



IZSAM G.CAPORALE  
TERAMO

  *Campylobacter*  
Laboratorio Nazionale di Riferimento

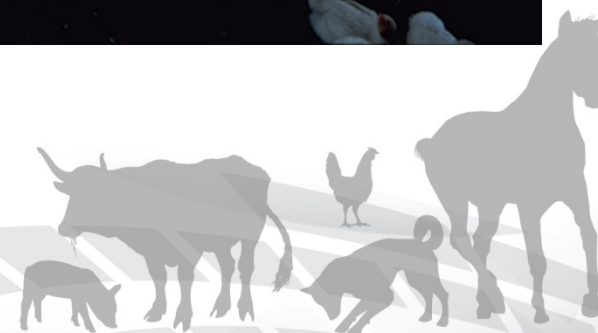
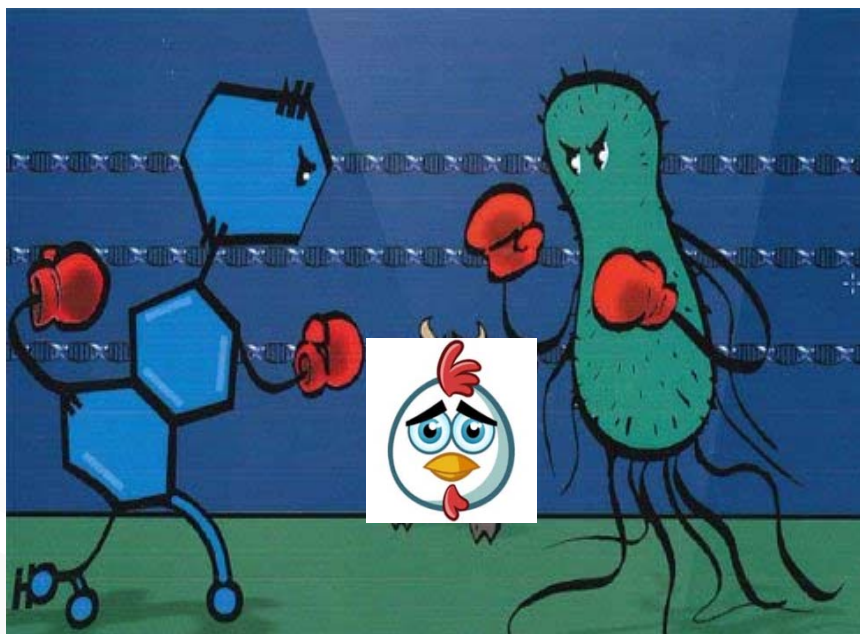
## Resistenza di *Campylobacter* ai chinoloni e fluorchinoloni e sequenziamento girasi





# Antibiotico resistenza

 *Campylobacter*  
Laboratorio Nazionale di Riferimento

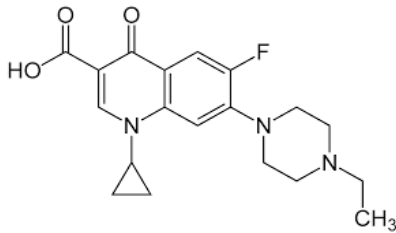




**Campylobacter**  
Laboratorio Nazionale di Riferimento

# Utilizzo antibiotici in zootecnia... implicazioni

## ENROFLOXACINA



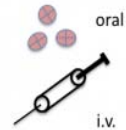
Clin

### Fluoroquinolone-Resistant *Campylobacter* Species and the Withdrawal of Fluoroquinolones from Use in Poultry: A Public Health Success Story

Jennifer M. Nelson,<sup>1,2</sup> Tom M. Chiller,<sup>1</sup> John H. Powers,<sup>3</sup> and Frederick J. Angulo<sup>1</sup>

## Fluoroquinolone Uses

### Routes:



Infections of bone, joints & soft tissues

### Mechanism:

Inhibits DNA Gyrase & Topoisomerase IV



bactericidal

Ophthalmic infections

Respiratory Infections, Inhaled Anthrax, Mycobacteria (TB)

GI & Abdominal Infections

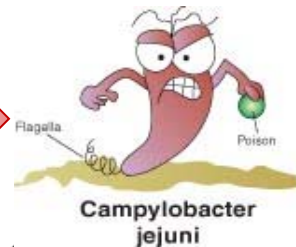
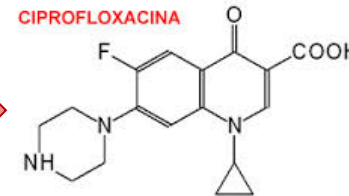
Prostatitis

