

**Therapy with fragments of *Mycobacterium tuberculosis* after a short-term chemotherapy with isoniazid in a new latent tuberculosis infection model in mini-pigs is safe and effective.**

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**OBJECTIVE.** The aim of this study was to evaluate the safety and therapeutic effect of fragments of vaccine RUTI® in a newly-developed experimental model of (LTBI) in mini-pigs. RUTI is a therapeutic vaccine based on *M. tuberculosis* (MTB) fragmented cells.

**METHODOLOGY.** 18 *spf* mini-pigs 1,5-month-old were infected by transthoracic (TT) inoculation of H37Rv Pasteur *M. tuberculosis* strain (2x10<sup>3</sup> CFUs) in the left lung. After 5 weeks post infection (pi.), three experimental groups were defined: non-treated; treated with INH (300 mg twice a week until w9 p.i.); and treated with INH plus two inoculations of RUTI® (at w9 and w12 pi). Cellular and humoral immunological response was evaluated through time. Animals were sacrificed on w21, for histological bacteriological analysis to evaluate the dissemination of the infection.

**RESULTS.** One week after the inoculation of RUTI, a marked increase of IFN- IL-12 and TNF levels was evidence after stimulating peripheral blood with PPD, BCG, and 85B, 16 kDa and ESAT-6 *M. tuberculosis* antigens using ELISA and ELISPOT assays. Neither IL-4 nor IL-10 were detected in any case. Antibody response against PPD was also induced after the second vaccine RUTI® inoculation. INH treatment caused a marked reduction in the granulomatous infiltration and dissemination in the lungs. Inoculation of vaccine RUTI® enhanced this effect and reduced the bacillary load, causing neither systemic nor local adverse effects. Mini-pigs showed human-like lesions and a good control of the bacillary load through time, becoming a reliable experimental animal model for LTBI.

**CONCLUSION.** In this newly-developed swine experimental model of latent tuberculosis infection, administration of vaccine RUTI® has demonstrated to be safe and effective. **ACKNOWLEDGEMENTS:** BIO BIO2005-07949-C02-02/, Programa de becas FPU del Ministerio de Educación y Ciencia, Plan Nacional I+D+I FIS CM06/00123, Archivel Farma, s.l., and Esmeralda Cano, Raquel Maeso and Maite Martín.