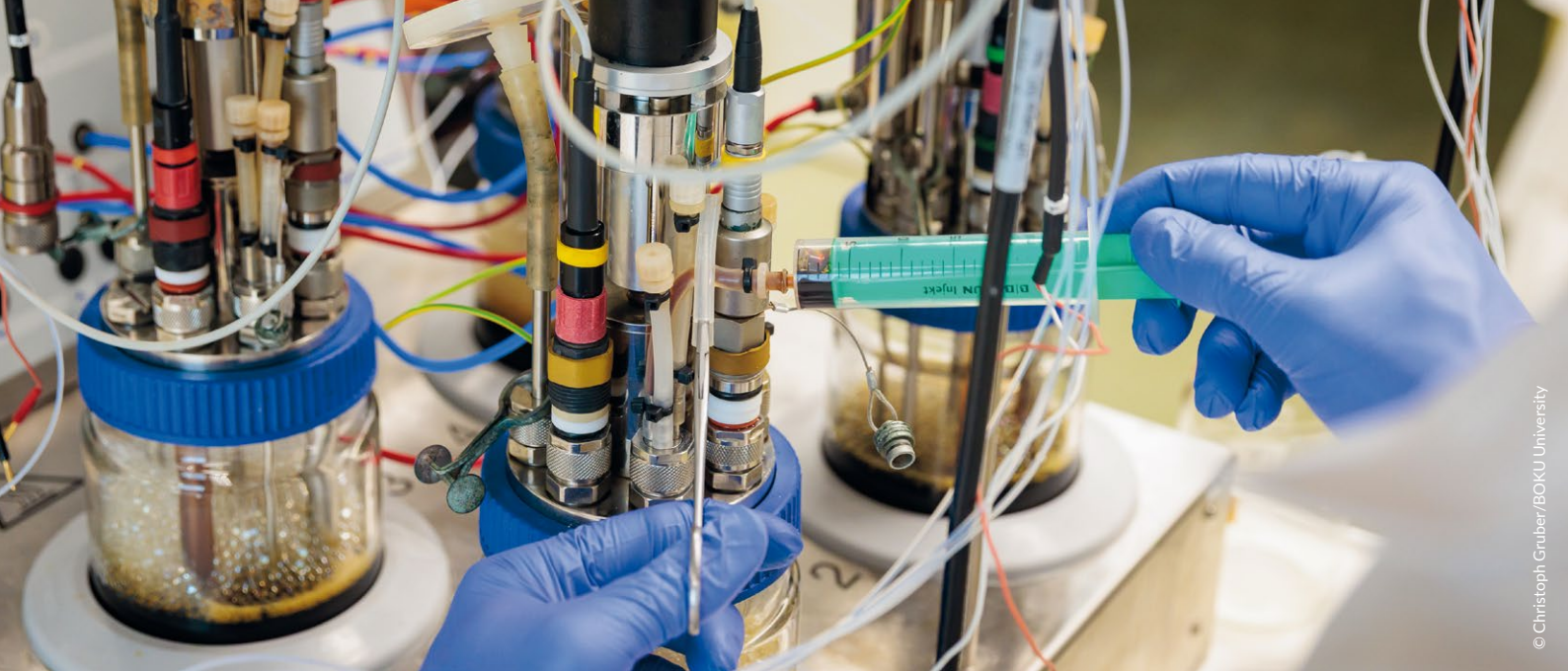




A paradigm shift in protein production

Many sectors, ranging from food to pharmaceutical production, require proteins in high quality and quantity. But how can they be produced as efficiently and sustainably as possible?
A CD Laboratory has the answer.

What is at issue?

Proteins are extremely important 'building blocks' for the biopharmaceutical industry, the food industry and as technical enzymes; they should be available in the highest possible quality and in large quantities. A tried-and-tested method for producing proteins is the use of yeast cultures, as these secrete proteins. The problem with this is that yeasts are single-celled fungi and, as such, like all other microorganisms, they strive to grow – that is, to produce biomass. In the context of yeast-based protein production, however, biomass is an undesirable by-product: the more biomass that is produced, the more energy must be expended on aeration and cooling, which results in additional costs and environmental impact. If yeast only secretes proteins whilst it is growing, it seems almost impossible to make this process more efficient.

The research question: Proteins vs. biomass

When the CD Laboratory for Growth-decoupled protein production in yeast was launched in 2017, the fact that yeast only secretes proteins whilst it is growing was taken for granted. However, Head of Laboratory Brigitte Gasser and her team turned this challenge on its head in an ingenious way: what if it were possible for yeast to secrete proteins even at near-zero growth – in other words, if the proteins could be transported out of the yeast cells without simultaneously producing ever-increasing amounts of biomass?



