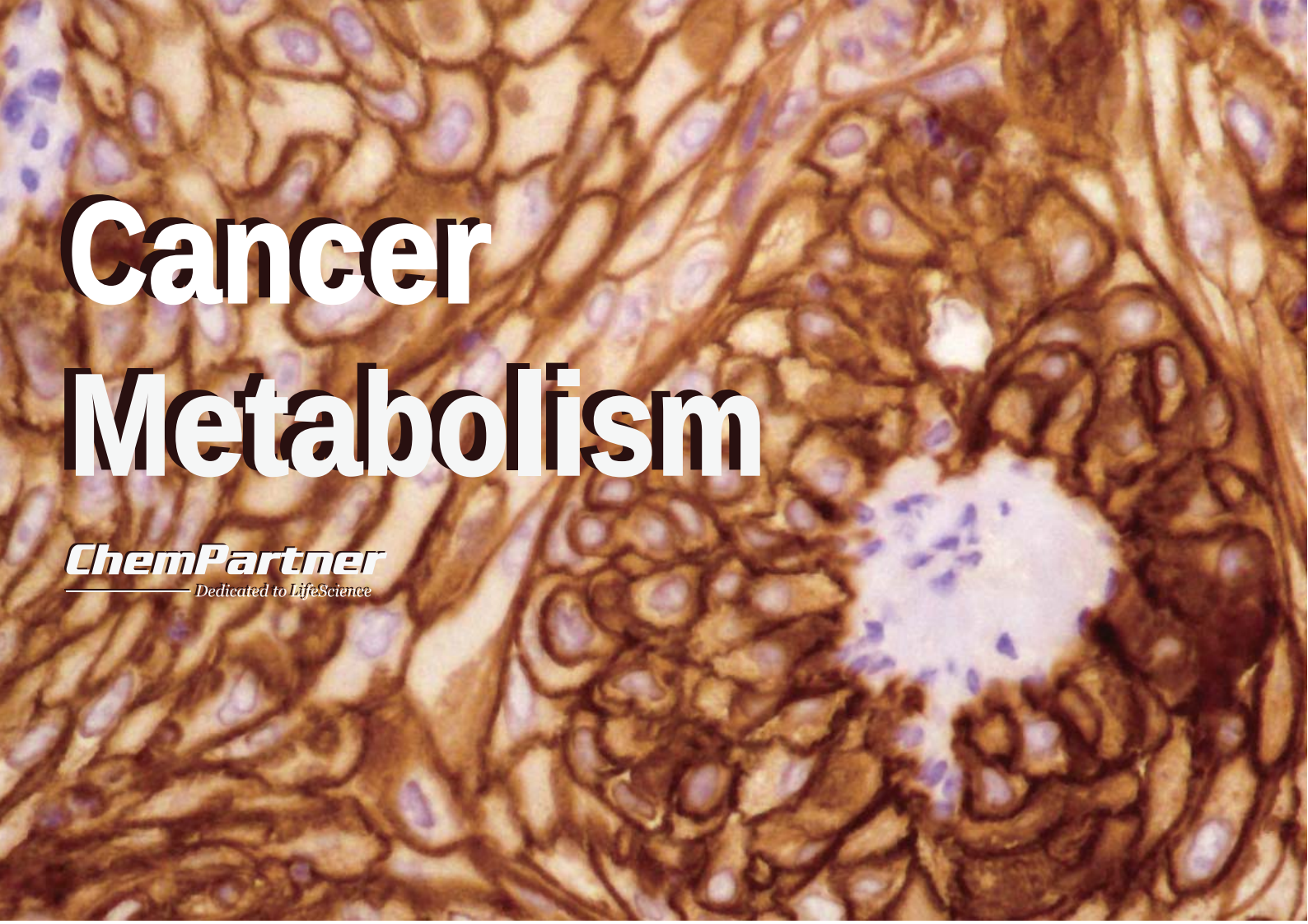

Cancer Metabolism

ChemPartner
Dedicated to LifeScience

Target Validation → Biochemical Assays → Cell-based Assays → *In Vivo* PK/PD Efficacy → Clinical Biomarker

Supported by UV-Vis/Fluorescence-based readout, metabolite quantification by LC/MS in various matrices, cellular functional readouts, etc.

