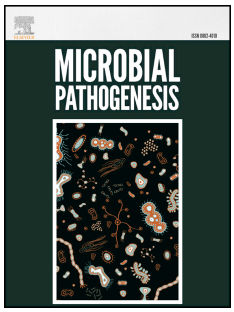
Accepted Manuscript



Assessment of antigenic supplementation of bovine purified protein derivative for diagnosis of subclinical infection with *Mycobacterium bovis* in cattle

A.H. Alvarez, A. Gutiérrez-Ortega, V. Gómez-Entzin, G. Pérez-Mayorga, J. Naranjo-Bastién, V. González-Martínez, F. Milián-Suazo, M. Martínez-Velázquez, S. Herrera-Rodríguez, E. Hinojoza-Loza

PII: S0882-4010(16)30649-0

DOI: 10.1016/j.micpath.2017.05.012

Reference: YMPAT 2256

To appear in: *Microbial Pathogenesis*

Received Date: 13 October 2016

Revised Date: 3 May 2017

Accepted Date: 4 May 2017

Please cite this article as: Alvarez AH, Gutiérrez-Ortega A, Gómez-Entzin V, Pérez-Mayorga G, Naranjo-Bastién J, González-Martínez V, Milián-Suazo F, Martínez-Velázquez M, Herrera-Rodríguez S, Hinojoza-Loza E, Assessment of antigenic supplementation of bovine purified protein derivative for diagnosis of subclinical infection with *Mycobacterium bovis* in cattle, *Microbial Pathogenesis* (2017), doi: 10.1016/j.micpath.2017.05.012.

Full Scientific Report

Assessment of antigenic supplementation of bovine purified protein derivative for diagnosis of subclinical infection with *Mycobacterium bovis* in cattle

Alvarez AH[1*], Gutiérrez-Ortega A[1], Gómez-Entzin V[1], Pérez-Mayorga G[1], Naranjo-Bastién J[1], González-Martínez V[1], Milián-Suazo F[2], Martínez-Velázquez M[1], Herrera-Rodríguez S[1], Hinojoza-Loza E[3]

[1]Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco A.C. Av. Normalistas 800, C.P. 44270. Guadalajara, Jal. México.
[2]Facultad de Ciencias Naturales, Universidad Autónoma de Querétaro, Av. de las Ciencias s/n, C.P. 76230. Querétaro, Qro. México.
[3]Instituto Tecnológico de Tlajomulco, Km 10 to San Miguel Cuyutlán, C.P. 45640. Tlajomulco de Zúñiga, Jal. México.

*Correspondence: A.H. Alvarez, Medical and Pharmaceutical Biotechnology, Centro de Investigación y Asistencia en Tecnología y Diseño del Estado de Jalisco A.C., Av. Normalistas 800, Col. Colinas de la Normal, C.P. 44270, Guadalajara, Jalisco, México. Tel: (+52) 3333455200 ext. 1307; fax: (52) 3333455200 ext. 1001; aalvarez@ciatej.mx

Abstract

Bovine tuberculosis (bTB) is usually diagnosed *in vivo* and *ex vivo* on the basis of delayed hypersensitivity reactions with a complex pool of antigens named bovine tuberculin (PPDB). The IFN-γ release assay (IGRA) for bTB is a blood-based assay that improves detection of infected cattle at early stages that escape skin testing. Improvements to IFN-γ testing with specific proteins have been performed to increase sensitivity. DosR regulon-related antigens are well known mycobacterial proteins expressed during the non-replicative phases of infection, this has been useful to improve the diagnosis of subclinical forms of TB in suspected individuals. Transcripts of DosR genes *mb2054c*, *mb2057c*, and *mb2660c* have been identified by our group in lymph nodes of IFN-γ test negative cattle . This led us to hypothesize that DosR-related proteins may potentiate the IFN-γ response to PPDB in animals with a false negative IFN-γ test, making evident subclinical infection . Three hundred animals were evaluated by means of IGRA and post-mortem microbiological analysis of tissue samples to validate *M. bovis* infection. We found that 176 out of 300 animals showed an overall increased OD in complemented IGRA with two purified protein cocktails in comparison to PPDB