CD Laboratory for
Growth-decoupled
protein production in yeast

Head

Univ.Prof. DI Dr. Brigitte Gasser,
BOKU University

Duration

01.03.2017 – 29.02.2024

Commercial partner

Lonza AG

Thematic Cluster

Life Sciences and the Environment

Three questions for ...



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Univ.Prof. DI Dr. Brigitte Gasser, BOKU University
Head of the CD Laboratory
for Growth-decoupled protein
production in yeast

Why is basic research so important for innovation?

In biotechnology, it is essential to understand the fundamental metabolic processes and their regulation within cells as comprehensively as possible, in order to derive the necessary steps and strategies for optimising the cells to produce the desired products – in our case, proteins. Application-oriented basic research is therefore the driving force behind innovation.

What are the advantages and challenges of collaborating with companies?

The advantages include a clear path to translating scientific findings into practice and direct feedback from commercial partners: results and newly developed technologies are both scientifically exciting and practical, with real-world applications, and our team gains insight into academic and industrial career perspectives. The challenges lie in shifts of the company's R&D focus.

What do you particularly appreciate about the CD Laboratories' funding model?

CD Laboratories are unique in that they simultaneously promote high-quality, excellent research and collaboration with companies. A seven-year funding period and the unbureaucratic administration by the CDG enable focused, in-depth scientific work as well as the rapid transfer of research results to industry and, consequently, their swift implementation for the benefit of society.

The ambitious, central focus of the research was therefore to understand microbial (yeast) cells at zero growth, analyse them system-wide and, in doing so, derive strategies to decouple growth from protein secretion: given the current state of research, success here would lead to a true paradigm shift whilst simultaneously enabling more efficient, sustainable and cost-effective protein production.

Cooperation at the CD Laboratory

In the biopharmaceutical sector, commercial partner Lonza AG operates as a CDMO (Contract Development and Manufacturing Organisation); in other words, it does not manufacture its own products in the traditional sense, but collaborates with other firms, enabling them – through its expertise and equipment – to carry out biotechnological production themselves, such as protein production using yeast.

The excellent collaboration between the CD Laboratory and the commercial partner allowed Prof. Gasser and her team to address Lonza AG's industrial challenges (such as the potential reduction of biomass generated during protein production) with considerable scientific freedom: it was only through this that the innovative approach of decoupling cell growth from protein production emerged, from which the commercial partner in turn benefited.

Results: A true paradigm shift

The starting point was the tried-and-tested 'Retentostat' cultivation technique, which allows (yeast) cells to be placed in a nutrient-limited yet still metabolically active state: on this basis, the researchers were able to carry out extensive analyses of the yeast cells' states. In this way, they came to understand how the secretion of proteins by these cells is linked to their growth, and how this link can be broken. One of the outcomes of this research is the now award-winning method of bringing the yeast species 'Pichia pastoris' into a state in which it secretes proteins even when growth is virtually zero.

For the research, the main findings therefore represent significant scientific insights into the coupling of the cellular processes of growth and protein secretion: on this basis, technologies were developed in the CD Laboratory which, in turn, can be utilised by Lonza AG and its external customers to achieve the decoupling of both processes. Consequently, the research findings have not only provided Lonza AG with a competitive advantage in the highly competitive international market for protein production, but have also enabled the sustainable production of proteins in large quantities and of high quality with significantly reduced resource consumption – a benefit to society as a whole.

Added value for the company

The technologies, processes and strategies developed at the CD Laboratory have already been implemented directly by the commercial partner: indeed, Lonza AG is already successfully offering them to customers, i.e. other companies. The collaboration with the CD Laboratory has contributed significantly to the creation of the commercial partner's intellectual property (IP), which has been integrated into its main platform, 'Lonza's XS(R) Pichia Expression Platform'. A new commercial education platform was also created for the company's customer service projects.

Scientific challenge

From a scientific perspective, the CD Laboratory focused in particular on the cell's translational machinery – the mechanism by which genetic information is translated into amino acid chains, i.e. proteins: How can this machinery be made to produce the desired proteins in greater quantities? Which factors act as limiting factors and which ones boost protein production? Which regulatory elements trigger the translation of the desired proteins, and what effect do additional copies of these elements in the genome have? The insights gained not only represent a step forward for protein production; they also greatly deepen our fundamental understanding of one of the central processes of life.