Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna, Reggio Emilia, Italy

Correspondence: Alessandra Carattoli (alessandra.carattoli@iss.it)

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>

Article submitted on 27 July 2017 / accepted on 03 August 2017 / published on 03 August 2017

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

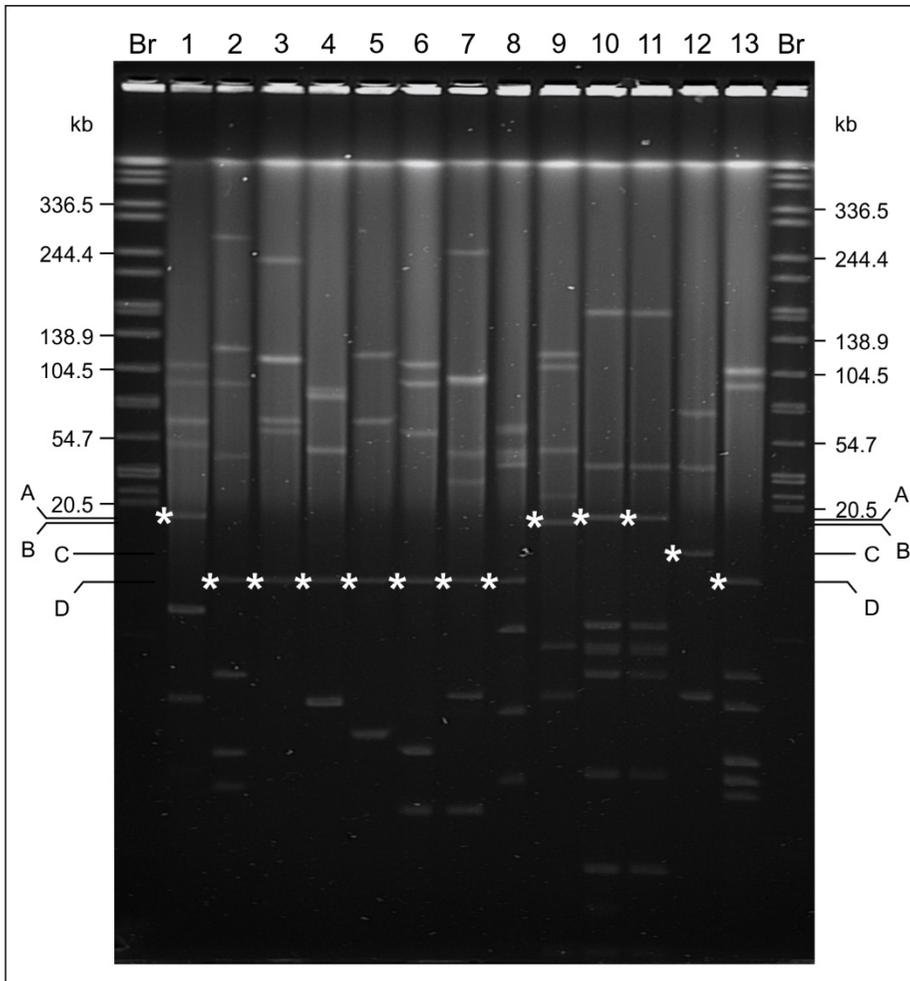
ID	Isolationsjahr	Herkunft	Bundesland	<i>mcr-4</i> -Variante
0761	2010	Kalb, Kot	Niedersachsen	<i>mcr-4.3</i> (Gln331→Arg)
1699	2011	Mastschwein, Kot	Nordrhein Westfalen	<i>mcr-4.2</i> (Val236→Phe)
1740	2011	Mastschwein, Kot	Niedersachsen	<i>mcr-4.2</i> (Val236→Phe)
2249	2011	Mastschwein, Kot	Nordrhein 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