UTIs (MDR strains) & STDs (Chlamydia)

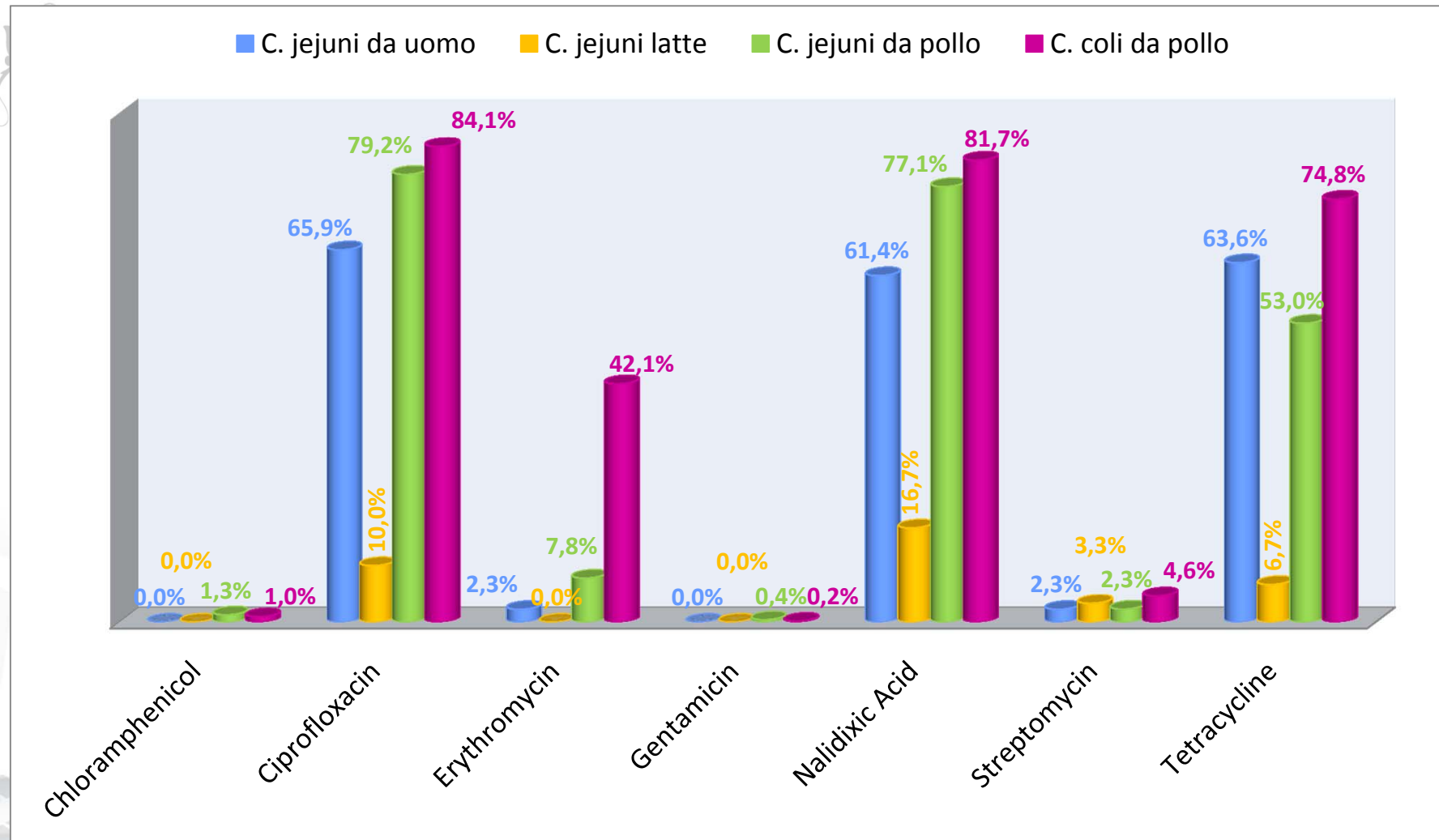
### Adverse Effects:

- Tendon rupture
- Children <18 yo (cartilage)
- Pregnancy Category C
- Seizures, prolong QT
- Dizziness, Confusion
- Photosensitivity

