



JOURNAL OF INTEGRATED OMICS

A METHODOLOGICAL JOURNAL

HTTP://WWW.JIOMICS.COM



POINT OF VIEW | DOI: 10.5584/jiomics.v4i1.165

Differential proteomics has emerged as a tool to understand carbapenem resistance in *Acinetobacter baumannii*

Vishvanath Tiwari*

Department of Biochemistry, Central University of Rajasthan, Ajmer, Rajasthan, 305801, India.

Received: 05 April 2014 Accepted: 30 June 2014 Available Online: 30 June 2014

Acinetobacter baumannii is one of the opportunistic pathogens described by Infectious Disease Society of America [1]. Due to its pathogenicity, it is grouped into ESKAPE pathogens, a group of pathogens causing hospital-acquired infections [2-3]. *Acinetobacter baumannii* has emerged as a threat to soldiers, wounded during military operations in Iraq and Afghanistan [4-5], and also isolated from natural resources [6]. It causes pneumonia, respiratory infections and urinary tract infections. It can grow on artificial surfaces, utilize ethanol as a carbon source [7], resist desiccation, survive at various temperatures, and pH conditions [8]. These abilities make it a 'lethal' pathogen. Prevalence of *Acinetobacter baumannii* in clinical setup increases gradually [9]. Commonly prescribed drug against *A. baumannii* are carbapenems which belongs to the β -lactam group of antibiotics [10]. *Acinetobacter baumannii* has emerged resistance against carbapenem which is a significant health problem and responsible for high morbidity & mortality [11]. This makes it one of the major health concerns [9, 12-13].

Proteomics emerged as a tool to study the differential proteome under diverse conditions. With the development of methods used in the proteomics, a considerable progress has been made in the recent years in the field of differential proteomics. Various methods have been employed to study the differential proteomics. These methods include gel based methods like DIGE [14], gel free methods like ICAT [15], iTRAQ [16], SILIC [17], ICPL [18], and mass spectrometry based methods like SRM [19]. Isotope labels can be incorporated into peptides chemically or enzymatically or metabolically or inverse labeling-based [20]. In label free proteomics mass spectrometer recognizes the mass difference and their

quantification are achieved by comparing their respective signal intensities.

Differential proteomics between wild type and carbapenem resistance strain of *Acinetobacter baumannii* was first reported by the Vila and colleagues [21]. Similarly, Siroy et al also performed the differential global comparison of the membrane sub-proteomes of multidrug-resistant *Acinetobacter baumannii* strain and a reference strain [22]. Using differential proteomics approach, Soares et al showed that *Acinetobacter baumannii* displays a robust and versatile metabolism [23]. With the help of differential outer membrane proteomics, Kwon et al, studied the secretion of outer membrane vesicles (OMVs) from a clinical *A. baumannii* isolate and analysed the comprehensive proteome of *A. baumannii*-derived OMVs [24]. Similarly, high-end isoelectric point (pH 6-11) differential proteome analysis of *Acinetobacter radiore-sistens* S-13 reveals that envelope stress responses can be induced by aromatic compounds [25]. Biofilm formation is one of the important causes for the persistence of *Acinetobacter baumannii* on the surface of host epithelial cells. Cabral et al, performed differential proteomics of *Acinetobacter* cultured in three different conditions (exponential, late stationary phase and biofilms stage) and they also checked the effects of biofilm inhibitory compound (salicylate) on the biofilm formation. This multiple-approach strategy showed a unique lifestyle of *A. baumannii* involved in biofilms formation [26]. Yun et al, performed differential quantitative proteomic analysis of cell wall and plasma membrane fractions from multidrug-resistant *Acinetobacter baumannii* and reported that carbapenem induces the expression of resistance-nodulation-cell division transporters, protein kinases and suppress outer

