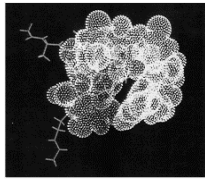


GLYCOPEPTIDE ANTIBIOTICS

from Old Mississippi mud ...



... to molecular mechanisms:

Glycopeptides (FARM 2146)

10-Feb-05

1

Glycopeptide story: from natural to semi-synthetic derivatives

~ 1950 :
discovery of vancomycin in Mississippi mud

~ 1985 :
large clinical use in USA
Gram(+) infections and digestive tract decontamination

Problem:

- toxicity of vancomycin due to impurities
➔ better purification procedures

~ 1980 :
discovery of teicoplanin, as a natural GP with improved PK
▪ largely used in Europe

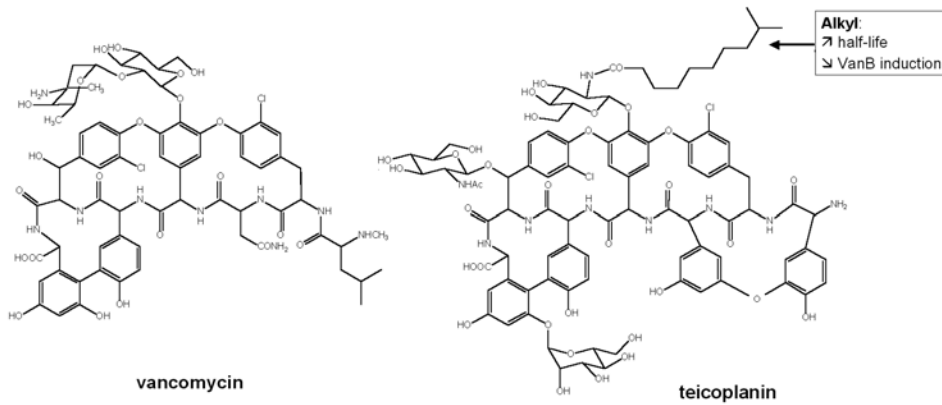


Glycopeptides (FARM 2146)

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2

vancomycine - téicoplanine

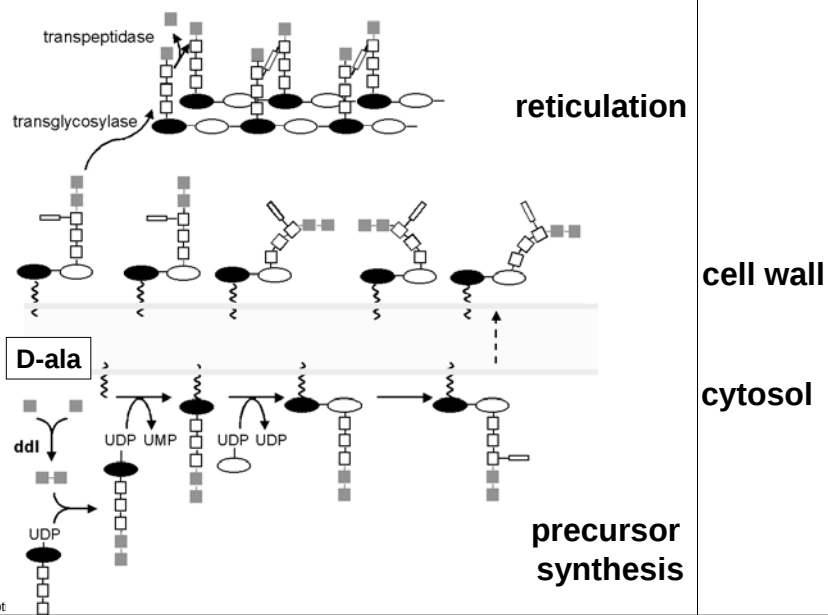


Glycopeptides (FARM 2146)