## CIPROFLOXACINA



# Antibiotico resistenza *Campylobacter*

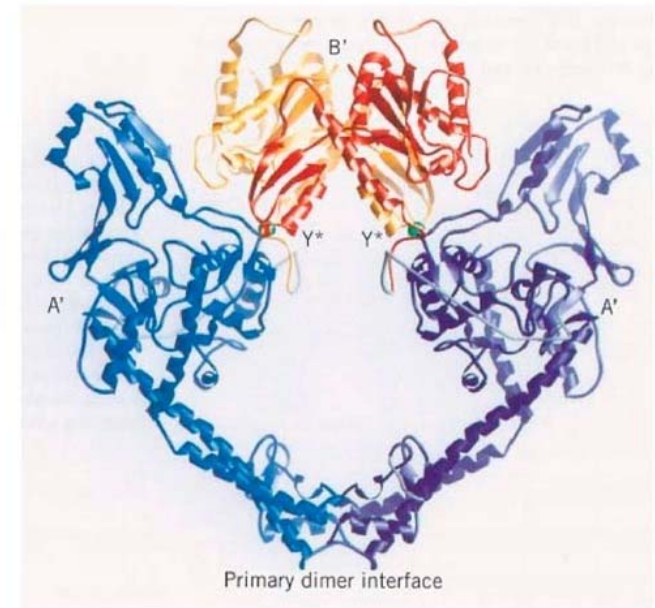
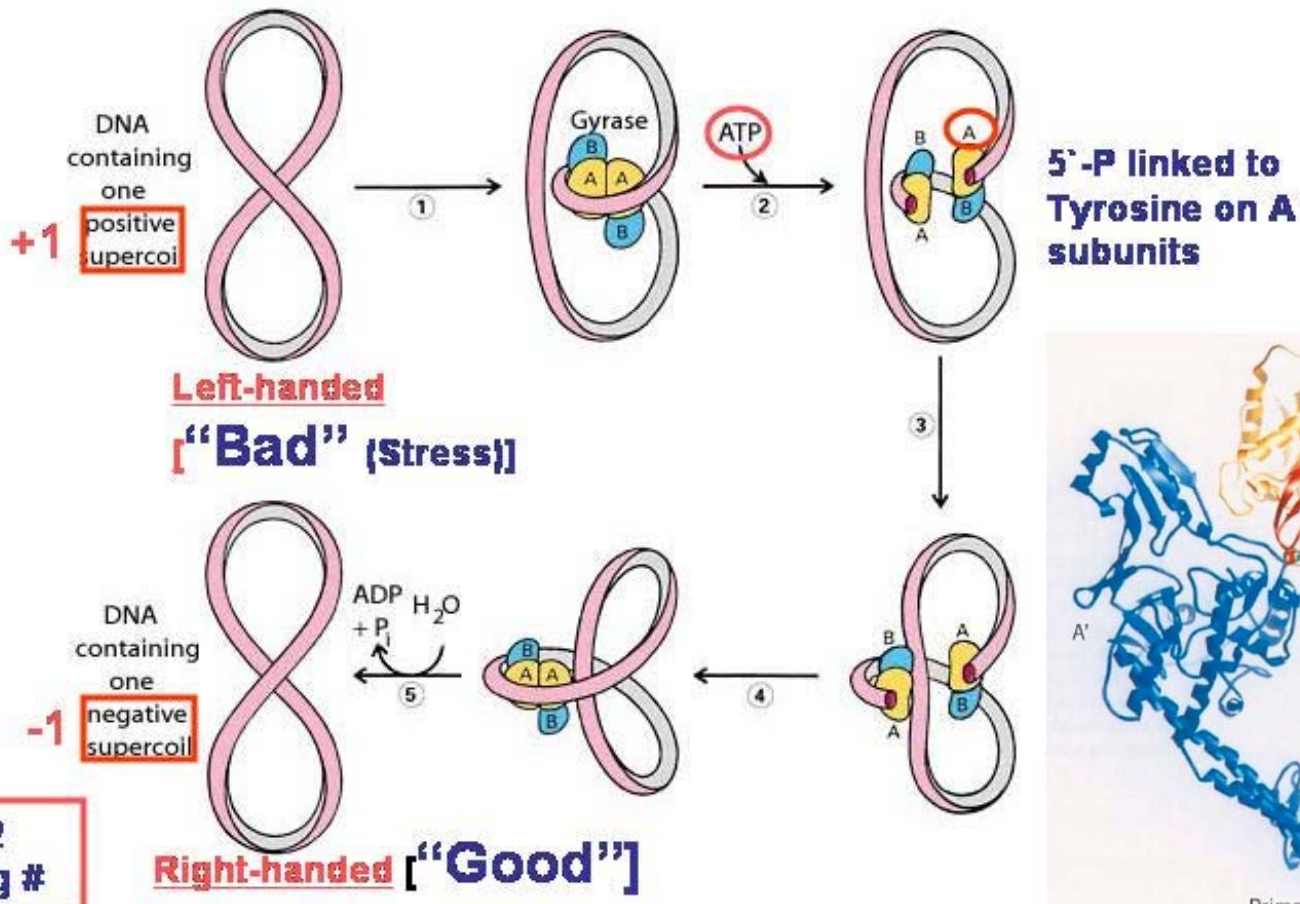