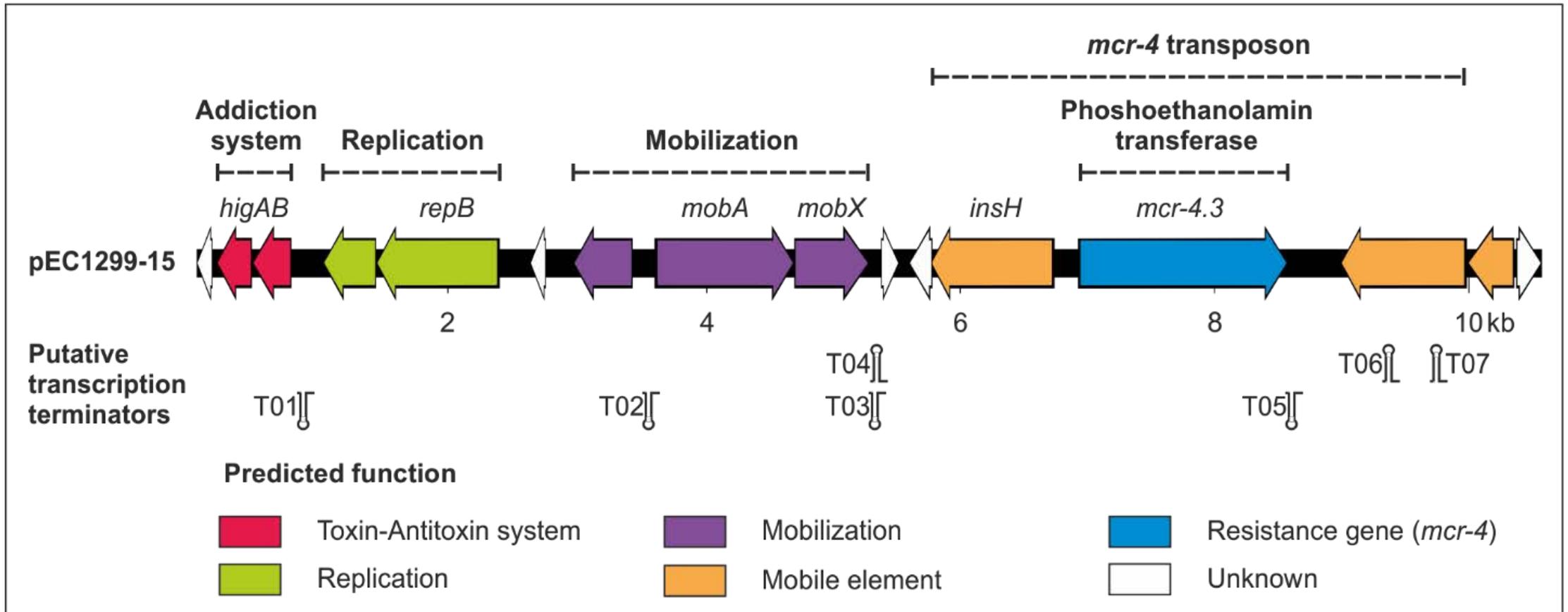
[mg/L]

