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Investigating the reverse Warburg effect: How high extracellular lactate alters breast cancer metabolism

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Realtime prediction and control of glycoform profile of mammalian cell cultures using *in silico* glycosylation model coupled with extracellular metabolites

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Abstract

In silico mechanistic models for glycosylation are investigated for biotherapeutics development and production. The models systematically describe the transport-kinetics of glycosylation process and serve as a prediction framework for glycan profile. However, inputs for those models are generally limited to intracellular parameters, such as enzymatic activity and nucleotide sugar concentration. These intracellular metabolites are unfortunately inaccessible in process. To modulate those models for glycoform prediction in culture process, linkage between measurable culture variations and the intracellular metabolites change will be thoroughly investigated. The measurable metabolites and intracellular variables associated with *in silico* glycosylation model are integrated in the modeling. Despite a few efforts, the mechanism of nucleotide sugar synthesis is not being fully understood and the accuracy of linking model is not at practical level. Here we propose development of mathematical models bridging in-process extracellular metabolites and variation of intracellular glycosylation related metabolites with experimental validation. In order to assess the model robustness, in-process extracellular and intracellular metabolites are generated via a few feeding strategy study with mammalian CHO cell cultures.