Supplementary Material to the Publication

Mastering the Gram-Negative Bacterial Barrier – Chemical Approaches to Increase Bacterial Bioavailability of Antibiotics

Henni-Karoliina Ropponen*, Robert Richter*, Anna K. H. Hirsch#, Claus-Michael Lehr#

Abstract: To win the battle against resistant, pathogenic bacteria, novel classes of anti-infectives and targets are urgently needed. Bacterial uptake, distribution, metabolic and efflux pathways of antibiotics in Gram-negative bacteria determine what we here refer to as bacterial bioavailability. Understanding these mechanisms from a chemical perspective is essential for anti-infective activity and hence, drug discovery as well as drug delivery. A systematic and critical discussion of *in bacterio*, *in vitro* and *in silico* assays reveals that a sufficiently accurate holistic approach is still missing. We expect new findings based on Gram-negative bacterial bioavailability to guide future anti-infective research.

E-mail: Anna.Hirsch@helmholtz-hips.de or Claus-Michael.Lehr@helmholtz-hips.de

3. Antibiotics and pathways of bacterial uptake, metabolism and efflux

3.1. Clinically approved antibiotic classes

Table S1. Classes of antibiotics for the treatment of Gram-negative infections and representatives

Antibiotic class		Panel
Aminoglycosides		Streptomycin, Tobramycin, Kanamycin, Amikacin
Penicillins		Ampicillin, Amoxicillin Piperacillin, Sultamicillin, Pivampicillin, Bacampicillin
Cephems		Cefuroxime, Ceftibuten, Flomoxef, Cefminox, Loracarbef
Carbapenems		Imipenem, Meropenem, Ertapenem, Doripenem, Thienamycin
Monobactams		Tabtoxin, Aztreonam, Carumonam Nocardicin A, Tigemonam
β-Lactamase inhibitors	1st Generation	Clavulanic acid Enmetazobactam Sulbactam Tazobactam
	2nd Generation	Avibactam Durlobactam Nacubactam Relebactam Zidebactam
	3rd Generation	Taniborbactam Vaborbactam
Fluoroquinolones		Ciprofloxacin, Sparfloxacin, Gemifloxacin, Garenoxacin, Clinafloxacin, Prulifloxacin
Tetracyclines		Tetracycline, Minocycline, Tigecycline, Meclocycline, Lymecycline
Sulfonamides		Sulfamethoxazole, Sulfaguanidin, Sulfadimidin, Sulfadoxin
Polymyxins		Colistin A, Colistin B, Polymyxin A, Polymyxin B