

Discovery and Validation of Immunological Biomarkers in Milk for Health Monitoring of Dairy Cows - Results from a Multiomics Approach

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Abstract

At onset of milk production and in early lactation highly producing dairy cows are most susceptible for inflammatory diseases due to functional suppression of immune cells. Intensive supervision of the animals is essential and implementation of new technologies to on-farm routines will be the next step to provide automation and improvement of herd health monitoring programs. Objective of our study was to identify and validate immunological biomarkers in milk that indicate extra-mammary inflammatory diseases to characterize the general health status of highly-producing dairy cows. In total 89 healthy and 75 diseased animals (German Holstein cows) were included. Diseases were distinguished by either systemic (extra-mammary) occurrence or those affecting the mammary gland (mastitis) and further classified by their severity. For protein biomarker discovery we used a top-down approach to narrow down a broad range of secreted gene products of the milk cell transcriptome (microarray) and proteome to a few promising candidates which were validated using real-time PCR and ELISA. The most promising biomarker candidates were statistically evaluated. Receiver operating characteristic analysis revealed haptoglobin, secretory component, lactoferrin and vascular endothelial growth factor showing the highest discriminatory capability for diseased vs. healthy cows. Values for sensitivity at a specificity of 94% were 82% for haptoglobin, 59% for secretory component, 55% for lactoferrin and 67% for vascular endothelial growth factor. Statistical evaluation by multinomial logistic regression and k-nearest neighbor method confirmed haptoglobin as the best single-use biomarker. In combination with secretory component or lactoferrin an increase in overall sensitivity or specificity, depending on the classification method, could be achieved. The application of the validated health biomarkers in

combination with an easy high-throughput detection system would offer a solution to adapt dairy herd management to changing requirements on animal welfare, farming efficiency, milk supply and food safety in modern agriculture.

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