*Corresponding author: Vishvanath Tiwari, Department of Biochemistry, Central University of Rajasthan, Ajmer, Rajasthan, 305801, India; Phone No.: + 91-1463-238652; Fax No: + 91-1463-238722; E-mail address: vishvanath7@yahoo.co.in

membrane proteins expression [27]. Lee et al explain the mechanism of hetero-resistance induced by imipenem (a member of carbapenem group) in the multidrug resistance *Acinetobacter baumannii* [28]. Rajeswari et al showed the importance of outer membrane in the carbapenem resistance using differential outer membrane proteomics of carbapenem resistance strain of *Acinetobacter baumannii* [29]. Tiwari et al identified the importance of the metabolism in the carbapenem resistance of *Acinetobacter* using differential inner membrane proteomics [13]. Role of iron in the survival of ATCC strain and carbapenem resistance strain of *Acinetobacter baumannii* in human host has also been studied using differential proteomics [30-31]. Proteome of the human host also changed during *Acinetobacter baumannii* infection. Soares et al, identified alterations in the plasma proteome of individuals infected with *Acinetobacter baumannii* as compared to healthy controls using DIGE based differential proteomic approach [32].

These updates show that differential proteomics has now emerged as an important tool to understand the mechanism of carbapenem resistance in *Acinetobacter baumannii*. Differential proteomics also helps to understand the role of different environments/conditions in the survival of *Acinetobacter baumannii* and its adaptation as a notorious pathogen.

