Integrative analysis of transcriptomics and metabolomics data: adaptation of *Propionibacterium freudenreichii* to long-term survival in nutritional shortage

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Propionibacterium freudenreichii is a bacterial species belonging to Actinobacteria phylum, known for its survival in long periods under adverse environmental conditions. This bacterium is widely used in dairy industry for the ripening process of Swiss-Type cheeses, such as Emmental and also presents potent strain-specific probiotic effects. In this study, *P. freudenreichii* CIRM-BIA 138 was grown for 11 days in a culture medium with nutritional shortage. Bacterial survival rate was assessed by optical density and CFU counting. Gene expression and biochemical analysis were also conducted to investigate the bacterial adaptive response to nutritional shortage condition. This strain maintained a high population level of 10^8 CFU/ml for the entire period. The available carbon and free amino acids sources and organic acid produced by the strain were monitored in the bacterial supernatant throughout survival for 11 days. Lactate was the first carbon source for *P. freudenreichii* CIRM-BIA 138 to be exhausted in the medium. RNA-seq analysis demonstrated different metabolic behaviors across the conditions of stationary entry phase and exponential phase. At the beginning of stationary phase, *P. freudenreichii* CIRM-BIA 138 dramatically reduces several metabolic processes as glycolysis, oxidative phosphorylation and Wood-Werkman Cycle, seeking an alternative metabolism facing pathways that promote new energy sources, such as carbon and nitrogen. Moreover, it is noted that, the processes of transcription, translation and secretion of proteins are decreased at the stationary growth phase. The transcriptomic and metabolomic data integration allowed us to deduct the strategies involved in adaptation, persistence and long-term survival of *P. freudenreichii* in nutritional shortage.

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