

Popular science summary of the PhD thesis

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Title of the PhD thesis	dDNP as a method to assess altered cellular metabolism <i>in vitro</i>
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Science summary

Lifestyle diseases are expanding global health problems that are contributing to the global burden of chronic diseases. To link diet to metabolic outcome, it is necessary to understand the metabolic fate and interaction of the nutritional components in living organisms. The objective of this project is to study perturbed metabolism using dissolution Dynamic Nuclear Polarization (dDNP) in several cell models, representing various human diseases.

In the first part of the thesis, dDNP is used to probe slow biochemical reactions in combination with Stable Isotope Resolved Metabolomics (SIRM). The method is applied on insulin-producing β -cells to study early response to excessive sugar concentrations, a condition mimicking the development of type 2 diabetes. Glucose-derived pyruvate is found to correlate with a high fuel burden for the cells and is hypothesized to be a potential biomarker in the early handling of excessive sugars, before the development of insulin impairment is established.

In the second part of the thesis, dDNP is applied to study metabolism in live pancreatic cancer cells in real time. For this purpose, a bioreactor with a home-built flow cell was constructed and tested. The bioreactor was found suitable for longitudinal cell studies over several hours, but also revealed limitations such as flow stress for such experiments.

The third part of the thesis concerns three different bioprobes for novel applications: N-acetylcysteine (NAC), alpha-ketoglutarate (α KG) and γ -Glu-[1- 13 C]Gly. The sample formulations were optimized to achieve highest possible DNP polarization for further studies, and preliminary tests in cell- and animal models were performed.

In summary, this thesis shows the versatility of dDNP for metabolic research and potential diagnostic applications demonstrated by the polarization of 13 C labeled substrates in cell systems.