Key features in cancer metabolism

- Aerobic glycolysis (Warburg effect)
- Enhanced nutrient uptake
- Re-organization of metabolic pathways to support biosynthesis and balance redox

Target cancer metabolism

- Glucose/glutamine metabolism
- Fatty acid/ lipid synthesis
- Amino acid/nucleotide synthesis
- Metabolic enzyme that are mutated in cancer

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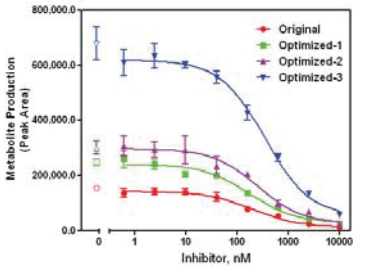
Extensive Experience in Cancer Metabolism

- Chemical synthesis of potent inhibitors targeting various cancer metabolism pathways
- Screening of compounds in biochemical reactions
- Screening of compounds in cell based assays
- Drug sensitivity test using cancer cell panels
- LC-MS based assays for cancer metabolite detection and quantification
- *In vivo* testing in different tumor models of therapeutics targeting cancer metabolism

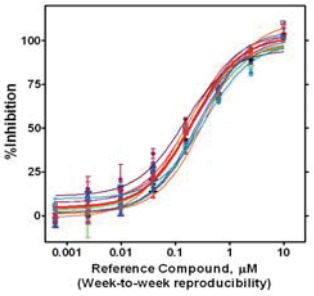
mpounds

Conditional Medium (secreted metabolites)

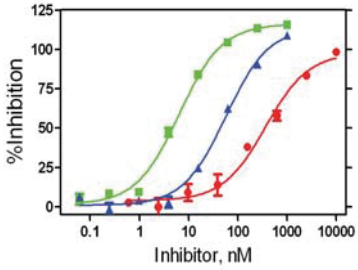
Cell Extracts (intracellular metabolites)



Assay Optimization
- Find the best condition that biologically makes sense and also is robust enough for routine screening



Assay Reproducibility
- Include a reference compound in each round of the screening as QC



Routine Screening
- High throughput, over 5,000 data points per assay per week

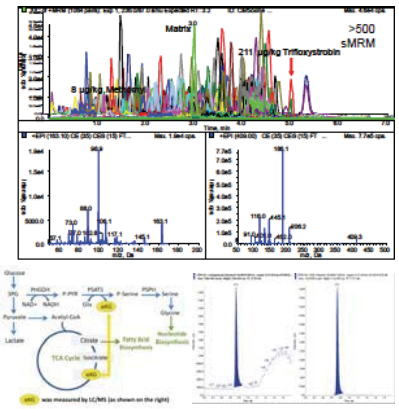
Capability of Using LC-MS for Cancer Metabolite Quantification

Assay development and validation;
More than 200 metabolite monitoring in a single assay;
Application of assay developed for routine compound screening;
Typical metabolite quantitations include:
- Products of the Krebs Cycle (acetyl-CoA, lactate, pyruvate, malate, oxaloacetate, etc)
- Fatty acids and lipids (Myristoleic acid, Myristic acid, Palmitic acid, Stearic acid, Eicosanoic acid, Acachidic acid etc
- Amino acids (e.g. Serine, Glutamine)
- Glucose and its derivatives

Turnaround time:
- 5 -15 working days depending on the nature of assay specifics

Instrumentation:
- ABI5500 and 6500, Waters Q-Tof G2-S, UPLC including Multiplex

Instrumentation allows up to 300 analytes to be quantified simultaneously in each run



ChemPartner made the following contributions to the Nature article:

- Produced 9 mutant proteins, 2 at large quantities to support crystallography.
- Conducted enzymology work to characterize all the mutants Km, Vmax, pH and metal ion effects, forward and reverse kinetics, Ki.

ARTICLES

Cancer-associated IDH1 mutations produce 2-hydroxyglutarate

ChemPartner co-authored in an article published in Biochemistry 2011

- Produced 5 glutaminase isoforms and mutants
- Measured Km, kcat, phosphate activation and sensitivity to the allosteric inhibitor

BIOCHEMISTRY

Full-Length Human Glutaminase in Complex with an Allosteric Inhibitor

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