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Control of bovine mastitis in the 21st century: Immunize or tolerize?





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# ACCEPTED MANUSCRIPT

### Control of bovine mastitis in the 21st century: immunize or tolerize?

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#### Introduction

Bovine mastitis still underlies huge losses and represents one of the main causes of early cull for dairy cows. There is definitely a correlation between prevalence of mastitis and high milk yield (Ingvartsen, 2003). Interestingly, whereas milk somatic cell counts have substantially decreased, this is not true of clinical mastitis cases, still causing large drug usage on farm (**Ruegg, 2017**).

#### The correlation between high milk yield and mastitis

The innate immune system can mount a response to both infectious and non-infectious stressors. Among non-infectious stressors, the metabolic ones play a crucial role: products of metabolic stress like non-esterified fatty acids (NEFA) can signal to the innate immune system and sometimes lead to a dysregulated inflammatory response (Amadori, 2016).

The above concepts should underlie modern, updated disease control programs on farm. Accordingly, most cases of production diseases like mastitis take place in the early lactation phase, in the framework of inflammatory responses to metabolic stress and immunosuppression.

#### The two strategies of the immune system

In a continuous trade-off, the host offsets the elimination of microbial stressors against the need to avoid tissue damages and waste of metabolic energy. This is the crucial, strategic knot which dictates the final type and outcome of the response, finely tuned by mechanisms developed along the phylogenetic evolution.

Accordingly, two major options are available to both innate and adaptive immune systems:

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