Dati LNRC (1391 ceppi)

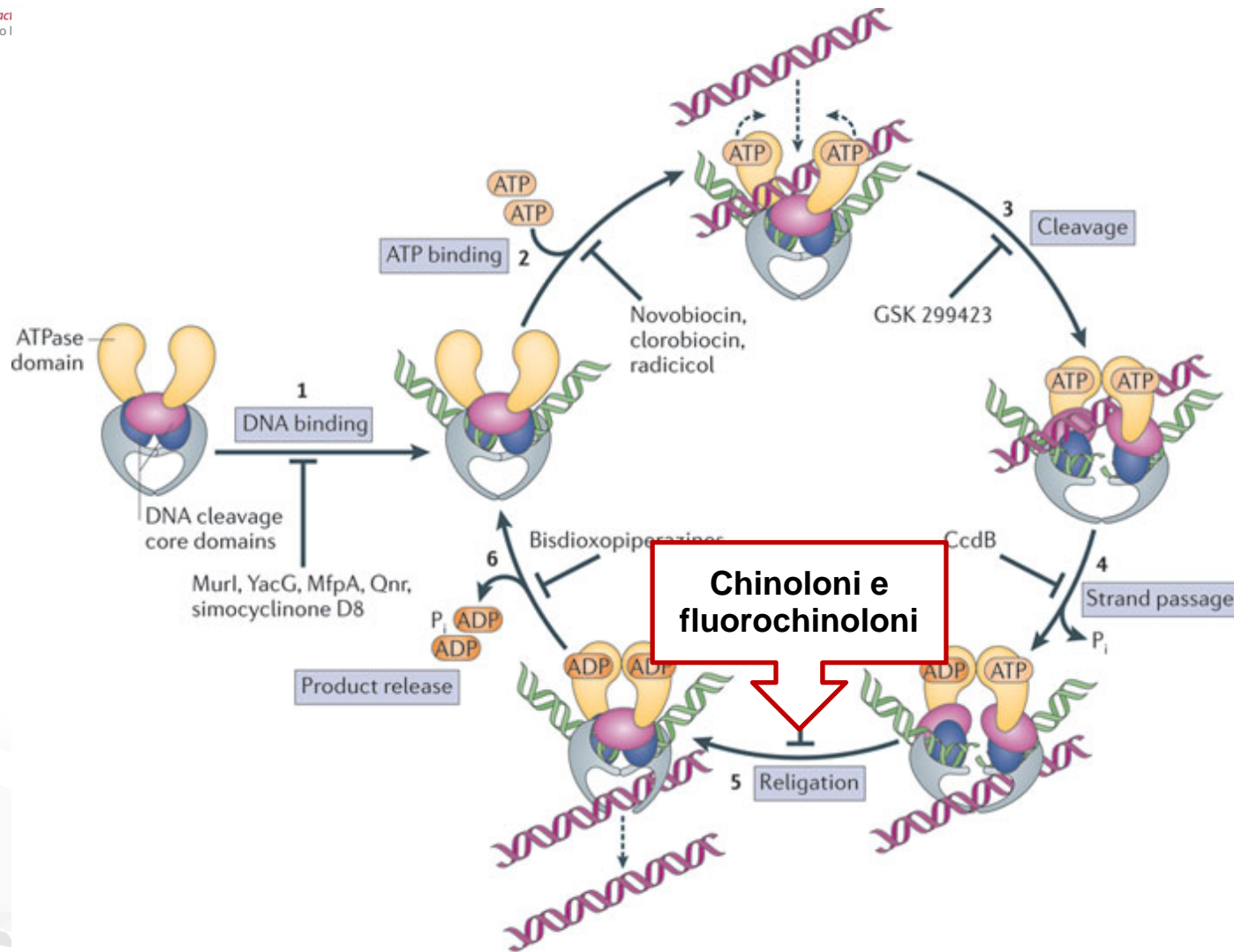


# DNA girasi

## Mechanism of DNA Gyrase (a Topoisomerase II)



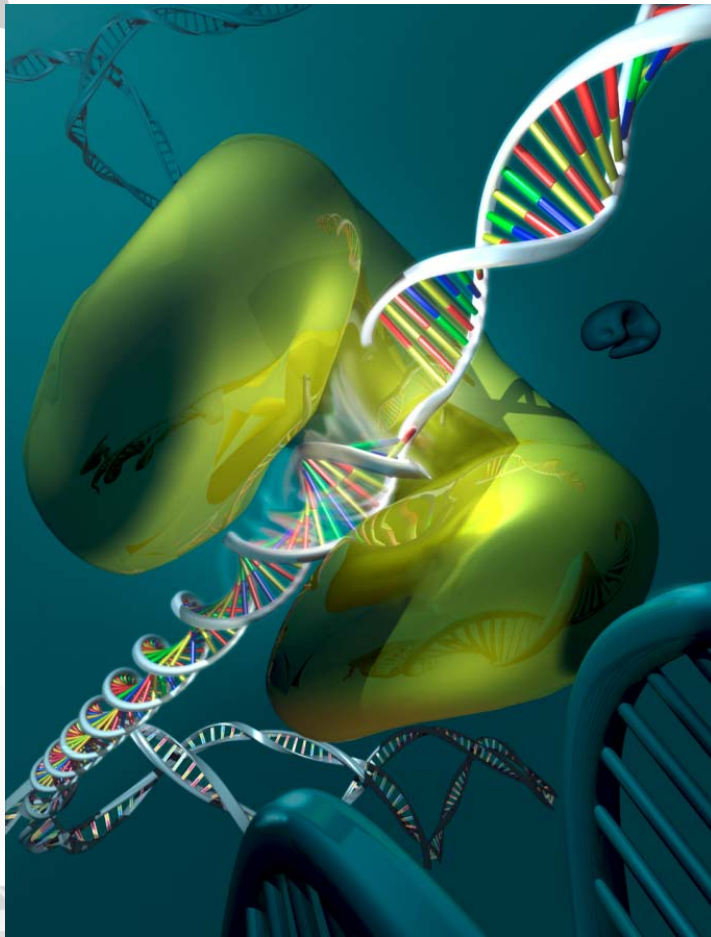
# Ciclo di reazione della DNA girasi



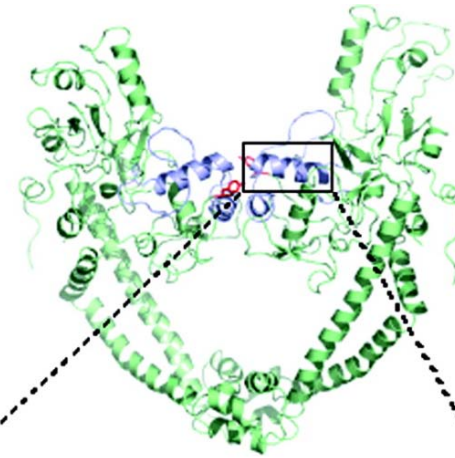


 *Campylobacter*  
Laboratorio Nazionale di Riferimento