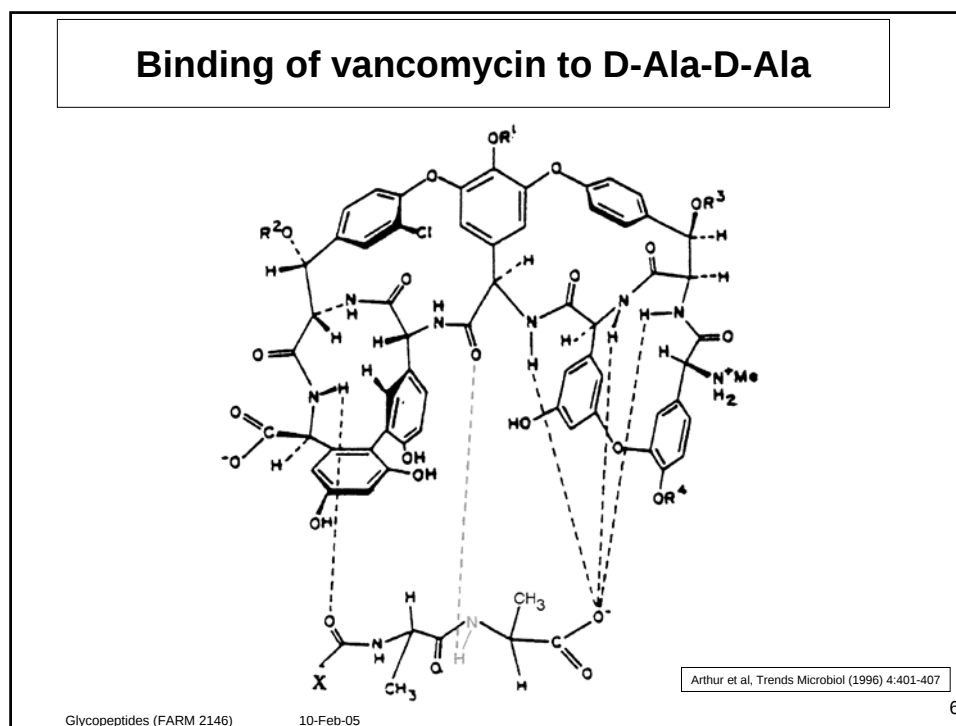
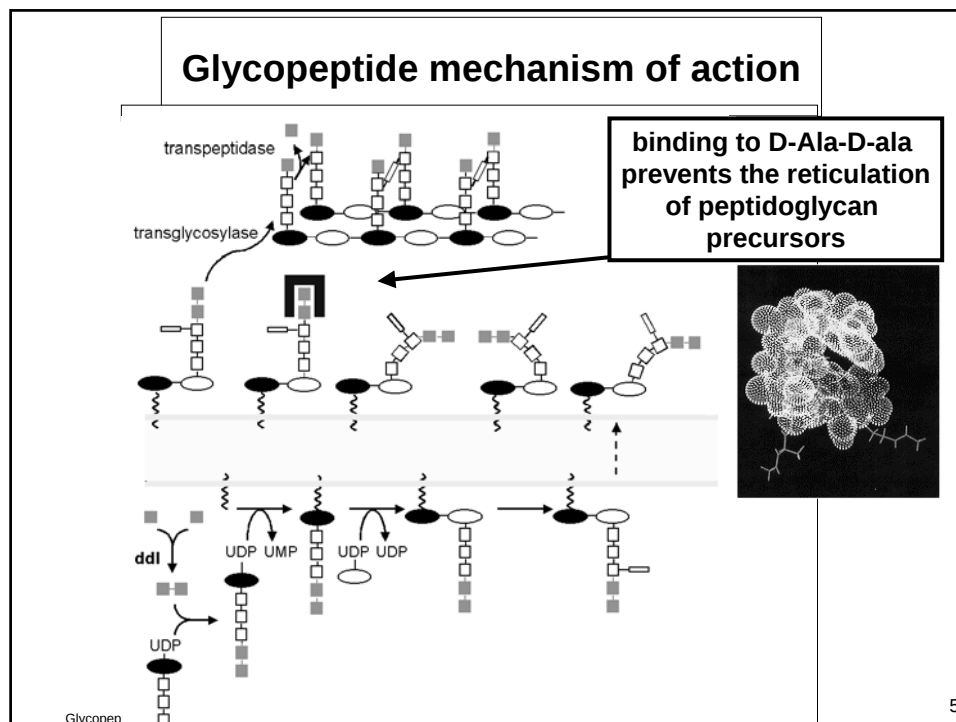
10-Feb-05

