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## **Pichia production host engineering by systemic host changes**

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## PICHIA PRODUCTION PLATFORM ENGINEERING BY SYSTEMIC CHANGES

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Protein production has a continuous need for the improvement of production systems regarding product titers and quality, but also processability, robustness and reliability. Systemic changes affect many parts of a system and can help to overcome limitations of existing systems or enable new applications or processes.

Here, we show two examples for *Pichia pastoris* (syn. *Komagataella phaffii*) wherein systemic changes of the production platform led to extensive changes of protein production and host performance. The consequences for the development of production process will also be highlighted.

New promoter system to dramatically reduce fermentation time and complexity to enable yeast production processes in “bacterial” fermentation times of 2-3 days with high space time yields.

Transcription factor knock-out impacting various cellular processes including transcriptional activity, mating, respiration, cellular membranes, cell cycle genes, etc.

Such approaches of changing basic parameters of a production system to create “novel” *Pichia* production hosts instead of incrementally increasing an existing system have the potential to overcome intrinsic limitations of the system. However, the far-reaching changes of the production host will have consequences not only for strain generation and screening, but also for the whole production process.

Related presentations:

- Brigitte Gasser: “Flo8 – A versatile regulator for improving recombinant protein production in *Pichia pastoris*”
- Jennifer Staudacher: “Going beyond the limit: Impact of increasing global translation activity on the productivity of recombinant secreted proteins in *Pichia pastoris*”