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

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

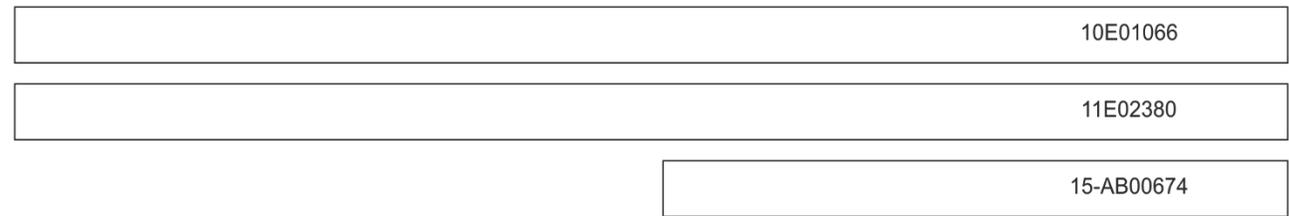
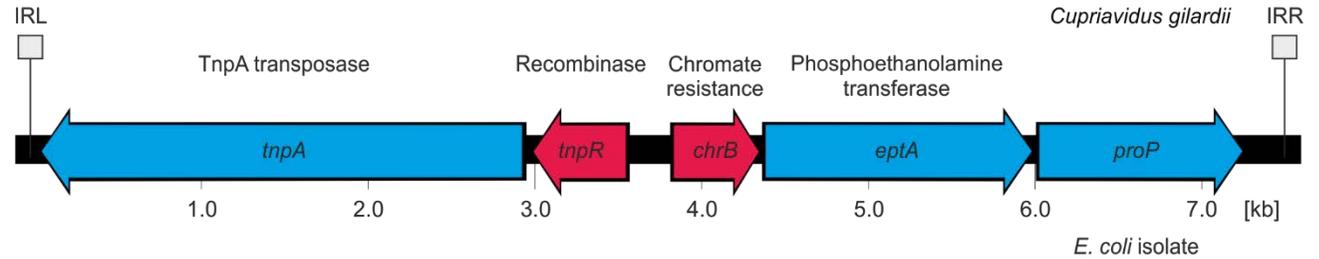
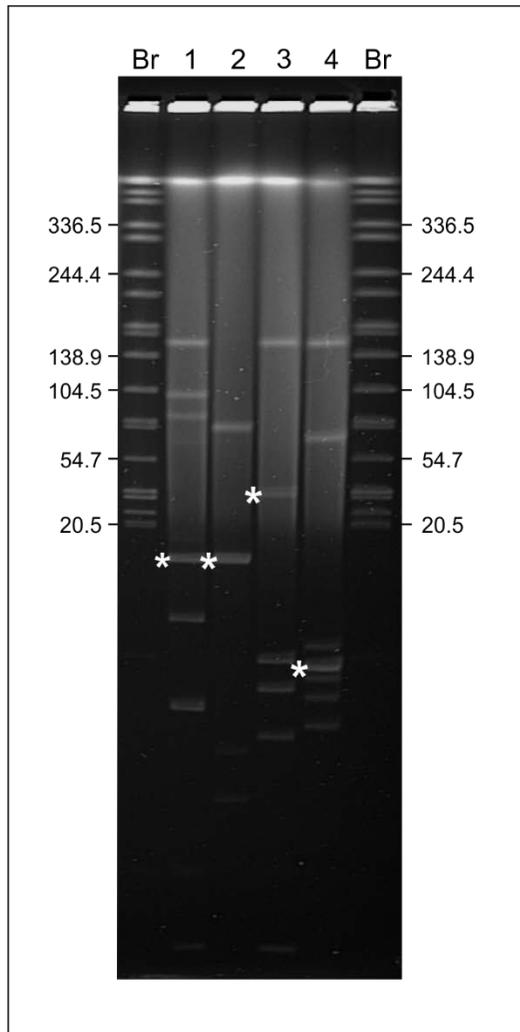
Maria Borowiak¹, Jennie Fischer¹, Jens A. Hammerl¹, Rene S. Hendriksen², Istvan Szabo¹ and Burkhard Malorny^{1*}

¹German Federal Institute for Risk Assessment, BfR, Department for Biological Safety, Berlin, Germany; ²National Food Institute, Technical University of Denmark, WHO Collaborating Center for Antimicrobial Resistance in Foodborne Pathogens and European Union Reference Laboratory for Antimicrobial Resistance, Kgs Lyngby, Denmark

*Corresponding author. Tel: +49-30-18412-2237; E-mail: Burkhard.Malorny@bfr.bund.de