3

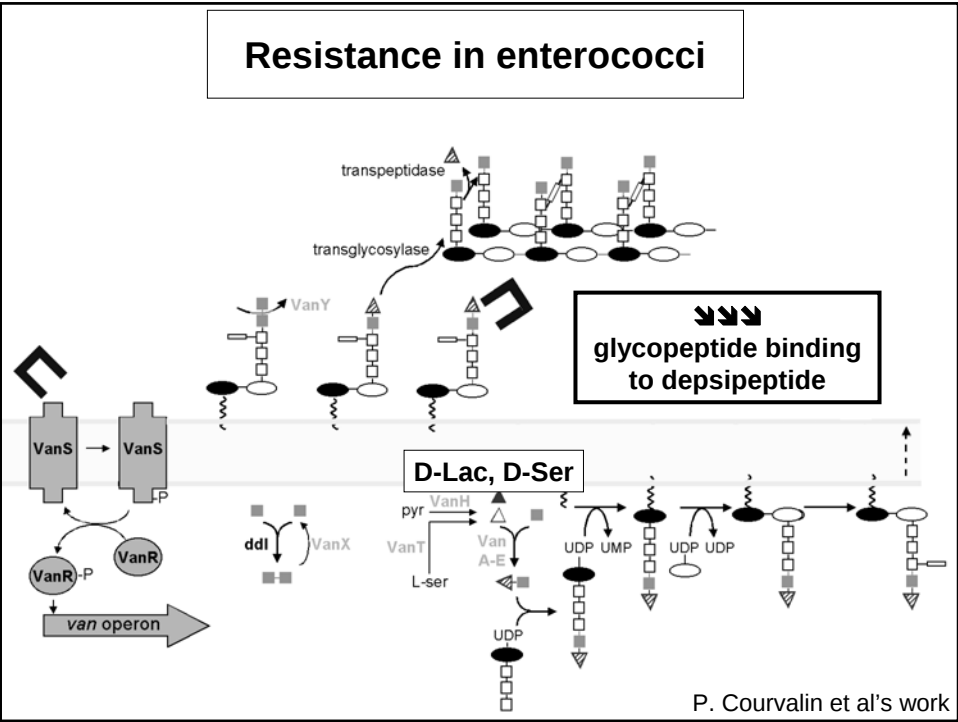
Peptidoglycan synthesis



4



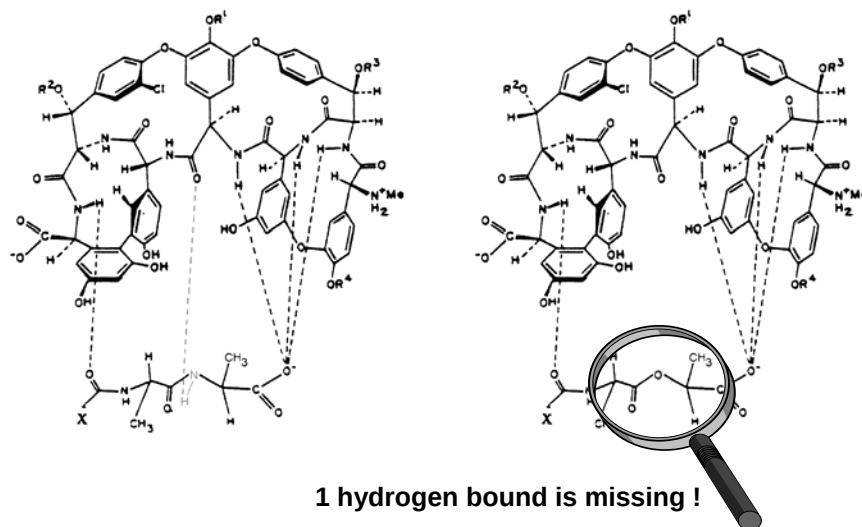
Resistance in enterococci



Resistance in enterococci

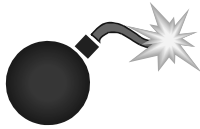
from susceptible ...

