Omics Technologies: A Hope for Translational Research in Bovine Tuberculosis

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Abstract

Bovine tuberculosis diagnosis is one of the main challenges faced by animal and public health systems. The incidence of *M. bovis* infections remains undefined in developed countries. So it is necessary to carry out an extensive study and surveillance to determine the status of bovine tuberculosis as an urgent need for control eradication program. Furthermore, developed countries, microbiological (bacteriological) and immunological (histochemistry) techniques are still used, making more difficult to homogenize epidemiological knowledge of bTB. Recent reports describing the potential of microarray technology not only to explore subunit vaccine agents (biomarkers), but to pinpoint immunomodulation, and signatures in the journey of pathogen interaction with the host in bovine tuberculosis. Omics and next generation high-throughput technologies have risen as promising tools that will enable translational research (development of prognostic and diagnostic methods with high accuracy and sensibility) and in depth molecular analysis even at single cell level to underpin dynamics in the transcripts regulation of the host response in bTB.

What We have in Terms of Detection and IdentiẐcation of *M. bovis*

In the last decades, a huge of group have been focused in the development of molecular detection of *M. bovis* which in general terms started with isolation from tissue homogenate with lesion, seeding in Middlebrook brook solid medium supplemented with OADC and THF followed by DNA extraction, nested PCR and multiplex PCR amplifcation of specifc regions of the *M. bovis* genome [8-14], a screening test used to prevent infection and introduction of disease in healthy herds. T e application of the PCR technology, have been seen as a reliable and accurate diagnostic development [8-14]. Moreover, real-time Multiplex PCR was standardized with reference to Mycobacterium strains and was subsequently tested with 66 clinical isolates [15-17]. T e sensitivity and specifcity of the designed primers were for each one as follows: 100% for MTC, *M. abscessus*, *M.fortuitum*, *M. aviumcomplex*, *M. kansasii*, and *M. gordonae*. While the sensitivity and specifcity of the primers designed for the genus Mycobacterium were between 96 and 100% [15-17]. By other hand, epidemiological analysis using techniques such as spoligotyping, VNTRs, RFLPs, for typifcation of *M. bovis* substrains and for simultaneous diferentiation of other members of the Mycobacterium complex with ther mycobacterial species not included in the complex. Non-tuberculous mycobacterial species (NTM) that may have a clinical signifcance and interference with the detection and identifcation of *M. tuberculosis* [18-20] were analysed. T us, MTBC and NTM were simultaneously evaluated in respiratory specimens using real-time PCR multiplex and RFLPs. and the Geno Blot Advan Sure Mycobacteria trial (LG Life Sciences). T e data obtained using this approach, is that species commonly detected in mixed cultures were *M. intracellulare* (29.0%) and *M. abscessus* (29.0%) [18-20] to carry out a rapid and simultaneous detection of the *M. tuberculosis* complex (MTC), as well as of diferentiation with *M. bovis*; a multiplex assay based on microspheres was developed using xMAP technology [21]. Briefy, these methods detects 4 target sequences, including the insertion-specifc elements IS6110 and IS1081 of the MTC, a specifc fragment of 12.7-Kb for *M. tuberculosis*, and an uninterrupted sequence of 229 sub specifc for *M. bovis* [17,22]. T e specifcity of the assay was validated by testing 13 reference strains of mycobacteria; 22 isolates of

of the species, the macrophage gene expression program is different even both pathogens share 99.5% homology, they still have some percentages of different routes depending of the host human or bovine.

Proteomics

Proteomics is also a powerful tool that should be integrated to the study of bTB [45], to deep insight in protein-protein interactions, to characterize proteins that suffer post-transductional modifcations, to study stability, abundance of key role of proteins, glycoprotein, when and how are expressed and migrate, protein patterns and if the proteome overall at the level of cells (macrophages, dendritic or lymphocytes cells) or tissues are afected in response to M. bovis infection. All these issues can be studied, by spectrometric mass (SELDITOFF) [27,45]. Moreover, recent research in this aspect indicate that the knowledge of the antigenic targets of T cells in bTB as well as the increasing knowledge of the subset of T cells and their interactions with infected macrophages with M. bovis can help for the development of better methods of control of disease. In biologic systems based in the integration of data generated by omics studies are a potential approach that can be used to identify transcriptional gene signatures to predict or to correlate parameters of protection in vaccinated calves versus unvaccinated, and also 188 to predict vaccination protocol efectiveness, until now mostly applied to human tuberculosis [26,27,31,45,46] (Figure 1).

Conclusion

Despite of the development and improvement of the DNA technologies for diagnostic and prognostic test, in the last decade there have been a raise in the technologies of the new generation which certainly are giving an enormous advance either to epidemiological molecular studies as well as in the knowledge of the epigenetics and deep insight in the knowledge of mutations, genetic markers (SNP), biomarkers, defnition of spectrum of disease. Omics technologies and third next generation high-throughput technologies have emerged as a potent technologies that cover the totality of the genome wide studies and importantly the functionality and dynamic of the genomes, transcriptomes, and proteomes that will enable to integrate the complete and defne as it was possible to determine for humans, the landscape in the spectrum of the infectious disease, the progression and/or the genetic predisposition to mycobacterial diseases for (Figure 1) and make feasible translational research.

Conẑict of interest

None.