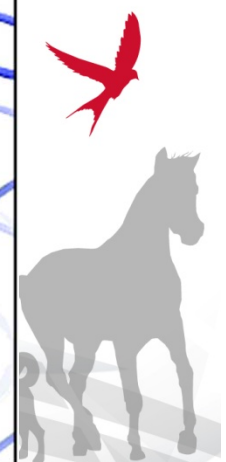
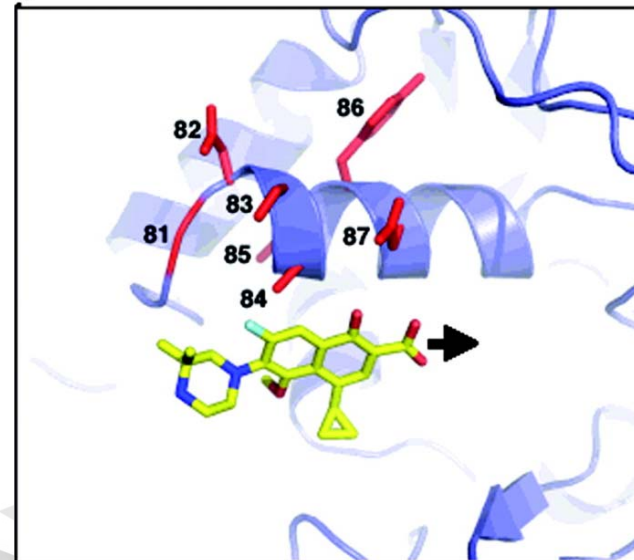
# QRDR: Quinolone Resistance Determining Region



A



B







 *Campylobacter*  
Laboratorio Nazionale di Riferimento

# Sequenziamento *gyrA* *Campylobacter*

JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 1999, p. 3276-3280  
0095-1137/99/\$04.00+0

