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NMR-based metabolomics analysis of 2D with 3D (Spheroids) of breast cancer cells

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Findings in 2D tumor cell models only partly translate to experimental outcome *in vivo*. Chemotherapy strategies target proliferating cells adjacent to blood vessels with sufficient supply of oxygen and nutrients. In poorly vascularized regions of the tumor cells adapt to survive and are resistant to chemotherapy. 3D Spheroids of tumor cells resemble characteristics of invasive tumors and are an interesting model to target the inner core of tumors. We used NMR-based metabolomics to study the metabolic differences of T47D breast cancer cells cultivated in 2D and 3D conditions. Additionally tumor spheroids were treated with compounds targeting the inner core of the spheroids. After 48 h incubation cells were quenched and harvested with an ice-cold MeOH/Chloroform/H2O mixture. The freeze dried sample extracts were reconstituted in phosphate-buffered saline and high-resolution 1H-NMR spectra were measured with a 600 MHz Bruker Biospin equipped with a cryo-probe and sample jet system. Baseline and peak shift corrected spectra were divided into 0.04 ppm buckets and integrated. Multivariate data analysis was performed on bucketed spectra to identify difference between 2D and 3 D control conditions. Afterwards metabolites were annotated using the Chenomx Profiler software. Metabolite differences showed signatures indicative for glucose deprivation in spheroids accompanied with limited capacity to perform synthesis and cell division to maintain cell hemostasis and resulting in tumor dormancy. Studied compounds targeting the specific inner core region of tumor spheroids resemble metabolic profiles similar to inhibitors of mitochondrial respiration like Antimycin A or Oligomycin.

Biography

Bjoern Riefke completed his PhD in Biology in 1994 from Heinrich-Heine-University in Duesseldorf, Germany. Since 1994 he has worked in various positions in research and development of former Schering AG, and since 2006 in Bayer Pharma AG. He is Head of Metabolic Profiling and Clinical Pathology Group in Toxicology and since then involved in the establishment of metabolic profiling platform supporting projects in toxicology, biomarker research and pharmacology.

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