

## **The bovine mammary gland microbiota as a resource for the design of new strategies against mastitis**

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Mastitis is a mammary gland inflammatory disease often due to bacterial infections. Mastitis is responsible for considerable economic losses in dairy farms and preventive and curative strategies that mainly rely on antibiotic therapies are not totally effective and contribute to antibiotic resistance dissemination, prompting the need for alternative or complementary strategies. Given the relationship between microbiota composition and health that was reported in several contexts in both human and animals, we explored a potential role of the bovine mammary gland microbiota in udder health. The bovine teat microbiota was investigated using metataxonomics on the 16s rRNA gene in quarters which were all free of inflammation at sampling time but which had different histories regarding mastitis: from no episode of mastitis on all the previous lactations (Healthy quarter, Hq) to one or several clinical mastitis events (Mastitic quarter, Mq). Our results revealed a higher diversity in Hq compared to Mq quarters and allowed to identify taxonomic markers of the health status of quarters. These results indicated a link between teat microbiota composition and bovine mastitis even at distance from the infectious episode. To further decipher the relationships between teat microbiota and immune and microbial responses, we used a switch from twice- to once-daily milking (ODM) in initially healthy quarters of dairy cows to trigger an udder perturbation. Our results clearly support a temporal relationship between initial teat microbiota composition and richness, the immune response to ODM, and mastitis development. Quarters with a higher richness and specific taxonomic markers displayed early inflammation following transition to ODM but without developing mastitis (no infection). Altogether, these results suggest a role of the bovine teat microbiota composition and richness in the immune response of the mammary gland during perturbations such as transition to ODM or pathogen entrance. They invite us to consider strategies that can preserve teat microbiota diversity as well as taxa associated to a healthy status of the bovine mammary gland for the design of next-generation probiotics.