Vol. 37, No. 10

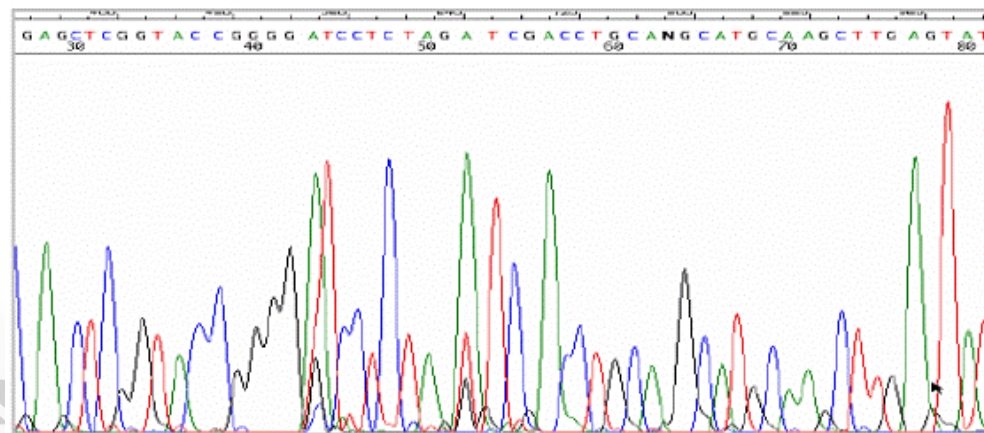
## Ciprofloxacin Resistance in *Campylobacter jejuni* Isolates: Detection of *gyrA* Resistance Mutations by Mismatch Amplification Mutation Assay PCR and DNA Sequence Analysis

GERALD ZIRNSTEIN,\* YU LI, BALA SWAMINATHAN, AND FREDERICK ANGULO



GZ*gyrA*5: 5'-ATTTTTAGCAAAGATTCTGAT-3'

GZ*gyrA*6: 5'-CCATAAATTATTCCACCTGT-3'





# Sequenza parziale *gyrA* *Campylobacter jejuni* NCTC 11168

GZgyrA5

ATGGAGAATATTTTGTAGCAAAGATCTGATATTGAACTTGTAGATATAGAAAATTCTATAAAAAGTAGTT  
 M E N I F S K D S D I E L V D I E N S I K S S  
 M E N I F S K D S D I E L V D I E N S I K S S  
 ATTTAGACTATTCTATGAGTGTATTATAGGTCGTCGCTGACGCAAGAGATTAAGCCTGT  
 Y L D Y S M S V I I A R P V  
 Y L D Y S M S V I I A R P V  
 TCATAGAAGAATTTTATATGCTATGCAAAACACAGATTCAGCC  
 H R R I L Y A M Q N D E A K S P T D F V K S A  
 H R R I L Y A M Q N D E A K S P T D F V K S A  
 CGTATAGTGGGTGCTGTTTACCCACATGGAGATACAGCAGTTTATGATGCTTTGGTTT  
 R I V G A V H P H G D T A V Y D A L A70-T  
 R I V G A V H P H G D T A V Y D A L  
 GAATGGCTCAAGATTTTCTATGAGATATCCAAGTATTACAGGACAAGGCAACTTTGGATCTATAGATG  
 R M A Q D F S M R Y P S I T G Q G N F G S I D G  
 R M A Q D F S M R Y P S I T G Q G N F G S I D G  
 TGATAGTGCCGCTGCGATGCGTTATACTGAAGCAAAAATGAGTAAACTTTGCTTTTAAAAGAT  
 D S A A A M R Y T F A K M S K L S E L L K D  
 D S A A A M R

T86-I; T86-A  
T86-L; T86-V

D90-N  
D90-Y

P104-S

A70-T

ELSEVIER

International Journal of Antimicrobial Agents 31 (2008) 307–315

www.isc

Review

Quinolone resistance in the food chain

Anna Fàbrega, Javier Sánchez-Céspedes, Sara Soto, Jordi Vila\*

*Journal of Antimicrobial Chemotherapy* (2003)  
DOI: 10.1093/jac/dkg033

**Fluoroquinolone resistance in  
animals: detection of mutations in topoisomerase genes**

Laura J. V. Piddock\*, Vito Ricci, Lilian Pumbwe, Martin J. Everett and Deborah J. Griggs