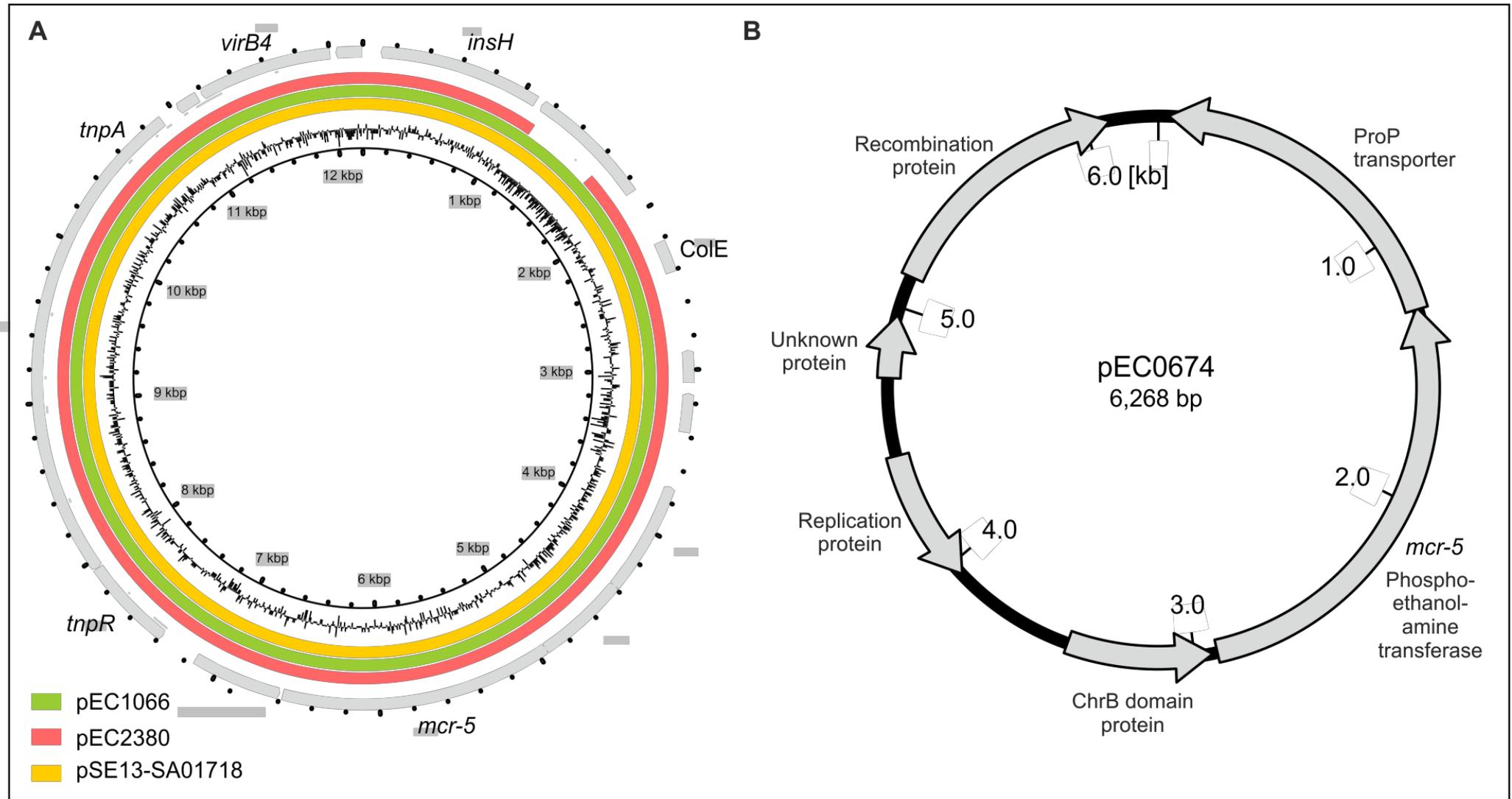
Received 23 June 2017; returned 17 July 2017; revised 4 August 2017; accepted 4 August 2017

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

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

[Go to](#)

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.
 FEATURES
 source Location/Qualifiers
 1..1617
 /organism="Moraxella sp. MSG47-C17"
 /mol_type="genomic DNA"
 /strain="MSG47-C17"
 /isolation_source="caecal contents"
 /host="porcine"
 /db_xref="taxon:1935434"
 /country="United Kingdom"
 /collection_date="May-2015"
 /note="Moraxella cf. pluranimalium"

NCBI Resources How To

Nucleotide Nucleotide Advanced

GenBank

Klebsiella pneumoniae strain SC20141012 plasmid pSC20141012, sequence

GenBank: MG267386.1

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

[Go to](#)

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
 FEATURES
 Location/Qualifiers
 source 1..65631
 /organism="Klebsiella pneumoniae"
 /mol_type="genomic DNA"
 /strain="SC20141012"
 /host="Chicken"
 /db_xref="taxon:573"
 /plasmid="pSC20141012"
 /country="China"

NCBI Resources How To

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](#)

[Go to](#)

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.
 FEATURES
 source Location/Qualifiers
 1..1898
 /organism="Klebsiella pneumoniae"
 /mol_type="genomic DNA"
 /strain="KP91"
 /isolation_source="feces"
 /host="pig"
 /db_xref="taxon:573"
 /plasmid="pKP91"
 /country="China"

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

Bundesinstitut für Risikobewertung

Max-Dohrn-Str. 8-10 • 10589 Berlin

Tel. 030 - 184 12 - 0 • Fax 030 - 184 12 - 47 41

bfr@bfr.bund.de • www.bfr.bund.de