Enzootic bovine leucosis is an infectious viral disease of cattle distributed worldwide that affect dairy cattle over 2 years of age. This disease produces changes in the animal’s immune system that may affect vaccine efficacy. During the last 10 years many reports have highlighted the association of BLV infection with a diminished or modified immune response against routinely used cattle vaccines. Our group has focused on studying the possible role of BLV infection on the immune response elicited by foot-and-mouth disease primo or multiple vaccinations making use of serological assays aimed to characterize the antibody response in terms of IgG-subtypes and avidity. These tools demonstrated to be very useful for analyzing the effects of BLV in FMD vaccine immunity. The use of simple high-throughput assays delving on the quality of the antibody response is paramount for assessing vaccine efficacy and can help in analyzing the impact of BLV infection at herd level.

Keywords: Bovine leucosis; Foot-and-mouth disease vaccines; Immune response; Serological tools
well-controlled in many South-American countries. In Argentina, vaccination campaigns are applied under the supervision of the national authorities, certifying cold chain and correct application. Another advantage is the availability of ELISAs that allow a precise correlation with that can be used to study FMD-vaccine efficacy in the field [15,16]. Apart from assays measuring total antibodies, like liquid phase blocking ELISA used since the late eighties [17], there are also simple high-throughput serological tools to characterize the quality of the antibody response [14].

The quality of vaccine-induced antibodies, defined by isotype profile and avidity, has been identified as a defining factor in efficacy. FMDV isotype ELISAs for cattle sera were developed in the nineties [13]. They are indirect tests used to titrate anti FMDV IgG1 and IgG2 in sera. The rate between IgG1 and IgG2 titers has been related to protection against FMDV specially when studying cross- protection [14,18]. Isotypes bring information of the type of immune response, if it is related to antibody-mediated cellular responses or if they are mainly neutralizing responses. Avidity is another parameter of the “functional affinity” of specific antibodies. It is related to the interaction between polyclonal antibodies in a sample and the bound antigen. Avidity is influenced by the antibody serotype, their epitope-paratope affinity, the number of antibodies and their aminoacidic sequence. When vaccines stimulate the acquired immunity, antigen-specific B cells undergo somatic hypermutation and affinity-based selection, resulting in B cells that produce antibodies with increased avidity over germline antibodies. Avidity can be considered a landmark of efficient vaccination [19] and has been related to protection for many vaccines and diseases [20], used to discriminate between chronic and acute infections [21] and correlated to capacity of antibodies to neutralize viral infection in cultured cells [20,22].

Analysis of the isotypes of the antibodies induced against a virus strain in primo-vaccinated cattle revealed that IgM, IgG1 and IgG2 titres increased in both positive (BLV+) and negative (BLV-) heifers following FMD immunization, although IgM and IgG1 titers were higher in non-infected animals [5]. Levels of IgG2 can explain why the difference in antibody titers was only marginally significant when total antibodies were measured. The avidity index was lower in seropositive animals than that seronegative, meaning a reduced capacity of developing a protective immune response. These results demonstrated that BLV infection in dairy cattle modified the profile of antibody response to FMD primo-vaccination, biasing the isotype switch towards IgG2 though total antibody levels were marginally affected. These differences may be caused by the cytokine modulation exerted by BLV.

In a larger study [23] we measured anti FMDV antibodies from two-hundred milking cows (>2 years old) selected based on their BLV-serologic status (100 BLV+ and 100 BLV-). The animals were in two large farms in Argentina (500 animals each), one with low and another with high BLV prevalence. The aim of this study was to investigate if BLV-status could interfere with the efficacy of the FMDV-vaccination campaign. This is of interest in FMDV-endemic regions since the total FMDV-antibody titers induced through vaccination are necessary to prevent disease outbreaks. Here we showed that after repeated vaccination, levels and avidity of anti-FMD antibodies were similar between BLV + and BLV- animals. Although primo-vaccination may be affected [5], repeated vaccination probably weakens this effect at a herd level, as animals may get infected with BLV at different times before or after their primo-vaccination. The use of avidity in this study allowed detecting individual vaccine failures that cannot be accounted by just measuring total antibodies. Our results suggested that BLV-status did not compromise the efficacy of routine FMDV-vaccination in cattle.

The use of serological high-throughput assays allowed to study if FMD vaccination was affected by the animal’s BLV serological status. These simple tools were useful to characterize the immune response at individual level and get a closer insight on the effects of this important viral disease of dairy cattle, revealing individual vaccine failures and helping to better characterizing the effect of BLV infection on the immune response induced by vaccination, at a herd level. These serological assays constitute important tools to assess vaccine performance in the field.

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