TAGAAGAG  
E E  
E E



# Mutazioni amminoacidiche in *gyrA*

*Campylobacter*  
Laboratorio Nazionale di Riferimento

Sostituzione amminoacidica	Percentuale dei ceppi (N°)
Assente	0,59% (2)
Thr86-Ala	0,89% (3)
Thr86-Ile	97,33% (328)
Thr86-Val	0,30% (1)
Thr86-Ile; Asn57-Ala	0,59% (2)
Thr86-Ile; Phe99-Leu	0,30 % (1)

ATGGAGAATATTTTAGCAAAGATTCTGATATTGAACTTGTAGATATAGAAAATTCTATAAAAAGTAGTT  
M E N I F S K D S D I E L V D I E N S I K S S  
 M E N I F S K D S D I E L V D I E N S I K S S  
ATTTAGACTATTCTATGAGGGTCGTGACGCAAGAGATGGTTTAAAGCCTGT  
Y L D Y S M S V I G R A R D G L K P V  
Y L D Y S M S V I G R A R D G L K P V  
TCATAGAAGAATTTTATATGCTATGCAAAATGATGAGAACAGATTTTGTCAAATCAGCC  
H R R I L Y A M Q N D E A K S R T D F V K S A  
H R R I L Y A M Q N D E A K S R T D F V K S A  
CGTATTTTATAGGTCGTTATCACCCACATGGAGATACAGCAGTTTATGATGCTTTGGTTA  
R I V G A V I G R Y H P H G D T A V Y D A L V  
R I V G A V I G R Y H P H G D T A V Y D A L V  
GAATGGCTCAAGATTTTCTATGAGATATCCAAGTATTACAGGACAAGGCAACTTTGGATCTATAGATGG  
R M A Q D F S M R Y P S I T G Q G N F G S I D G  
R M A Q D F S M R Y P S I T G Q G N F G S I D G

N57-A

T86-I  
T86-A  
T86-V

F99-L



# MIC *Campylobacter*

MIC Ciprofloxacina  
( $\mu\text{g/ml}$ )

MIC  
Acido Nalidixico  
( $\mu\text{g/ml}$ )

Mutazione *gyrA*

$\leq 0,06$	32	T86-I T86-A
2	32	T86-I
2	64	T86-I
4	$\leq 2$	T86-I
4	8	T86-I
4	16	T86-I
4	32	T86-I T86-A T86-I; F99-L T86-I; N57-A
4	64	T86-I T86-A T86-V T86-I; N57-A





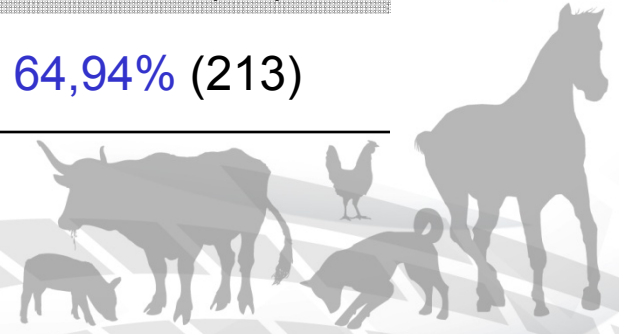


# MIC *Campylobacter* vs Thr86-Ile

 *Campylobacter*  
Laboratorio Nazionale di Riferimento



MIC Ciprofloxacina (µg/ml)	MIC Acido Nalidixico (µg/ml)	Percentuale Campioni T86-I (N°)
≤0,06	32	0,30% (1)
2	32	0,30% (1)
2	64	0,92% (3)
4	≤2	4,27% (14)
4	8	0,92% (3)
4	16	5,18% (17)
4	32	23,17% (76)
4	64	64,94% (213)



# Meccanismi alternativi di resistenza



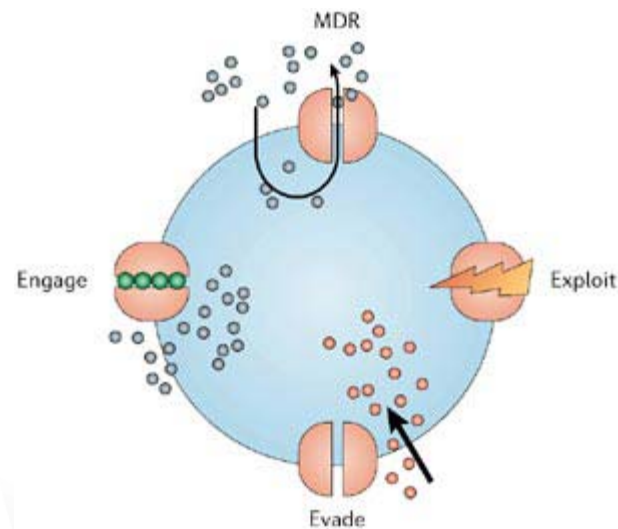
 *Campylobacter*  
Laboratorio Nazionale di Riferimento

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 2005, p. 3347–3354  
0066-4804/05/\$08.00+0 doi:10.1128/AAC.49.8.3347–3354.2005  
Copyright © 2005, American Society for Microbiology. All Rights Reserved.

