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Quantifying metabolic fluxes in cancer and stem cells

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Despite their different origin, cancer and stem cells share the feature of fast growth and unlimited proliferation. It is under debate if their mode of proliferation should require likewise distinct demands of precursors for biosynthesis or energy; regardless both cell types favoring aerobic glycolysis. In our lab we combine MS-based 'omics'-technologies (LC-MS / GC-MS) to deliver relative and absolute quantitative information about enzyme abundance and metabolite concentrations of the central carbon metabolism (CCM). We have developed pulsed stable isotope resolved metabolomics (pSIRM) to monitor how cells utilize substrates like glucose and glutamine to meet their energetic requirements. Finally, the integration of quantitative and time-resolved isotope incorporation in a mathematical framework enables the calculation of the metabolic fluxes; the only functional readout of a cell. Isotopically non-stationary (INST) metabolic flux analysis uses the collected data (absolute poolsizes, extracellular rates) in combination with a network model (material balances, carbon transitions) to jointly estimate intracellular metabolic fluxes and pool sizes in cell culture experiments. The complete workflow-from the petri dish to the metabolic flux map-has been applied to track the rerouting of carbon usage during pluripotency, reprogramming and differentiation. We applied stable isotope labeled substrates and analyzed their fate in fibroblasts and their pluripotent counter parts (iPSC), in breast cancer MDA-MB231 and in human embryonic stem cells (hESC). The analysis endorsed the switch from a glycolytic to respiratory metabolism after differentiation both in hESC and iPSC-derived fibroblasts. Specifically the comparison of the metabolic profiles of stem cells and cancer cells revealed distinct metabolic features of these cell types.

Biography

Christin Zasada studied Biosystems engineering at the Otto-von-Guericke University Magdeburg, Germany. In 2011 she started her PhD thesis in the lab of Stefan Kempa (Integrative Proteomics and Metabolomics) at the Berlin Institute of Medical Systems Biology at the Max-Delbrueck-Center for Molecular Medicine in Berlin, Germany.

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