Systems biology applied to cheddar production

Duration: 2014-2019

Highlights

- One of the challenges in the milk processing industry is producing high quality cheeses on a consistent basis.
- Many factors influence quality, including the microbiological composition of milk and the effectiveness of starter cultures and bacteriophages.
- This project investigates these factors using a "systems biology" approach to better understand the impact of the microbiological network on cheddar production.
- Systems biology integrates different levels of information to develop an operating model for the entire system.
- Systems biology uses techniques to quantify changes in the genome, transcriptome, proteome and metabolome in response to a given situation (cheddar, in this case).
- This very ambitious project has generated new results that pave the way for a better understanding of the cheese-making ecosystem.
- Functional assembly (from the genome to the metabolome) will also provide added-value in order to better understand and intervene in regards to the major variables affecting these products.

Objectives

- Objective 1: Determine the microbiome and virome of milk and cheddar.
- Objective 2: Determine the microbial and viral transcriptome of milk and cheddar.
- Objective 3: Determine the microbial and viral proteome of milk and cheddar.
- Objective 4: Determine the metabolome of milk and cheddar.
- Objective 5: Determine the biology of the cheddar system.

Results and potential benefits

The main achievements of this project are as follows:

1.1) Development of a protocol for isolating the genetic material of various viruses based on dairy product samples (milk, cheese).

1.2) Updating of a protocol for isolating the genome of various bacteria based on dairy product samples (milk, cheese).

1.3) A number of new genomes (draft) of *Lactococcus lactis* are now available.

1.4) Creation of a database containing genomic sequences of the cheese microbiome.

2) Development of a protocol for isolating the DNA of dairy product samples (milk, cheese).

3.1) By using various proteomic approaches and an *L. lactis* phage-bacteria model system, we were able to detect 78% (39/50) of the phage proteins and 56% (1332/2383) of the bacteria proteins.

3.2) We identified 209 *L. lactis* proteins that are expressed only when infected by the phage p2.

4.1) Two extraction methods to detect a broader profile of metabolites are now available.

4.2) Evaluation of different sources of high-speed ionization for the metabolomic analysis of cheese.

4.3) A list of ions corresponding to the normal ripening of cheddar as well as potential identifications for these ions.

5.1) The results of the metabolomic analysis are promising in order to quickly determine a cheddar aging profile or signature.

5.2) However, in order to validate the results obtained, numerous other cheese samples will have to be analyzed, including cheeses with a variety of organoleptic profiles.

Innovative aspects

- Development of several protocols for "omic"-type studies on cheese samples.
- First study of the proteome of a lactic acid bacterium infected by a phage (https://www.ncbi.nlm.nih.gov/pubmed/30679258).
- Rare study on the metabolome of cheddar cheese.

Professionals trained

- **Marie-Laurence Lemay**, PhD student in microbiology.
- **Pier-Luc Plante**, PhD student in bioinformatics.
- **Alexia Lacelle-Côté**, master's student in microbiology.
- **Frédéric Raymond**, post-doctoral researcher in bioinformatics.
- **Simon Labrie**, post-doctoral researcher in microbiology.
- **Jessie Bélanger**, undergraduate student in microbiology.

For further information

- Fraud, S., and S. Moineau. 2018. Phages. Le fromage. 4th édition. J.-C. Gillis and A. Ayerbe (Eds.). Lavoisier. p. 293-302.
- Lemay, M.-L., A. Otto, S. Maaß, K. Plate, D. Becher and S. Moineau. 2019. "Investigating *Lactococcus lactis* MG1363 Response to Phage p2 Infection at the Proteome Level". *Molecular & Cellular Proteomics*. 18:704-714.

Other articles of interest on phages of mesophilic starter cultures:

- Geagea, H., A. Gomaa, G. Remondetto, S. Moineau and M. Subirade. 2015. "Investigation of the protective effect of whey proteins on lactococcal phages during heat treatment at various pH". *Int. J. Food Microbiol*. 210:33-41.
- Geagea, H., S.J. Labrie, M. Subirade and S. Moineau. 2018. "The Tape Measure Protein is Involved in the Heat Stability of *Lactococcus lactis* Phages". *Appl. Environ. Microbiol.* 84:e02082-17.
- de Melo, A.G., S. Levesque and S. Moineau. 2018. "Phages as friends and enemies in food processing". *Curr. Opin. Biotechnol*. 49:185-190.
- Dion, M., F. Oeschlin and S. Moineau. 2020. "Phage diversity, genomics and phylogeny". *Nature Reviews Microbiology*. In press.

Financial contributions

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- Fonds de recherche du Québec – Nature et technologies
- Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec
- Novalait

The industrial partner has provided cheese and starter cultures.

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