

β -lactam resistance in ESKAPE pathogens mediated through modifications in Penicillin-

Binding Proteins: An overview

Dhiviya Prabaa Muthuirulandi Sethuvel¹, Yamuna Devi Bakthavachalam¹, Maruthan Karthik¹,
Irulappan Madhumathi¹, Rahul Shrivastava², Hariharan Periasamy², *Balaji Veeraraghavan¹

¹Department of Clinical Microbiology, Christian Medical College, Vellore-632004

²Wockhardt Research Centre, Aurangabad, India.

***Corresponding Author**

Balaji Veeraraghavan

Professor

Department of Clinical Microbiology

Christian Medical College, Vellore-632004

Email: vbajali@cmevellore.ac.in

Table: S1 – DBO molecule recently identified to inhibit β -lactamases and bind PBPs of ESKAPE pathogens

DBO molecules that can inhibit β -lactamases and bind PBPs	Effective against	References
Avibactam	<i>Klebsiella pneumoniae</i>	Sutaria DS, Moya B, Green KB, Kim TH, Tao X, Jiao Y, Louie A, Drusano GL, Bulitta JB. First penicillin-binding protein occupancy patterns of β -lactams and β -lactamase inhibitors in <i>Klebsiella pneumoniae</i> . <i>Antimicrobial agents and chemotherapy</i> . 2018 May 25;62(6):e00282-18.
Relebactam	Enterobacteriaceae; low activity against <i>Klebsiella pneumoniae</i>	Bush, K., Bradford, P.A., 2016. β -lactams and β -lactamase inhibitors: an overview. <i>Cold Spring Harb. Perspect. Med.</i> 6, a025247. http://dx.doi.org/10.1101/cshperspect.a025247 .
Nacubactam	Enterobacteriaceae and non-ESBL-producing <i>K. pneumoniae</i>	Morinaka, A., Tsutsumi, Y., Yamada, M., Suzuki, K., Watanabe, T., Abe, T., Furuuchi, T., Inamura, S., Sakamaki, Y., Mitsuhashi, N., Ida, T., Livermore, D.M., 2015. OP0595, a new diazabicyclooctane: mode of action as a serine β -lactamase inhibitor, antibiotic and β -lactam “enhancer”. <i>J. Antimicrob. Chemother.</i> 70, 2779–2786. http://dx.doi.org/10.1093/jac/dkv166
Zidebactam	<i>Pseudomonas aeruginosa</i>	Moya, B., Barcelo, I.M., Bhagwat, S., Patel, M., Bou, G., Papp-Wallace, K.M., Bonomo, R.A., Oliver, A., 2017. WCK 5107 (zidebactam) and WCK 5153 are novel inhibitors of PBP2 showing potent “ β -lactam enhancer” activity against <i>Pseudomonas aeruginosa</i> , including multidrug-resistant metallo- β -lactamase-producing high-risk clones. <i>Antimicrob. Agents Chemother.</i> 61, 16–e02529. http://dx.doi.org/10.1128/AAC.02529-16 .
ETX2514	<i>Escherichia coli</i> and <i>Klebsiella pneumoniae</i> and	Durand-Réville, T.F., Guler, S., Comita-Prevoir, J., Chen, B., Bifulco, N., Huynh, H., Lahiri, S., Shapiro, A.B., McLeod, S.M., Carter,

	<i>Acinetobacter baumannii</i>	N.M., Moussa, S.H., Velez-Vega, C., Olivier, N.B., McLaughlin, R., Gao, N., Thresher, J., Palmer, T., Andrews, B., Giacobbe, R.A., Newman, J.V., Ehmann, D.E., de Jonge, B., O'Donnell, J., Mueller, J.P., Tommasi, R.A., Miller, A.A., 2017. ETX2514 is a broad-spectrum β -lactamase inhibitor for the treatment of drug-resistant Gram-negative bacteria including <i>Acinetobacter baumannii</i> . Nat. Microbiol. 2, 17104. http://dx.doi.org/10.1038/nmicrobiol.2017.104 .
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