

Antibody and cell-mediated immune responses to *Staphylococcus aureus* small colony variants and their parental strains associated with bovine mastitis

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Abstract:

Persistence of bovine *Staphylococcus aureus* mastitis may be associated with the small colony variant (SCV) form that is adapted to intracellular life and resists elimination by the immune system. This study evaluated antibody-mediated (AMIR) and cell-mediated immune responses (CMIR) to two bovine SCV forms and their parent strains isolated from cows with mastitis. Four groups of healthy cows, five cows/treatment group, were challenged by the intramammary route with naturally occurring bovine SCV Heba3231, its parent strain 3231, a hemB mutant displaying the SCV phenotype or its parent strain, Newbould 305. Blood and milk samples were collected at day 0 before challenge and at days 1, 14, 21 and 36 post-challenge to determine antigen-specific immunoglobulin (Ig) IgG1 and IgG2 antibody responses as indicators of type 2 and type 1 responses, respectively. At day 24 post-challenge cows in each group were inoculated with the UV-killed homologous strain intradermally in the neck to induce delayed-type hypersensitivity (DTH) as an indicator of CMIR. The SCV Heba3231 and 3231 strains induced significant IgG1 and IgG2 antibody responses in sera and in sera and milk whey, respectively. The hemB SCV mutant and Newbould 305 strains induced significant IgG1 antibody in milk whey, and in sera and milk whey, respectively. The SCV Heba3231 and 3231 strains induced DTH, the hemB mutant induced intermediate hypersensitivity, and Newbould 305 failed to induce DTH. These results indicate marked differences in immune responses induced by parent and SCV forms of the same strain of *S. aureus* and by the two wild-type strains. This is the first study to evaluate both AMIR and CMIR in the context of persistent bovine mastitis to different and genetically characterized strains of *S. aureus* including two SCVs. The findings expand our understanding of immune responses to persistent *S. aureus* mastitis.