

Cultivated milk from in vitro grown milk cells

A new research project funded by the Danish Dairy Research Foundation places Denmark on the roadmap of new initiatives relative to cultivated milk. The project idea is based on secretion of milk components from mammary cells isolated from milk.

The milk-producing cells and cultivated milk

The complex composition of milk comes from the synthesis of milk constituents by the mammary epithelial cells (MECs) lining the alveoli in the mammary gland, as they contain the whole machinery for making e.g. milk proteins with the right decorations, like calcium binding. These cells are responsible for the major part of the components found in milk, including the major and many of the minor milk proteins, as well as the fat globules and lactose. In addition to the components made by MECs, some milk components are transferred from blood or secreted by immune cells or microorganisms present in milk. To obtain MECs there are two strategies: isolation from mammary tissue of slaughtered cows, or non-invasively from milk itself. Cow's milk contains what is called the somatic cells, which are mainly immune cells being part of the cow's defense system against invading microorganisms that can otherwise result in mastitis. However, a tiny part, around 1-2 % of this cell pool present in milk is constituted of MECs. A major part of the project is to study the viability and optimal growth conditions of these isolated cells

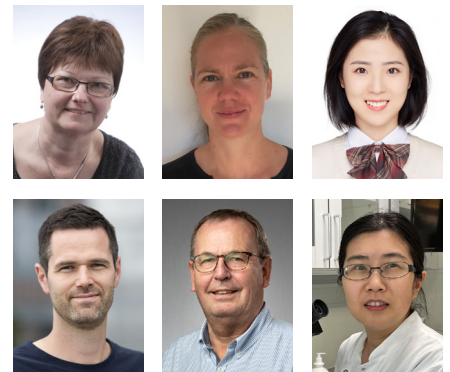
and not least, the conditions for secretion of milk components. Collected secretions will be characterized in relation to their composition using proteomics, mineral content determination, metabolomics, and micelle and fat globule formation, as well as hopefully, the functional properties of the "cultivated milk".

Isolation and growth of cells from milk

In the project, called "CleanMilk", cells are isolated from milk immediately after milking (Figure 2). At present, cells have been isolated from milk of 19 cows (representing 3 lactation stages, 2 parities and 3 biological replicates) from Danish Cattle Centre at Aarhus University in Foulum. The somatic cells are isolated from the milk by centrifugation and washing. Subsequently, the epithelial cells are isolated from these by special density centrifugation, and then grown in flasks with culture medium and their cellular origin is confirmed by microscopy and immunohistochemistry.

Target of the project

The overall target of the "CleanMilk" project is to provide a scientific basis for potential future use of lab (in vitro) grown MECs for



PROFESSOR LOTTE BACH LARSEN, ASSOCIATE PROFESSOR NINA AAGAARD POULSEN, PHD STUDENT JING CHE, ASSISTANT PROFESSOR ULRIK KRÆMER SUNDEKILDE, DEPARTMENT OF FOOD SCIENCE, AARHUS UNIVERSITY. SENIOR RESEARCHER, ADJUNCT PROFESSOR STIG PURUP, POSTDOC YUAN YUE, DEPARTMENT OF ANIMAL AND VETERINARY SCIENCES, AARHUS UNIVERSITY

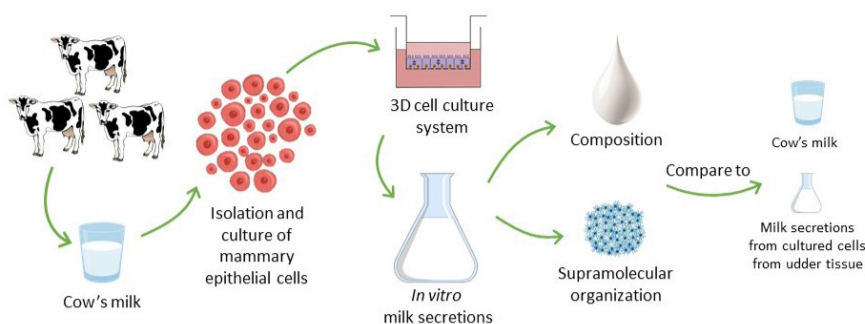


Figure 1. Project illustration



Project Info

Project title: CleanMilk - from in vitro grown milk cells

Project leader: Professor Lotte Bach Larsen, Department of Food Science, Aarhus University, Agro Food Park 48, 8200 Aarhus N, e-mail: lbl@food.au.dk, tlf. 22 81 92 82

Partners: Department of Animal and Veterinary Sciences, Aarhus University.

Project period: 2020-2024

Main aim: To provide a scientific basis for potential future use of lab grown (in vitro) bovine mammary cells for production of milk constituents of potential benefit in future scenarios. *Projects under Danish Dairy Research Foundation*

production of milk constituents of potential benefit in future scenarios. Comparison with cow's milk will be central, both in terms of composition, but also macromolecular structures, and for example to decipher if the cells can secrete caseins in the form of micelles and fat in the form of milk fat globules.

We do not foresee that these solutions will replace cows to produce milk constituents on a large scale but the research opens a possibility to enter the international scene and have competent and qualified research ongoing in this area, contributing to evaluating the potential and new areas for these

solutions and approaches. This will contribute to examining if such systems in the long perspective help reduce climate gases and thereby contribute to fulfilling Danish climate goals.

New concepts for milk

At present, concepts and solutions about milk production are intensively being debated in light of the sustainability agenda. Production of milk constituents by single cells (bacteria, yeast cells) using genetically modified microorganisms (GMO) is one future scenario being internationally consid-

ered, and where companies and research projects have been initiated on the international scene. However, only proteins encoded by the gene inserted in the microorganism will be synthesized in these systems. Milk contains a wealth of components from macro to micro components, that all together give the milk its specific nutritional, biological, and functional properties, both for off-spring and for consumers of dairy products.

Summary

In the project, MECs will be isolated from milk and grown in vitro, and their milk-like secretions will be characterized and compared with cow's milk in composition, structural features, and properties relative to dairy utilization. A central part of the project relates to growth, viability, and secretion conditions for the isolated epithelial cells. One PhD student is affiliated with the project.

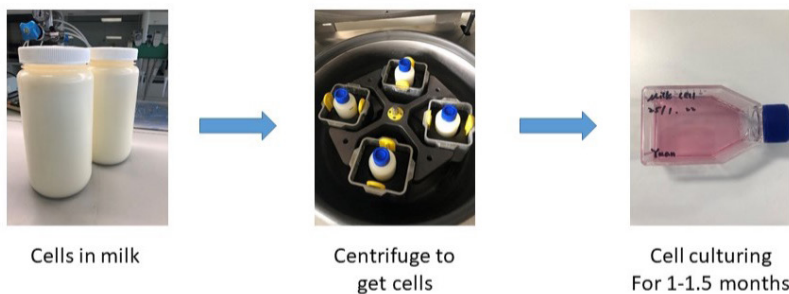


Figure 2. Milk cell isolation – cell isolation in lab