Vol. 49, No. 8

## Role of Efflux Pumps and Topoisomerase Mutations in Fluoroquinolone Resistance in *Campylobacter jejuni* and *Campylobacter coli*

Beilei Ge,<sup>1,2</sup> Patrick F. McDermott,<sup>3</sup> David G. White,<sup>3</sup> and Jianghong Meng<sup>1\*</sup>





 *Campylobacter*  
Laboratorio Nazionale di Riferimento

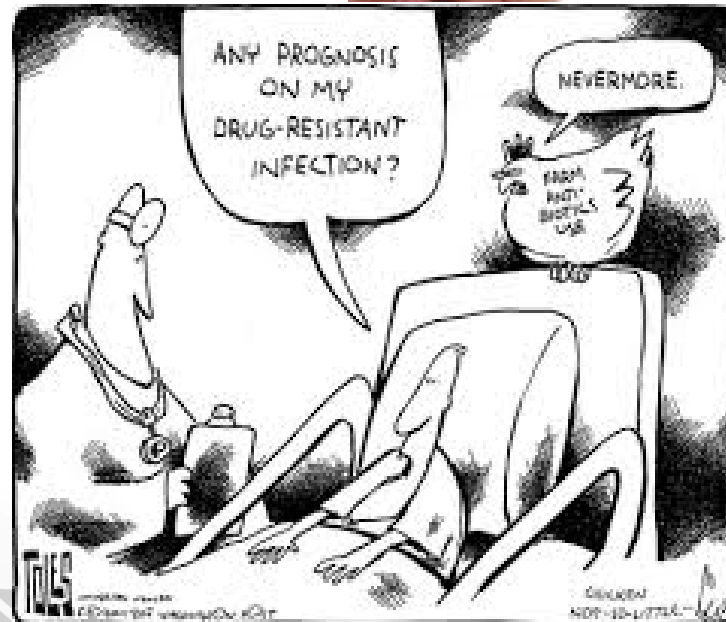
## ...riassumendo

- Mutazione più diffusa in *gyrA* è Thr86-Ile.
- Il 64,94% dei *Campylobacter* con sostituzione T86-I in *gyrA* mostra valori elevati di MIC sia per Ciprofloxacina che per Acido Nalidixico.
- Comparsa di nuove sostituzioni doppie, associate a MIC elevate:
  - Thr86-Ile; Phe99-Leu
  - Thr86-Ile; Asn57-Ala





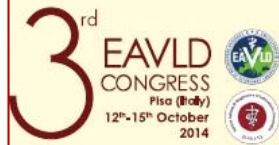
# ...se li conosci li eviti!!!






# ...esistono alternative?!

 *Campylobacter*  
Laboratorio Nazionale di Biferimento



## Effects of dietary inclusion of synbiotic on *Campylobacter jejuni* infection in broiler



 *Campylobacter*  
National Reference Laboratory

Gabriella Di Serafino<sup>1</sup>, Giuliano Garofolo<sup>1</sup>, Diana Di Gioia<sup>2</sup>, Loredana Baffoni<sup>2</sup>, Ilenia Platone<sup>1</sup>, Guido Di Donato<sup>1</sup>, Elisabetta Di Giannatale<sup>1\*</sup>

OPEN ACCESS Freely available online



## Impact of a Single Phage and a Phage Cocktail Application in Broilers on Reduction of *Campylobacter jejuni* and Development of Resistance

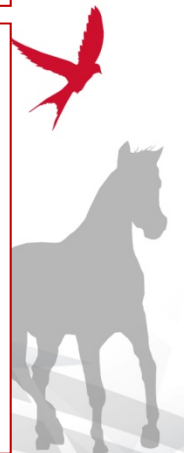
Samuel Fischer<sup>1\*</sup>, Sophie Kittler<sup>2</sup>, Günter Klein<sup>2</sup>, Gerhard Glünder<sup>1</sup>



Full Text (PDF)

## Effects of feeding plant-derived agents on the colonization of *Campylobacter jejuni* in broiler chickens

*Poultry Science* (September 2014) 93 (9): 2337-2346  
first published online July 7, 2014





IZSAM G. CAPORALE  
TERAMO



*Campylobacter*  
Laboratorio Nazionale di Riferimento



# GRAZIE PER L'ATTENZIONE!