... to resistant



Arthur et al. Trends Microbiol (1996) 4:401-407

8



Resistance in staphylococci (GISA)

Methicillin-resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility

J Antimicrob Chemother 1997; **40**: 135–136

K. Hiramatsu^{a*}, H. Hanaki^a, T. Ino^b, K. Yabuta^b, T. Oguri^c and F. C. Tenover^d

^aDepartment of Bacteriology; ^bDepartment of Pediatrics, Juntendo University, Tokyo; ^cClinical Laboratory, Juntendo Hospital, Tokyo, Japan; ^dNosocomial Pathogens Laboratory, Centers for Disease Control and Prevention, Atlanta, GA, USA

	AB	MIC
AMP		64
VAN		8
GEN		128
RIF		2048
LVX		8
TET		128
SMX		0.125
Q-D		0.5
LZD		2

Glycopeptides (FARM 2146)

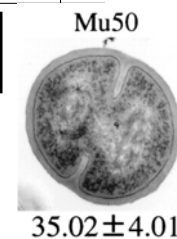
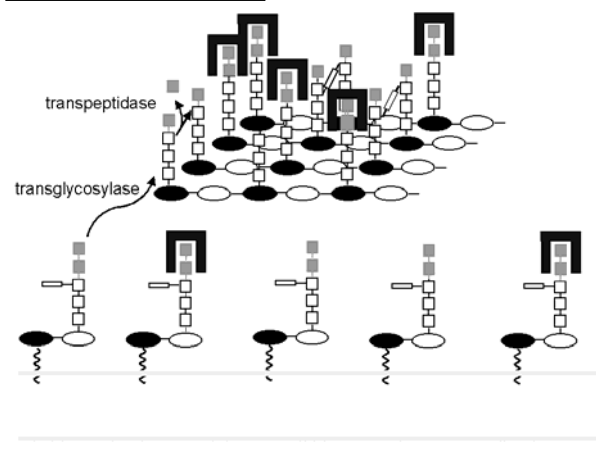
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9

Resistance in staphylococci (GISA)

multiplication of the target !

tickened Cell wall



Hiramatsu Lancet ID (2001) 1:147-155

Cui et al J Clin Microbiol (2003) 41:5-14



Resistance in staphylococci (GRSA)



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BRIEF REPORT

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April 3, 2003

Number 14

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Infection with Vancomycin-Resistant *Staphylococcus aureus* Containing the *vanA* Resistance Gene

Soju Chang, M.D., M.P.H., Dawn M. Sievert, M.S., Jeffrey C. Hageman, M.H.S., Matthew L. Boulton, M.D., Fred C. Tenover, Ph.D., M.P.H., Frances Pouch Downes, Dr.P.H., Sandip Shah, M.S., James T. Rudrik, Ph.D., Guy R. Papp, D.P.M., William J. Brown, Ph.D., Denise Cardo, M.D., Scott K. Fridkin, M.D., for the Vancomycin-Resistant *Staphylococcus aureus* Investigative Team



42nd Annual

TOC

San Diego

MICs and kill kinetics of antibacterials against vancomycin resistant *Staphylococcus aureus* (VRSA) with *vanA* gene isolated at Penn State Hershey Medical Center

B. Bozdogan¹, J. Chaitram², P. C. Appelbaum¹, C. Whitener¹, F. A. Browne¹, F. C. Tenover²

¹Penn State Hershey Medical Center, Hershey, PA, ²Centers for Disease Control and Prevention, Atlanta, GA

AB	MIC
VAN	32
TEC	4

Glycopeptides (FARM 2146)

10-Feb-05