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Comparative analysis of four lipoproteins from *Mycoplasma mycoides* subsp. *mycoides* Small Colony identifies LppA as a major T-cell antigen

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Abstract

Control of contagious bovine pleuropneumonia (CBPP), caused by *Mycoplasma mycoides* subsp. *mycoides* Small Colony (*Mmm*SC), remains an important goal in Africa. Subunit vaccines triggering B and T-cell responses could represent a promising approach. To this aim, the T-cell immunogenicity of four *Mmm*SC lipoproteins (LppA, LppB, LppC and LppQ), present in African strains and able to elicit humoral response, was evaluated. *In vitro* assays revealed that only LppA was recognized by lymph node lymphocytes taken from three cattle, 3 weeks after *Mmm*SC exposure. Maintenance of the LppA-specific response, relying on CD4 T-cells and IFNγ production, was then demonstrated 1 year after infection. LppA is thus an important target for the CD4 T-cells generated early after *Mmm*SC infection and persisting in the lymph nodes of recovered cattle. Its role as a protective antigen and ability to *in vivo* trigger both arms of the host immune response remain to be evaluated.

Keywords: Contagious bovine pleuropneumonia; *Mycoplasma mycoides* subsp. *mycoides* S.C.; Antigen; Vaccine; Cell-mediated immunity; Cattle; Tropical disease

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Résumé

Le contrôle en Afrique de la péripneumonie contagieuse bovine (PPCB), causée par *Mycoplasma mycoides* subsp. *mycoides* SC (*Mmm*SC), reste problématique. Le développement de vaccins sous-unités pourrait apporter une solution. Dans ce but, la capacité d'induction d'une réponse immunitaire cellulaire de quatre lipoprotéines de *Mmm*SC (LppA, LppB, LppC and LppQ), présentes dans les souches Africaines et responsables de réponses humorales, a été analysée *in vitro*. Les résultats ont révélé que seule la LppA était reconnue par des lymphocytes ganglionnaires issus de bovins, trois semaines après infection par *Mmm*SC. La réponse spécifique de la LppA, médiée par des lymphocytes CD4 et une production d'IFNγ, a également été détectée un an après infection. La LppA de *Mmm*SC est donc un antigène intéressant, capable d'induire une stimulation précoce de lymphocytes CD4 dont une sous-population persiste dans les ganglions d'animaux guéris. Son rôle dans la protection face à la PPCB reste à confirmer.

Mots-clés : Péripneumonie contagieuse bovine ; *Mycoplasma mycoides* subsp. *mycoides* S.C. ; antigène ; vaccin ; Immunité à médiation cellulaire ; bovins ; pathologie tropicale

1. Introduction

Contagious bovine pleuropneumonia (CBPP), caused by *Mycoplasma mycoides* subsp. *mycoides* biotype Small Colony (*Mmm*SC), is one of the most serious cattle diseases in Africa. The disease is responsible for heavy economic losses due to mortality, loss of weight, reduced working ability or in fertility. CBPP is included in the list of pathologies of the Office International des Epizooties (OIE) requiring official declaration. Infected countries are thus excluded from international trade. The development of an improved vaccine is the only realistic prophylaxis to achieve eradication of CBPP in Africa. Indeed, the combination of stamping-out, control of cattle movement and quarantine used in other continents to successfully eradicate CBPP is impracticable in the African continent where cattle raising rely on nomadism and transhumance. Development of optimized vaccines against CBPP is thus a necessity, requiring identification of the protective immune parameters and *Mmm*SC components triggering this immune response [1].

Previous studies have demonstrated the systematic occurrence of *Mmm*SC-specific CD4 IFNγ-secreting T-cells in recovered cattle either in blood circulating mononuclear cells [2] or in the respiratory lymph nodes [3,4]. Recovered animals are known to be protected against new *Mmm*SC infection since they develop long-term immunity to reinfection [5]. CD4 T-cell activation and IFNγ secretion can, therefore, be retained as relevant criteria to select *Mmm*SC components for vaccine development.

Four *Mmm*SC membrane lipoproteins (Lpps) have been identified, namely LppA (also known as P72), LppB, LppC and LppQ, and their role in the *Mmm*SC-specific humoral response has been shown [6–10]. It is known that several proteins might display both B-cell and T-cell epitopes [11–13]. Furthermore, studies also reported the strong potential of mycoplasmal Lpps to trigger immune responses, the lipid moiety acting with adjuvant-like proinflammatory activity while epitopes expressed by the protein part evoke the immune response [14,15].