References

- [1] H.W. Boucher, G.H. Talbot, J.S. Bradley, J.E. Edwards, D. Gilbert, L.B. Rice, M. Scheld, B. Spellberg, J. Bartlett, Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 48 (2009) 1-12. doi: 10.1086/595011
- [2] R.M. Klevens, J.R. Edwards, F.C. Tenover, L.C. McDonald, T. Horan, R. Gaynes, Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 42 (2006) 389-391. doi: 10.1086/499367
- [3] H.W. Boucher, G.R. Corey, Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 46 Suppl 5 (2008) S344-349. doi: 10.1086/533590
- [4] K.A. Davis, K.A. Moran, C.K. McAllister, P.J. Gray, Emerging Infectious Diseases, 11 (2005) 1218-1224. doi: 10.3201/1108.050103
- [5] C. Camp, O.L. Tatum, Laboratory Medicine, 41 (2010) 649-657. doi: 10.1309/Im90ijnnddwri3re
- [6] M. Kempf, J.M. Rolain, G. Diatta, S. Azza, B. Samb, O. Mediannikov, A. Gassama Sow, S.M. Diene, F. Fenollar, D. Raoult, PLoS one, 7 (2012) e39495. doi: 10.1371/journal.pone.0039495
- [7] S. Navon-Venezia, R. Ben-Ami, Y. Carmeli, Curr Opin Infect Dis, 18 (2005) 306-313. doi: 10.1097/01.qco.0000171920.44809.f0
- [8] E. Bergogne-Berezin, K.J. Towner, Clinical microbiology reviews, 9 (1996) 148-165. doi:
- [9] V. Tiwari, A. Kapil, R.R. Moganty, Microbial pathogenesis, 53 (2012) 81-86. doi: 10.1016/j.micpath.2012.05.004
- [10] P.M. Hawkey, A.M. Jones, The Journal of antimicrobial chemotherapy, 64 Suppl 1 (2009) i3-10. doi: 10.1093/jac/dkp256
- [11] D.M. Sengstock, R. Thyagarajan, J. Apalara, A. Mira, T. Chopra, K.S. Kaye, Clinical infectious diseases : an official publication of the Infectious Diseases Society of America, 50 (2010) 1611-1616. doi: 10.1086/652759
- [12] V. Tiwari, I. Nagpal, N. Subbarao, R.R. Moganty, Journal of molecular modeling, 18 (2012) 3351-3361. doi: 10.1007/s00894-011-1346-3
- [13] V. Tiwari, J. Vashist, A. Kapil, R.R. Moganty, PLoS one, 7 (2012) e39451. doi: 10.1371/journal.pone.0039451
- [14] M. Unlu, M.E. Morgan, J.S. Minden, Electrophoresis, 18 (1997) 2071-2077. doi: 10.1002/elps.1150181133
- [15] S.P. Gygi, B. Rist, S.A. Gerber, F. Turecek, M.H. Gelb, R. Aebersold, Nature biotechnology, 17 (1999) 994-999. doi: 10.1038/13690
- [16] C.S. Gan, P.K. Chong, T.K. Pham, P.C. Wright, Journal of proteome research, 6 (2007) 821-827. doi: 10.1021/pr060474i
- [17] S.E. Ong, Molecular & Cellular Proteomics, 1 (2002) 376-386. doi: 10.1074/mcp.M200025-MCP200
- [18] J. Kellermann, Methods in molecular biology, 424 (2008) 113-123. doi: 10.1007/978-1-60327-064-9_10
- [19] S. Elschenbroich, T. Kislinger, Molecular bioSystems, 7 (2011) 292-303. doi: 10.1039/c0mb00159g
- [20] H.M. Santos, D. Glez-Pena, M. Reboiro-Jato, F. Fdez-Riverola, M.S. Diniz, C. Lodeiro, J.L. Capelo-Martinez, Electrophoresis, 31 (2010) 3407-3419. doi: 10.1002/elps.201000251
- [21] S. Marti, J. Sanchez-Cespedes, E. Oliveira, D. Bellido, E. Giral, J. Vila, Proteomics, 6 Suppl 1 (2006) S82-87. doi: 10.1002/pmic.200500323
- [22] A. Siroy, P. Cosette, D. Seyer, C. Lemaitre-Guillier, D. Valenet, A. Van Dorsselaer, S. Boyer-Mariotte, T. Jouenne, E. De, Journal of proteome research, 5 (2006) 3385-3398. doi: 10.1021/pr060372s
- [23] N.C. Soares, M.P. Cabral, J.R. Parreira, C. Gayoso, M.J. Barba, G. Bou, Proteome science, 7 (2009) 37. doi: 10.1186/1477-5956-7-37
- [24] S.O. Kwon, Y.S. Gho, J.C. Lee, S.I. Kim, FEMS microbiology letters, 297 (2009) 150-156. doi: 10.1111/j.1574-6968.2009.01669.x
- [25] R. Mazzoli, P. Fattori, C. Lamberti, M.G. Giuffrida, M. Zapponi, C. Giunta, E. Pessione, Molecular bioSystems, 7 (2011) 598-607. doi: 10.1039/c0mb00112k
- [26] M.P. Cabral, N.C. Soares, J. Aranda, J.R. Parreira, C. Rumbo, M. Poza, J. Valle, V. Calamia, I. Lasa, G. Bou, Journal of proteome research, 10 (2011) 3399-3417. doi: 10.1021/pr101299j
- [27] S.H. Yun, C.W. Choi, S.O. Kwon, G.W. Park, K. Cho, K.H. Kwon, J.Y. Kim, J.S. Yoo, J.C. Lee, J.S. Choi, S. Kim, S.I. Kim, Journal of proteome research, 10 (2011) 459-469. doi: 10.1021/pr101012s
- [28] H.Y. Lee, C.L. Chen, S.B. Wang, L.H. Su, S.H. Chen, S.Y. Liu, T.L. Wu, T.Y. Lin, C.H. Chiu, International journal of antimicrobial agents, 37 (2011) 302-308. doi: 10.1016/j.ijantimicag.2010.12.015
- [29] J. Vashist, V. Tiwari, A. Kapil, M.R. Rajeswari, Journal of proteome research, 9 (2010) 1121-1128. doi: 10.1021/pr9011188
- [30] C.C. Nwugo, J.A. Gaddy, D.L. Zimble, L.A. Actis, Journal of proteomics, 74 (2011) 44-58. doi: 10.1016/j.jprot.2010.07.010
- [31] V. Tiwari, R.R. Moganty, Journal of Proteomics & Bioinformatics, 06 (2013) 125-131. doi: 10.4172/jpb.1000270
- [32] A.J. Soares, M.F. Santos, M.R. Trugilho, A.G. Neves-Ferreira, J. Perales, G.B. Domont, Journal of proteomics, 73 (2009) 267-278. doi: 10.1016/j.jprot.2009.09.010