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References

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23. Jia K, Yu M, Zhang GH, Zhang J, Lin ZX, et al. (2012) Detection and identification of Mycobacterium tuberculosis and Mycobacterium bovis from clinical species using DNA microarrays. J Vet Diag Invest 24: 156-160.
24. De Ketalacre A, Grossens K, Peelman I, Burvenich C (2006) Technical note: Validation of internal control genes for gene expression analysis to bovine polymorphonuclear leucocytes. J Dairy Sci 89: 4066-4069.
25. Huang DW, Sherman BT, Lempicki RA (2009) Bioinformatics enrichment tools: paths toward the comprehensive functional analysis of large gene list. Nucleic Acids Res 37: 01-13.
26. Berry PRM, Graham MCh, McNab WF, Xu Z, Bloch AAS, et al. (2010) An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis. Lett Nature 466: 973-979.
27. Nakaya HI, Li S, Pulendran B (2011) Systems vaccinology: learning to compute the behavior of vaccine induced immunity. Wiley Interdiscip Rev Syst Biol Med 4: 193-205.
28. Malone JH, Oliver B (2011) Microarrays, deep sequencing and the true measure of transcriptome. BMC Biology 9: 34.
29. Aranday-Cortes E, Hogarth PJ, Kaveh DA, Whelan A.O, Villarreal-Ramos B, et al. (2012) Transcriptional profling of disease-induced host responses in bovine tuberculosis and the identification of potential diagnostic biomarkers. Plos one 7: e30626.
30. Mortazavi A, Williams BA, McCue K, Schafer I, Wold B (2008) Mapping and quantifying mammalian transcriptomes by RNA-seq. Nat Methods 5: 621-628.
31. Bhuju S, Aranday-Cortes E, Villarreal-Ramos B, Xing Z, Singh M et al. (2012) Global gene transcriptome analysis in vaccinated cattle revealed a dominant role of IL-22 for protection against bovine tuberculosis. PLoS Pathog 8: e1003077.
32. Meade KG, Gormley E, Park SD, Fitzsimons T, Rosa GJ, et al. (2006) Gene expression profling of peripheral blood mononuclear cells (PBMC) from Mycobacterium bovis infected cattle afer in vitro antigenic stimulation with purifed protein derivative of tuberculin (PPD). Vet Immunol Immunopathol 113: 73-89.
33. Meade KG, Gormley E, O'Farrelly C, Park DS, Costello E, et al. (2008) Antigen stimulation of peripherla blood mononuclear cells from Mycobacterium bovis infected cattle yields evidence for a novel gene expression program. BMC Genomics 9: 447.
34. Shukla SK, Shukla S, Chauhan A, Sarvjeet, Khan R, et al. (2017) Diferential gene expression in Mycobacterium bovis challenged monocyte-derived macrophages of cattle. Microb Pathog 113: 480-489.
35. Shukla SK, Shukla S, Khan R, Ahuja A, Singh LV, et al. (2018) Pathway analysis of diferentially expressed genes in Mycobacterium bovis challenged bovine macrophages. Microb Pathog 115: 343-352.
36. MacHugh DE, Gormley E, Park SD, Browne JA, Taraktsoglou M, et al. (2009) Gene expression profling of the host response to Mycobacterium bovis infection in cattle. Transbound Emerg Dis 56: 204-214.
37. Blanco FC, Soria M, Bianco MV, Bigi F (2012) Transcriptional response of peripheral blood mononuclear cells from cattle infected with Mycobacterium bovis. Plos one 7:e41066.
38. Magee DA, Conlon KM, Nalpas NC, Browne JA, Pirson C, et al. (2014) Innate cytokine profling of bovine alveolar macrophages reveals commonalities and divergence in the response to Mycobacterium bovis and Mycobacterium tuberculosis infection. Tuberculosis (Edinb) 94: 441-450.
39. McLoughlin KE, Nalpas NC, Rue-Albrecht K, Browne AJ, Magee DA, et al. (2014) RNA-seq transcriptional profling of peripheral blood leukocytes from cattle infected with M. bovis. Front Immunol 5: 396.
40. Nalpas NC, Park DDE, Magee DA, Taraktsuglou M, Browne JA, et al. (2013) Whole-transcriptome high-throughput RNA sequence analysis of the bovine macrophage response to M. bovis infection in vitro. BMC Genomics 14: 230.
41. Nalpas NC, Magee DA, Conlan KM, Browne JA, Healy C, et al. (2015) RNA sequencing provides exquisite insight into the manipulation of the alveolar macrophages by tubercle bacilli. Sci report 5: 13269.
42. Lin J, Zhao D, Wang J, Wang Y, Li H, et al. (2014) Transcriptome changes upon in vitro challenge with Mycobacterium bovis in monocyte-derived macrophages from bovine tuberculosis-infected and healthy cows. Vet Immunol Immunopathol 163: 146-156.
43. Churbanov A and Milligan B (2012) Accurate diagnostic for bovine tuberculosis based on High-throughput sequencing. Plos one 7: e50147.
44. Pan L, Wei N, Jia H, Gao M, Chen X, et al. (2017) Genome-wide transcriptional profling identifes potential signatures in discriminating active tuberculosis from latent infection. Oncotarget 8: 112907-112916.
45. Malone KM, Rue-Albrecht K, Magee DA, Conlon K, Schubert TO, et al. (2018) Comparative omics analyses diferentiate M. tuberculosis and M. bovis and reveal distinct macrophage responses to infection with the human and bovine tubercle bacilli. Microbial Genomics 4: e000163.
46. Mayorquin-Luna GA and Guerrero GG (2018) An study of the in vivo gene profle in M. bovis infected cattles from Mexico. Curr Analytical Biotech (inpress).